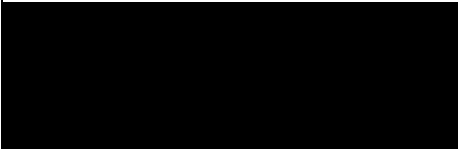


PMOS Information

Title	Long-term Documentation of the Safety, Effectiveness, and Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis during HUMIRA® (Adalimumab) Therapy in Routine Clinical Practice (AGIL) and Supplementary Documentation to Record Cardiovascular and Metabolic Risk Factors (AGIL-CV)
Study Identifier	P11-973 Final Report
Version Identifier of the Final Study Report	1.0
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Marketing Authorisation Holder(s)	AbbVie Deutschland GmbH & Co. KG.
Joint PASS	Not required for Non-PASS PMOS
Research Question and Objectives	<p>Primary employment-related objectives for this study were to examine therapeutic success with respect to improvements in:</p> <ul style="list-style-type: none"> • Number of missed working days due to sick leave • Self-assessed work ability (modified Work Productivity and Impairment questionnaire and modified Work Ability Index) <p>Primary clinical objectives for this study were to examine therapeutic success with respect to improvements in:</p> <ul style="list-style-type: none"> • Severity of clinical symptoms (Disease Activity Score – 28 joints [DAS28] and tender and swollen joint counts) • Levels of inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) • Patient-reported function (Health Assessment Questionnaire-Disability Index) and health-related quality of life (EuroQol 5-dimensions and Visual Analogue Scale) <p>The primary research questions for the cardiovascular (CV) substudy, AGIL-CV, were to:</p> <ul style="list-style-type: none"> • Determine changes from baseline in body measurements, vital signs, and lab chemistry blood parameters for glucose and lipid metabolism

Research Question and Objectives (continued)	<ul style="list-style-type: none">• Compare vital signs and lab chemistry blood parameters for glucose and lipid metabolism between DAS28 responders and nonresponders• Determine the time point and frequency of CV events
Country(-ies) of Study	Germany
Author	



Marketing Authorisation Holder(s)

Marketing Authorisation Holder(s)	AbbVie Deutschland GmbH & Co. KG Knollstrasse 67061 Ludwigshafen Germany
MAH Contact Person	

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1.0 Abstract

Title

Long-term Documentation of the Safety, Effectiveness, and Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis during HUMIRA[®] (Adalimumab) Therapy in Routine Clinical Practice (AGIL) and Supplementary Documentation to Record Cardiovascular and Metabolic Risk Factors (AGIL-CV)

Keywords

Adalimumab, rheumatoid arthritis, work ability, effectiveness, safety, cardiovascular disease

Rationale and Background

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by progressive joint destruction, loss of physical function, and reduced quality of life and work productivity. Effective therapy with agents such as adalimumab, a tumor necrosis factor inhibitor, is associated with improvements in patient function and work productivity and, in some studies, reduced cardiovascular (CV) risk. The AGIL study was designed to evaluate the effectiveness and safety of adalimumab over 5 years in routine daily clinical practice in Germany, with a focus on the impact of therapy on employment-related outcomes. A substudy of AGIL, AGIL-CV, evaluated the effect of therapy on CV risk factors, including lipid profiles.

Research Question and Objectives

Primary employment-related objectives were to examine changes in:

- Number of missed working days due to sick leave
- Self-assessed work ability

Primary clinical objectives for this study were to examine changes in:

- Severity of clinical symptoms
- Levels of inflammatory markers
- Patient-reported function and health-related quality of life

The primary research questions for AGIL-CV were to evaluate:

- Changes from baseline in body measurements, vital signs, and lab chemistry blood parameters for glucose and lipid metabolism
- Differences in these parameters between treatment responders and non-responders
- Time point and frequency of CV events

Study Design

This study was a prospective, multicenter, observational study of adult patients with RA who initiated adalimumab therapy during routine clinical care. Patient data were recorded at Months 3, 6, 12, 24, 36, 48, and 60 months (recommended visit schedule). Patients continued in the study for a maximum of 60 months or until discontinuation from adalimumab therapy.

Setting

Patients were enrolled at 326 clinical centers in Germany and seen during regular visits for routine clinical care.

Subjects and Study Size, Including Dropouts

Four patient cohorts were evaluated (N values represent baseline numbers): employed patients (patients employed full- or part-time at baseline) (N = 3285), full analysis set (FAS; patients with sufficient data for effectiveness analyses) (N = 4466), safety set (all enrolled patients who received at least one dose of adalimumab) (N = 7229), and the AGIL-CV substudy cohort (patients enrolled in AGIL-CV) (N = 260). At

Month 60, patient cohorts contained fewer than 20% of the baseline population. Study discontinuations were fairly evenly distributed between study withdrawals, most often due to lack of effectiveness, and patients lost to follow-up for unspecified reasons.

The study was stopped on 30 June 2017 after achieving the planned sample size for AGIL employment analyses (5000), and the number of patients needed for robust analyses of mean values at later time points (past the 24 month visit) was not attained.

Variables and Data Sources

Case report forms were the primary data source. Key variables included self-reported number of sick leave days and work ability, clinical symptoms, including the Disease Activity Score-28 joints (DAS28), tender and swollen joint counts, levels of inflammatory markers, and patient-reported function and health-related quality of life. The AGIL-CV substudy also included body measurements, vital signs, and lab chemistry parameters for glucose and lipid metabolism.

Results

During adalimumab therapy, mean sick leave days in the past 6 months decreased from 19.2 at baseline to 7.4 at Month 24 and remained near this level through Month 60 in patients who continued in the study. Because of asymmetric data distribution, the primary evaluation of sick leave days was a categorical analysis of patients with sick leave days within the normal range for the German population (0 to 5 days in the past 6 months) or higher than normal range (> 5 days in the past 6 months). At baseline, 55.3% of patients had sick leave days within the normal range; this figure significantly increased to 72.1% at Month 24 and was maintained at this level throughout the study. In patients with a higher than normal sick leave at baseline, 58.2% returned to normal values by Month 24 and 63.3% by Month 60. Improved work productivity was also observed during adalimumab therapy. Changes in employment-related outcomes were accompanied by significant improvements in clinical symptoms as assessed by objective assessments, including joint counts and

DAS28, and patient-reported evaluations, including function. Most improvements occurred by Month 6 and were maintained to Month 60 in patients remaining on therapy. No clear effect of adalimumab therapy on CV risk markers was observed, but AGIL-CV enrolled too few patients to allow valid conclusions. Over the 60-month period, 32.1% of patients reported an adverse event and 12.9% experienced a serious adverse event. Adverse events were consistent with the known adalimumab safety profile.

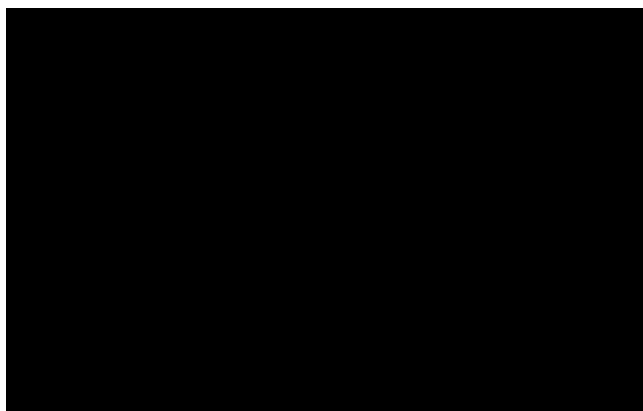
Discussion

Despite high discontinuation rates, the findings from AGIL indicate that long-term therapy with adalimumab results in significant improvements in employment-related outcomes and clinical outcomes for up to 60 months in adult patients with RA who remain on therapy. Continued improvements at later time points may have been influenced by responder bias. The findings of this observational study support the conclusion that adalimumab is effective and safe during long-term therapy of adult RA patients in Germany.

Marketing Authorisation Holder(s):

AbbVie Deutschland GmbH & Co. KG, 67061 Ludwigshafen, Germany

Names and Affiliations of Principal Investigators:



2.0 List of Abbreviations

AE	Adverse event
BMI	Body mass index
CCP	Cyclic citrullinated peptide
CRF	Case report form
CRP	C-reactive protein
CV	Cardiovascular
DAS28	Disease Activity Score-28 joints
DAS28-d _{crit}	Critical difference therapeutic response criterion for DAS28
DMARD	Disease-modifying antirheumatic drug
EQ-5D	EuroQuol 5 dimensions
ESR	Erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FAS	Full analysis set
HAQ-DI	Health Assessment Questionnaire-Disability Index
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
MedDRA	Medical Dictionary for Regulatory Activities
MTX	Methotrexate
NSAID	Non-steroidal anti-inflammatory drug
PMOS	Post-marketing observational study
PT	Preferred term
RA	Rheumatoid arthritis
RF	Rheumatoid factor
SD	Standard deviation
SOC	System organ class
SAE	Serious adverse event
SCORE	Systematic Coronary Risk Evaluation
SJC	Swollen joint count
TNF	Tumor necrosis factor
TJC	Tender joint count
Total-C	Total cholesterol
VAS	Visual analogue scale

WAI Work Ability Index
WPAI Work Productivity and Impairment Questionnaire

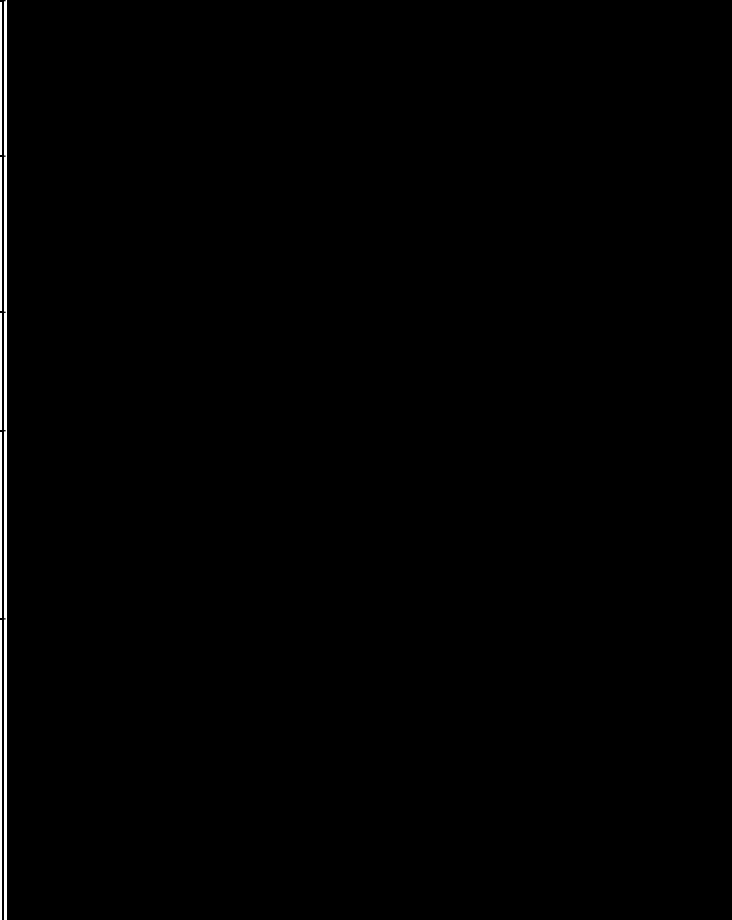
3.0 Investigators

The primary investigators for this study were:



Clinicians at 326 centers throughout Germany enrolled patients in this study.

4.0 Other Responsible Parties

Position	Name and Contact Information
Report author	
Project director	
Study-designated physician	
External medical advisor	
Statisticians	

5.0 Milestones

Milestone	Full Study (Actual Date)	CV Substudy (Actual Date)
Start of Data Collection:	12 January 2009	13 February 2013
End of Data Collection:	14 September 2017	12 July 2017
Ethics approval: ^a	18 May 2009	Not required
Registration in the EU PAS Register:	Not required for Non-PASS	Not required for Non-PASS
Study Progress Report X:	Not required for Non-PASS	Not required for Non-PASS
Interim Report X:	None	None
Final Report of Study Results:	29 March 2018 (current report)	29 March 2018 (current report)

- a. In Germany, ethics approval is not required for observational studies, so it was possible to begin data collection prior to ethics approval.

6.0 Rationale and Background

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by progressive joint destruction and loss of physical function.¹ In Germany, 2.5% of the adult population is affected by RA.² Tumor necrosis factor (TNF) is an important cytokine that mediates inflammation in RA.³ The introduction of TNF inhibitors 15 years ago revolutionized RA treatment and provided new options for disease control. Adalimumab, a human monoclonal antibody against TNF, is approved for RA treatment in the US (2002), the European Union (2003), and many other countries worldwide. Multiple clinical trials have shown that adalimumab reduces the clinical symptoms of RA, slows structural destruction of the joints, and improves physical function, thus improving health-related quality of life and employment-related outcomes.⁴⁻⁶

The goal of this study, known as the AGIL study (agil is the German word for "agile"), was to document the long-term effectiveness and safety of adalimumab as used in daily clinical practice to treat adult German patients with RA. A primary study objective was to evaluate the long-term impact of adalimumab on employment-related outcomes. The joint destruction and impaired physical function that occurs during the course of RA are often accompanied by a reduced ability to engage in productive work.⁷ The impact of RA

on work ability is associated with a large societal cost.^{8,9} Effective RA therapy has been shown to improve work-related outcomes, including sick leave absences and productivity.¹⁰ However, most studies have examined the impact of therapy over periods of 1 year or less, and often the patient population has been confined to patients with specific characteristics, such as early RA.¹⁰ There is thus a need to further characterize the effects of long-term treatment, particularly in patients with extended disease durations.

Observational, non-interventional studies can supplement clinical trials by providing data on the "real-world" clinical activity of a therapeutic agent.¹¹ Unlike clinical trials, non-interventional studies do not have selection criteria for patients or restrict its use in patients with comorbid conditions or concomitant medications.

Data for the study were collected from rheumatology outpatient departments and office-based rheumatologists who routinely treated patients with RA in Germany. No specific education was provided for doctors concerning adverse events (AEs) that could potentially be associated with drug administration or TNF inhibitors.

During the course of AGIL, an amendment to the study allowed collection of data relevant to cardiovascular (CV) and metabolic risk factors in patients with RA; this substudy is referred to as AGIL-CV. Patients with RA have a 1.5- to 2-fold increased risk for CV events compared with the general population;^{12,13} a recent study estimated that 30% of CV events in this population were attributable to RA characteristics.¹⁴ Systemic inflammation drives both RA and atherosclerosis and is an independent risk factor for CV disease.¹⁵ Accordingly, suppression of inflammation during effective RA therapy could also lower the risk of CV disease.¹⁵ Other potentially modifiable characteristics in patients at risk of CV disease include blood pressure and lipid profiles.¹⁶ Treatment with TNF inhibitors decreases the risk of CV events, but the mechanism behind this remains unclear.^{15,17} Studies in RA patients treated with adalimumab have found improved endothelial function,¹⁸ decreased aortic stiffness,¹⁹ and increases in high-density lipoprotein cholesterol (HDL-C) levels, resulting in improved lipid profiles.^{20,21} However, most studies have had small patient cohorts and short periods of treatment, so evidence for the effects of adalimumab on markers of CV and metabolic risk during long-term treatment

are lacking. The AGIL-CV substudy was designed to explore the impact of adalimumab on CV and metabolic risk factors.

This report represents the final results of AGIL (Study P11-973), an observational study of adalimumab in adult patients with RA in Germany, and its associated substudy, AGIL-CV.

7.0 Research Questions and Objectives

7.1 Employment-Related Objectives

Primary employment-related objectives for this study were to examine changes in:

- Number of missed working days due to sick leave
- Self-assessed work ability (modified Work Productivity and Impairment questionnaire [WPAI] and modified Work Ability Index [WAI]).

7.2 Clinical Objectives

Primary clinical objectives for this study were to examine changes in:

- Severity of clinical symptoms (Disease Activity Score – 28 joints [DAS28] and tender and swollen joint counts [based on a 28-joint assessment])
- Levels of inflammatory markers (C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR])
- Patient-reported function (Health Assessment Questionnaire-Disability Index [HAQ-DI]) and health-related quality of life (EuroQol 5-dimensions [EQ-5D] and Visual Analogue Scale [VAS])

Secondary clinical objectives included changes in:

- Number of physician visits
 - Number and duration of hospitalizations
 - Number of days of impairment in non-occupational activities
-

- Duration of morning stiffness
- Levels of pain and fatigue
- Concomitant medication
- Patient's assessment of adalimumab therapy compared with previous therapies

7.3 CV Substudy Questions and Objectives

The primary research questions for AGIL-CV were to:

- Determine changes from baseline in body measurements, vital signs, and lab chemistry blood parameters for glucose and lipid metabolism (CRP and fasting glucose and lipid profile)
- Compare vital signs and lab chemistry blood parameters for glucose and lipid metabolism between DAS28 responders and DAS28 non-responders
- Determine the time point and frequency of CV events

Secondary research questions were to:

- Investigate the impact of baseline personal characteristics and family medical history on changes in CV and metabolic parameters
- Determine individual CV risk and changes in risk over time by using the Systematic Coronary Risk Evaluation (SCORE) model

7.4 Safety Questions and Objectives

Target parameters for safety evaluations were:

- Documentation of AEs and serious adverse events (SAEs)
 - Assessment of safety and tolerability for subgroups of patients with pre-specified concomitant diseases
-

8.0 Amendments and Updates

Number	Date	Amendment	Reason
1	06 March 2012	Supplementary documentation AGIL-CV to record cardiovascular and metabolic risk factors in RA patients treated with adalimumab in routine clinical practice	RA patients have increased CV morbidity and mortality compared with the overall population. TNF plays a significant role in the inflammatory process, and reducing inflammation has the potential to favorably impact CV risk. This substudy was designed to evaluate the effect of adalimumab on CV risk factors.

9.0 Research Methods

9.1 Study Design

The study reported here was a prospective, multicenter, observational, non-interventional study (Clinicaltrials.gov trial registration NCT01076205, also referred to as GER0805 and AGIL) as defined in Section 4, Subsection 23 of the Arzneimittelgesetz (German Medicinal Products Act).²² A complete description of the study can be found in the AGIL protocol in [Appendix 1](#) (English translation). The primary objectives of this study were to determine the impact of adalimumab on employment related outcomes and obtain long-term documentation of the effectiveness and safety of adalimumab treatment as used in daily clinical practice in Germany to treat adult patients with RA over a time interval of 60 months. Secondary objectives included long-term documentation of additional variables as described in Section 6.0. An amendment to the study allowed the collection of additional data concerning CV risk factors, including laboratory blood chemistry variables ([Appendix 2](#)).

Data for the study were collected on a Case Report Form (CRF) ([Appendix 3](#) [English translation excerpt including Visit 0/Month 0 and Visit 1/Month 3; subsequent visits collected the same data as Month 3] and [Appendix 4](#) [complete original German version]). The observation period for each individual patient began with the administration of the

initial dose of adalimumab (Month 0) and lasted for a maximum of 60 months. Therapy follow-ups were recommended at Month 3, Month 6, Month 12, and then yearly in accordance with the following schedule:

- Visit 0 = baseline/Month 0
- Visit 1 = after 3 months
- Visit 2 = after 6 months
- Visit 3 = after 12 months
- Visit 4 = after 24 months
- Visit 5 = after 36 months
- Visit 6 = after 48 months
- Visit 7 = after 60 months

All patients were informed of the objectives of the observational study and gave written consent for their voluntary participation in the study and the anonymous use of personal data in statistical analyses. Ethics approval was obtained from the Ethics Commission of the Medical Department of Goethe University, Frankfurt am Main, Germany ([Appendix 5](#)).

9.2 Setting

Patients for the AGIL study were enrolled by clinicians at 326 different clinical sites throughout Germany. The first patient was seen on 12 January 2009 and the last visit occurred on 14 September 2017.

Not all sites had the capability or willingness to perform CV and metabolic tests, so only a subset of sites participated in the CV substudy. Patients for the AGIL-CV study were enrolled at 36 different clinical sites throughout Germany. The first patient was seen on 13 February 2013 and the last visit occurred on 12 July 2017.

9.3 Subjects

The study population for AGIL was a community non-probability (non-random) sample of patients with RA who resided in Germany and were preparing to initiate adalimumab therapy at the decision of the clinician. German regulations state that all patients are eligible for non-interventional studies as long as they are able to give consent and understand the language of the patient questionnaires; there are no exclusions. Doctors were instructed to enroll patients with moderate to severely active RA who had failed other anti-rheumatic drugs and patients with severe, active and progressive RA regardless of previous treatment; inclusion and exclusion criteria adhered with the European Medical Agencies Summary of Product Characteristics.²³ Doctors were also instructed to limit enrollment to adult patients (≥ 18 years of age) with RA. However, there was no means of preventing doctors from enrolling patients with other indications or patients younger than 18 years of age. All patients were required to provide informed consent.

Patients enrolled in AGIL-CV met the same criteria and additionally agreed to undergo the supplemental tests required for evaluating CV and metabolic risk factors.

The study was stopped by AbbVie due to achievement of the planned initial enrollment for AGIL. However, the number of patients needed for robust analyses of sick leave analyses at later time points was only partially attained.

9.4 Variables

9.4.1 Primary Objectives: Employment-Related Outcomes

Employment-related outcome measures are described in [Table 1](#).

Table 1. Description of Employment-Related Outcome Measures

Outcome Measure	Abbreviation	Description
Sick leave days	--	Sick leave days were based on patient recall. In Germany, a certificate from a doctor is required if more than 3 consecutive days are missed due to illness. In practice, shorter absences do not require documentation for most patients. For visits conducted at Months 0, 3, 6, and 12, employed patients were asked (English translation): "In the last 6 months, have you received a sick leave certificate from a doctor?" If the answer was "yes," patients reported the total number of days covered by the sick leave certificate. At Months 24, 36, 48, and 60, patients were asked to list the number of doctor-certified sick leave days over the past 12 months (since their last visit); this value was divided by 2 to be comparable to the previous reporting periods.
Work Productivity and Activity Impairment questionnaire: General Health	WPAI	The WPAI is a validated tool in RA ²⁴ that assesses work time missed due to illness (absenteeism), impairment at work due to health (presenteeism), total work productivity impairment due to health (an aggregate measure of both absenteeism and presenteeism), and total non-occupational activity impairment due to health. ²⁵ The WPAI is one of the tools recommended for use in measuring the effects of intervention on ability to work in Germany. ²⁶ This instrument consists of 6 questions (see Annex 3) and is based on patient recall of the previous 7 days. For this study, the WPAI was modified by the removal of Question 1, which concerns current employment, as this question was included elsewhere in the documentation. WPAI scores are expressed as impairment percentages, with higher scores indicating worse outcomes. ²⁷

Outcome Measure	Abbreviation	Description
Work Activity Index	WAI	The WAI is a tool designed to record the work ability of employees that was developed as part of a research project in Finland and has since been used in multiple contexts, including RA. ^{28,29} Along with the WPAI, the WAI is recommended for use in measuring the effects of intervention on ability to work in Germany. ²⁶ The WAI consists of 7 questions (see Annex 4). The modified WAI used in this study included Questions 1, 2, 4, 6, and 7 of the WAI. Question 3, which involves the number of current diseases diagnosed by a physician, was omitted because this parameter was unlikely to reflect change due to treatment. Question 5 (sick leave during the past year) was replaced with the previous question concerning sick leave days. WAI scores range from 7 (worst) to 49 (best).

9.4.2 Primary Clinical Objectives

Table 2 describes the outcomes used to assess the primary clinical objectives of this study.

Table 2. Description of Primary Clinical Objectives Outcome Measures

Outcome Measure	Abbreviation	Description
Disease Activity Score – 28 joints	DAS28	A validated instrument in which higher scores indicate greater disease activity; ^{30,31} DAS28 > 5.1 indicates high disease activity, DAS28 < 3.2 is considered low disease activity, and DAS28 < 2.6 is considered clinical remission. ³² DAS28 scores are derived from the swollen joint count (SJC), tender joint count (TJC), ESR, and the patient's assessment of global disease activity.
Tender and swollen joint counts	TJC and SJC	Joint status was assessed based on examination of 28 joints.
C-reactive protein and erythrocyte sedimentation rate	CRP and ESR	These blood markers reflect systemic inflammation and are recommended components of RA disease activity measures. ³³
Health-Assessment Questionnaire-Disability Index	HAQ-DI	The HAQ-DI is a patient-reported assessment of physical function that includes 20 items in eight categories representing a comprehensive set of functional activities, including dressing, eating, walking, and hygiene. Patients are asked about their ability to complete these tasks in the past week. ³⁴ This tool was developed and validated for use in RA and is a strong predictor of long-term outcomes, including work disability and mortality. ³⁵ Scores range from 0 (best) to 3 (worst).
EuroQol-5 Dimensions	EQ-5D	The EQ-5D is a patient-reported assessment of health-related quality of life that has been validated in RA. ³⁶ Patients are asked to describe their health on that day with respect to 5 categories: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The version used in this study was EQ-5D-3L. Each category is rated on a scale ranging from 1 (no problem) to 3 (extreme problems). ³⁷ These data can be used to create a country-specific index value, but data transformation requires proprietary data from EuroQol and was not performed for this study.

Outcome Measure	Abbreviation	Description
EuroQol Visual Analogue Scale	EQ VAS	The EQ VAS is a vertical, thermometer-like, VAS ranging from 0 to 100 that provides a patient-reported assessment of overall health. Patients are asked to mark how good or bad their health is on that day, with 100 meaning "the best health you can imagine" and 0 meaning "the worst health you can imagine." ³⁷

9.4.3 Secondary Clinical Objectives

Table 3 summarizes the key clinical parameters evaluated as secondary objectives.

Table 3. Description of Secondary Clinical Objectives Outcome Measures

Outcome Measure	Description
Number of physician visits and hospitalizations	At Months 0, 6, and 12, patients were asked to self-report how many physician visits and hospitalizations they had in the past 6 months. At Months 24, 36, 48, and 60, patients were asked to report physician visits or hospitalizations in the past 12 months. Patients who had been hospitalized were also asked how many days they were hospitalized. Values for 12-month time periods were divided by 2 to be comparable to the previous reporting periods.
Number of days of impairment in non-occupational activities	This outcome utilized the same reporting periods discussed above (past 6 months at Month 0, 6, and 12; past 12 months at Month 24, 36, 48, and 60). Patients reported the number of days that sickness affected non-occupational activities in four categories: household, child-rearing/parenting, education, and recreational (free-time). Values for 12-month time periods were divided by 2 to be comparable to the previous reporting periods.

9.4.4 Cardiovascular Outcomes in AGIL-CV Substudy

Key CV outcomes included changes in body measurements (weight, body mass index [BMI], abdominal girth, and weight circumference), vital signs (pulse and blood pressure), lab chemistry blood parameters for glucose and lipid metabolism (CRP, fasting glucose, and fasting lipid profile) and assessment of CV events (myocardial infarction and stroke) at baseline and during treatment. Analyses of these outcomes on the basis of DAS28 response, as described in Table 4, was also a primary objective.

Table 4. Description of DAS28 Response Assessments in AGIL-CV

Outcome Measure	Abbreviation	Description
European League Against Rheumatism response	EULAR response	EULAR responses are separated into 3 categories, as described below, and based on both current DAS28 state and change in DAS28. ³² Good EULAR response: DAS28 reduction > 1.2 and current state \leq 3.2 Moderate EULAR response: DAS28 reduction > 0.6 to \leq 1.2 and current state > 3.2 and \leq 5.1 No response: DAS28 reduction \leq 0.6 or > 0.6 with current state > 5.1
DAS28 critical difference response	DAS28 _{crit} response	The DAS28 critical difference response criterion is an individual assessment that represents a significant and clinically relevant change in disease activity determined by an analysis of variance model as described by Behrens et al. ³⁸ Patients with a DAS28 decrease of \geq 1.8 from baseline are considered to have a DAS28 _{crit} response.

9.4.5 Safety Outcomes

Safety outcomes are shown in [Table 5](#).

Table 5. Description of Safety Outcome Measures

Outcome Measure	Abbreviation	Description
Adverse events and serious adverse events	AEs and SAEs	<p>Medical Dictionary for Regulatory Activities (MedDRA) v20.1 was used for AE reporting by System Organ Class (SOC) and Preferred Term (PT). An AE was considered to be an SAE if any of the following criteria were met:</p> <ul style="list-style-type: none"> • Death of patient • Life-threatening event • Hospitalization • Prolongation of hospitalization • Congenital anomaly • Persistent or significant disability or incapacity • Important medical event requiring medical or surgical intervention to prevent serious outcome • Spontaneous or elective abortion
Safety in patients with pre-specified comorbidities	--	To determine whether patients with pre-specified comorbidities were at a higher risk of AEs, AE rates were evaluated in patients with and without that comorbidity.

9.5 Data Sources and Measurement

Data for each visit were documented on a CRF ([Appendix 3](#) and [Appendix 4](#)). Upon completion, the CRF was faxed, mailed, or submitted through an internet portal to the AbbVie office in Wiesbaden, Germany. The data collected by the physician ([Table 6](#)) and patient self-reports ([Table 7](#)) are summarized in the following tables. AEs were evaluated by the clinician at each visit. No specific diagnostic or laboratory tests were conducted to detect AEs.

Table 6. Physician Schedule for Data Reporting

Data	Month							
	0	3	6	12	24	36	48	60
Demographic data	•							
Indication for adalimumab	•							
Patient consent	•							
Tuberculosis and hepatitis screening	•							
First diagnosis of RA	•							
Rheumatoid factor (RF) and anti-cyclic citrullinated peptide anti-CCP status	•							
Prior conventional and biologic disease-modifying antirheumatic drug (DMARD) therapy	•							
Adalimumab therapy	•	•	•	•	•	•	•	•
Concomitant RA therapy	•	•	•	•	•	•	•	•
Joint surgeries	•		•	•	•	•	•	•
CRP	•	•	•	•	•	•	•	•
ESR	•	•	•	•	•	•	•	•
Physician global assessment of disease activity	•	•	•	•	•	•	•	•
Swollen and tender joint counts	•	•	•	•	•	•	•	•
Duration of morning stiffness	•	•	•	•	•	•	•	•
Comorbid conditions	•	•	•	•	•	•	•	•
Reason for termination of adalimumab therapy		•	•	•	•	•	•	•
Adverse events		•	•	•	•	•	•	•
Additional assessments for AGIL-CV								
Tobacco use	•	•	•	•	•	•	•	•
Alcohol consumption	•	•	•	•	•	•	•	•
Documentation of CV events (myocardial infarction, stroke)	•	•	•	•	•	•	•	•
Blood pressure	•	•	•	•	•	•	•	•
Height	•							

Data	Month							
	0	3	6	12	24	36	48	60
Additional body measurements (weight, waist and hip circumference)	•	•	•	•	•	•	•	•
Fasting laboratory parameters (glucose, lipid profile)	•	•	•	•	•	•	•	•

Table 7. Patient Schedule for Data Reporting

Data	Month							
	0	3	6	12	24	36	48	60
Personal data	•	•	•	•	•	•	•	•
Education	•							
Employment status	•		•	•	•	•	•	•
Enrollment in "Abbott Care" (AbbVie Care) program	•	•	•	•	•	•	•	•
Sick leave days in past 6 months	•		•	•				
Sick leave days in past 12 months					•	•	•	•
Modified WAI	•	•	•	•	•	•	•	•
Modified WPAI	•		•	•	•	•	•	•
Global disease activity (last 7 days)	•	•	•	•	•	•	•	•
Fatigue (last 7 days)	•	•	•	•	•	•	•	•
Pain (last 7 days)	•	•	•	•	•	•	•	•
HAQ-DI	•	•	•	•	•	•	•	•
EQ-5D and EQ VAS	•	•	•	•	•	•	•	•
Physician visits and hospitalizations in past 6 months	•		•	•				
Physician visits and hospitalizations in past 12 months					•	•	•	•
Days of impairment in non- occupational activities in past 6 months	•		•	•				
Days of impairment in non- occupational activities in past 12 months					•	•	•	•
Current therapy compared with previous therapies		•	•	•	•	•	•	•

9.6 Bias

9.6.1 Confounding Variables

As for all observational studies, this study did not have controlled, parallel cohorts or a placebo arm, and so outcomes measures were potentially confounded by multiple factors, including documented variables such as age, previous treatment, concomitant medication, baseline disease activity, and comorbid conditions. Because of the potential impact of confounding factors, post-hoc subgroup analyses should be interpreted with caution.

9.6.2 Variability in Reporting

Clinicians measured and reported all outcomes as was normal for their clinical practice. As is usual for non-interventional studies conducted in Germany, clinicians did not receive training to help make AE reporting more uniform nor were they educated concerning potential AEs associated with adalimumab. A central laboratory was not used in this study. Laboratory parameters were evaluated by local laboratories and utilized different normal ranges based on each laboratory's standard procedures.

9.6.3 Recall Bias

Certain outcome measures, such as AEs, sick leave days, physician visits, in-patient hospitalization, and impairment of daily activities, were based on patient recall of events occurring over the previous 6 to 12 months (depending on the visit). This time lag may have made it difficult for patients to fully and accurately report these outcomes. However, a study of RA patients conducted in Germany found that patient-reported data on days of sick leave were comparable to insurance claims data from payers in Germany over six 3-month periods, suggesting that patient recall may be reliable for certain outcomes.⁸

9.6.4 Responder Bias

Effectiveness analyses were influenced by responder bias; patients experiencing a favorable response to adalimumab therapy were more likely to continue treatment, while

those who were not experiencing a favorable response tended to discontinue treatment. Responder bias probably results in overestimates of effectiveness at later time points in the study.

9.7 Study Size

9.7.1 AGIL Target Sample Size

Because one of the primary objectives of AGIL was assessment of work productivity, which is captured in part by the number of missed working days, the sample size calculation was based on the results of an interim analysis of a documentation of adalimumab in RA with 4640 patients, of whom 1417 were employed part-time or full-time. The mean number of missed working days was 26 (standard deviation [SD] of 55 days) during the 12 months prior to initiation of adalimumab therapy. The correlation between baseline and follow-up had an estimated r value of 0.5. Based on these numbers, 850 employed patients would be required to detect a mean difference of 5 missed working days during a 12-month period at the 0.95 significance level (two-sided) with a power of 0.80. Since approximately 30% of patients are employed, a total number of about 2500 employed and non-employed patients would be required at Month 60 in order to detect the specified difference in missed working days. Assuming a discontinuation rate of 50% over 60 months, the study would require 5000 patients at baseline. There was no upper limit for the number of enrolled patients.

9.7.2 AGIL-CV Target Sample Size

For AGIL-CV, the target study size was 300 patients. This was based on published data concerning the blood pressure of RA patients³⁹ and the following assumptions:

- Alpha and beta error of 5% each
- 50% discontinuation over 60 months
- 128 patients required to detect a means systolic blood pressure difference of 10 mmHg (assuming a mean systolic blood pressure of 128 mmHg with a standard deviation of 11 mmHg)

- 136 patients required to detect a mean diastolic blood pressure difference of 5 mmHg (assuming a mean diastolic blood pressure of 74 mmHg with a standard deviation of 11 mmHg)

9.8 Data Transformation

9.8.1 Patient Recall Measures at 6 and 12 Months

Patients were asked to state the number of sick leave days in the past 6 months at Months 0, 6, and 12. At subsequent visits (Months 24, 36, 48, and 60), patients were asked to state the number of sick leave days in the past 12 months. The number of sick leave days in the past 12 months was divided by 2 in order to make data at these time points comparable to the earlier reporting periods. Data for physician visits, hospitalizations, and days of impairment in non-occupational activities had the same reporting time points and were handled similarly.

9.8.2 Modified WAI

Although modified WAI data were collected at Month 3, there was no question concerning the number of sick leave days. Accordingly, WAI scores were not calculated for the Month 3 visit.

9.8.3 DAS28

DAS28 calculations were performed on data submitted by the clinician.

For patients with ESR values, the DAS28 was calculated by the following formula:

$$\text{DAS28} = 0.56 * \text{sqrt}(\text{TJC}) + 0.28 * \text{sqrt}(\text{SJC}) + 0.70 * \ln(\text{ESR}) + 0.014 * \text{PGA}$$

where sqrt = square root; TJC = tender joint count (28 joints); SJC = swollen joint count (28 joints); ln = natural logarithm; ESR = erythrocyte sedimentation rate; and PGA = patient global assessment (scale of 1 – 100 mm)

Formulas that utilize the C-reactive protein (CRP) value are also available, but tend to underestimate disease activity.⁴⁰ Accordingly, this study utilized only ESR values for DAS28 calculations.

9.8.4 HAQ-DI

The HAQ-DI is a summary measure composed of 20 items in 8 categories. Each item is scored from 0 to 3 (higher scores indicate more functional impairment). To calculate the HAQ-DI, the highest sub-category score determines the value for each category. The category scores are then averaged into an overall HAQ-DI from 0 to 3.³⁴

9.8.5 Correction of Blood Chemistry Values

For some blood chemistry parameters, data cleaning revealed incorrect values that appeared to arise from the use of different units than the ones requested on the CRF. Only a few patients were affected by these differences, but in order to include as many patients as possible in AGIL-CV the decision was made to correct these errors so the data from these patients would be usable. Values requiring correction were chosen by the statistician and study physician based on the data distribution and the available data. The following correction calculations were made on specified values that fell outside the data cleaning range:

- Fasting glucose values < 20 were assumed to be reported as mmol/L rather than mg/dL and multiplied by 18.018.
- Low-density lipoprotein cholesterol (LDL-C) values < 16, HDL-C values < 18, and total cholesterol (Total-C) values < 20 were assumed to be reported as mmol/L rather than mg/dL and multiplied by 38.941.
- Triglyceride values < 14 were assumed to be reported as mmol/L rather than mg/dL and multiplied by 88.496.

9.9 Statistical Methods

9.9.1 Main Summary Measures

Statistical analyses were performed using SAS[®] statistical software (Version 9.4). All documented and derived variables (e.g., changes from baseline) were summarized using descriptive statistics (mean, standard deviation, median, minimum, maximum).

Categorical variables were summarized by using absolute frequencies. In this report, mean values are presented for normally distributed data. For data that were not normally distributed, median values are also presented. The complete data set, including median values for all outcomes, can be found in [Appendix 6](#) (employed patients), [Appendix 7](#) (full analysis set [FAS]), [Appendix 8](#) (CV substudy), and [Appendix 9](#) (safety set).

Change from baseline analyses were conducted for patients with data at both time points (baseline and the subsequent visit). Because DAS28 was a requirement for inclusion in the FAS, all patients with DAS28 (and its components, including SJC, TJC, ESR, and patient global assessment of disease activity) at a given visit had data for both time points.

The evaluation of safety was based on the number of reported AEs and SAEs coded with MedDRA v20.1 Frequency tables were summarized according to SOC and PT.

9.9.2 Main Statistical Methods

9.9.2.1 Categorical Analyses

Initial analyses revealed that data for sick leave days were asymmetrically distributed (positively skewed) due to the large number of patients with no sick leave days at baseline. Because asymmetrical distribution can compromise interpretation of mean values, we conducted categorical analyses based on the mean number of sick leave days in the overall German population during the years this study was conducted (2009 to 2017). According to the German Federal Statistical Office, the annual sick leave days in Germany from 2009 to 2015 (most recent data) ranged from 8.8 to 10.00, with a mean of 9.44 per year, or 4.72 per 6 month period.⁴¹ We rounded this number to 5 to create two subgroups: 0 to 5 days/6 month period (representing a normal number of sick leave

days in the overall population) and > 5 sick leave days/6 month period (representing an increased number of sick leave days compared with the overall population).

9.9.2.2 Statistical Significance

Changes in AGIL primary objectives from baseline (Month 0) to Month 24 and to Month 60 were evaluated for statistical significance; a P value ≤ 0.05 was considered statistically significant. Month 24 was chosen as the primary end point for evaluations of statistical significance based on the ability of adalimumab to maintain a sustained response through 24 months in a randomized clinical trial⁴ and the higher numbers of patients available at Month 24 compared with later time points due to termination of the study in 2017.

For the categorical analysis of sick leave days, the McNemar test for paired samples was used to evaluate statistical significance. The remaining primary objectives in AGIL and AGIL-CV were continuous variables and were evaluated by the Wilcoxon signed rank test.

9.9.2.3 Multiple Regression Models

For heterogeneous populations such as the RA patients enrolled in this study, stepwise regression analysis is the statistical method of choice to identify associations among relevant variables.⁴²⁻⁴⁴ Multiple regression models were used to explore variables that were significant predictors of changes in employment-related outcomes (sick leave weeks, modified WPAI absenteeism and presenteeism, and modified WAI) in the employed patient cohort from Month 0 to Month 24, and of DAS28 and patient function (HAQ-DI) in the FAS from Month 0 to Month 6 at a significance level of $P < 0.01$. The end point of Month 24 for employment outcomes was chosen as a long-term time point that still retained a large population of patients. A total of 41 patient and disease variables were included in the regression models for employment-related outcomes (see [Appendix 6 Table 7.1](#)). For disease-related outcomes, Germany rheumatology experts consider Month 6 to be the main visit for determining whether current therapy should be stopped,

continued, or modified with concomitant DMARD therapy. A total of 35 patient and disease variables were included in the regression models (see Appendix 7, [Table 6](#)).

9.9.3 Missing Values

Due to the documentary nature of the study, data were not available for all assessments and thus the sample size differed among parameters. Missing data were not imputed and last-observation carried forward analyses were not conducted.

9.9.4 Sensitivity Analyses

None.

9.9.5 Amendments to the Statistical Analysis Plan

None.

9.9.6 Deviations to Protocol

9.9.6.1 Study Termination

The study was stopped by AbbVie on June 30, 2017. Doctors were asked to stop enrolling patients and to finish documentation within the next 8 weeks. At this time, AGIL had met the target sample size (5000 patients) and achieved the necessary number of patients for effectiveness analyses (e.g., DAS28, HAQ-DI, and other key outcomes) based on previous documentation studies in RA. Because an exact computation of the number of employed patients at each visit was only possible after analysis of the data, the study enrolled sufficient employed patients for robust analyses of employment-related outcomes for most of the study and came close to achieving the target sample size of 850 at Month 60. The target sample size was based on mean values; analyses of categorical values, as described in Section [9.9.2.1](#), indicated that the available number of employed patients was sufficient for statistically significant results at all visits. The AGIL-CV sample size was not achieved.

9.9.6.2 Changes in Concomitant Medication

Although one of the secondary objectives of the study was to evaluate changes in concomitant medications during adalimumab therapy, the CRF did not have a structured format for this information; medication changes were entered as free text. Accordingly, it was not possible to extract consistent information concerning changes in concomitant medication.

9.9.6.3 Secondary Objectives in AGIL-CV

Evaluation of the SCORE risk factors and the impact of baseline characteristics on CV and metabolic parameters were secondary objectives of AGIL-CV. Due to a small sample size and the lack of observable changes in primary objectives, these analyses were not performed.

9.10 Quality Control

Each patient CRF was reviewed for completeness of the main primary variables and for the plausibility of responses, as detailed in the Data Validation Plan (Appendix 14 [AGIL main study] and Appendix 15 [AGIL-CV]). Briefly, for effectiveness variables, values outside of a pre-determined range of acceptable values were considered missing and excluded from the analysis for that visit. Other effectiveness variables and safety data were not affected by this decision. Blood chemistry values were adjusted as described in Section [9.8.5](#).

10.0 Results

10.1 Participants

Because the study was stopped early by AbbVie due to achievement of the planned sample size for effectiveness analyses in AGIL, 2532 patients who enrolled between 2013 and 2017 (35.0% of the safety set) did not have the opportunity to reach Month 60. Accordingly, analyses for the first 24 months of treatment are more robust than subsequent analyses. For employed patients, the target sample size (850 patients) was

achieved through Month 36. This target sample size was based on mean values; the categorical analyses used for employed patients had a sufficient sample size for meaningful results at all visits. The target sample size for AGIL-CV was not achieved and none of the patients in this substudy had the opportunity to reach the Month 48 and Month 60 visits.

10.1.1 Analyzed Populations

This report is based on four different populations (summarized in [Table 8](#)). The employed patient set, FAS, and safety set populations are described in the following sections. Disposition and characteristics of patients in AGIL-CV are described in [Section 10.4.3](#).

Table 8. Summary of Analyzed Populations

Population	Description	N at Baseline	Appendix
Employed patient set	Patients who were employed outside of the home, on either a part-time or full-time basis, at baseline	3285	6
FAS	Patients with sufficient data to evaluate clinical outcomes and baseline disease activity high enough to evaluate effectiveness	4466	7
CV subset	Patients enrolled in the AGIL-CV substudy	260	8
Safety set	All enrolled patients who received at least one dose of adalimumab	7229	9

10.1.2 Employed Patients

Of 7229 enrolled patients, 3285 (45.4%) were employed part- or full-time at baseline. [Table 9](#) shows the disposition of the employed patient set over 60 months, including the numbers of patients who discontinued the study or were lost to follow up (patients for whom no further documentation was received for unknown reasons). More than half of patients (58.3%) remained on study at Month 12, but this figure dropped to below 20% at Month 60.

Table 9. Disposition of Patients in the Employed Patient Set

Patients, n (% of Employed Patient Set)	Month After Inclusion							
	0	3	6	12	24	36	48	60
Total employed patient set	3285	3285	3285	3285	3285	3285	3285	3285
Ongoing patients at the end of visit	3285 (100)	2713 (82.6)	2348 (71.5)	1915 (58.3)	1349 (41.1)	961 (29.3)	701 (21.3)	527 (16.0)
Cumulative documented withdrawals (discontinuation rates)	-	323 (9.8)	564 (17.2)	831 (25.3)	1067 (32.5)	1194 (36.3)	1257 (38.3)	1312 (39.9)
Cumulative lost to follow up	-	130 (4.0)	271 (8.2)	475 (14.5)	806 (24.5)	1076 (32.8)	1274 (38.8)	1446 (44.0)
Single visit missing (a later visit is following)	-	119 (3.6)	102 (3.1)	64 (1.9)	63 (1.9)	54 (1.6)	53 (1.6)	0 (0.0)

Reference: Appendix 6 [Table 4.3](#)

For patients with documented withdrawals, the reasons for withdrawal are shown in [Table 10](#). The most common reason for study withdrawal was lack of effectiveness (21.3% of the employed patient cohort), followed by "other" (13.8%).

Table 10. Reasons for Discontinuation from the Employed Patient Set (N = 3285) by Visit

Patients, n (% of Employed Patient Set)	Month After Inclusion							Total
	3	6	12	24	36	48	60	
Documented withdrawals ^a	323 (9.8)	241 (7.3)	267 (8.1)	236 (7.2)	127 (3.9)	63 (1.9)	55 (1.7)	1312 (39.9)
Adverse drug reaction	53 (1.6)	30 (0.9)	21 (0.6)	13 (0.4)	2 (0.1)	4 (0.1)	1 (0.0)	124 (3.8)
Lack of effectiveness	173 (5.3)	153 (4.7)	156 (4.7)	131 (4.0)	55 (1.7)	18 (0.5)	15 (0.5)	701 (21.3)
Other reason	93 (2.8)	53 (1.6)	85 (2.6)	84 (2.6)	62 (1.9)	38 (1.2)	39 (1.2)	454 (13.8)
Unknown reason	4 (0.1)	5 (0.2)	5 (0.2)	8 (0.2)	8 (0.2)	3 (0.1)	0 (0.0)	33 (1.0)

a. There were no multiple answers; patients were asked to provide the most important reason for study discontinuation.

Reference: Appendix 6 [Table 4.2](#)

10.1.3 FAS (Clinical Outcomes)

Of the 7229 patients enrolled in AGIL, 4466 patients (61.8%) met criteria for inclusion in the FAS. Reasons for exclusion from the FAS are shown in [Table 11](#). Patients with low disease activity were excluded due to the difficulty in assessing effectiveness in patients whose disease is currently well controlled. The two most common reasons for exclusion were lack of DAS28 documentation at baseline and low disease activity (DAS28 \leq 3.2) at baseline. Of patients excluded for low disease activity, 929 (12.9% of the patient base) were excluded for this reason only.

Table 11. Reasons for Exclusion from the FAS

	n	%
Patient base	7229	100
At least one of the following criteria resulted in exclusion (multiple reasons were possible)	2763	38.2
Patients without DAS28 measurement at baseline	1097	15.2
DAS28 ≤ 3.2 at baseline	1097	15.2
Patients without post-baseline information (no visit dates)	556	7.7
Patients with prior adalimumab therapy	362	5.0

Reference: Appendix 7 [Table 1.1](#)

The disposition of the FAS during the 60-month study is shown in [Table 12](#). Of the 4466 patients, approximately 20% were available at month 60 for evaluations of clinical outcomes. About half of the 3740 patients who left the study withdrew and half were lost to follow-up for unknown reasons (no further documentation received). The termination of the study in 2017 likely influenced these numbers.

Table 12. Disposition of Patients in the FAS

Patients, n (% of FAS)	Month After Inclusion							
	0	3	6	12	24	36	48	60
Total FAS	4466	4466	4466	4466	4466	4466	4466	4466
Ongoing patients at the end of visit	4466 (100)	3936 (88.1)	3300 (73.9)	2618 (58.6)	1842 (41.2)	1318 (29.5)	975 (21.8)	726 (16.3)
Cumulative documented withdrawals (discontinuation rates)		380 (8.5)	797 (17.8)	1219 (27.3)	1553 (34.8)	1734 (38.8)	1826 (40.9)	1889 (42.3)
Cumulative lost to follow up		0 (0.0)	243 (5.4)	550 (12.3)	988 (22.1)	1347 (30.2)	1611 (36.1)	1851 (41.4)
Single visit missing (a later visit is following)		150 (3.4)	126 (2.8)	79 (1.8)	83 (1.9)	67 (1.5)	54 (1.2)	0 (0.0)

Reference: Appendix 7 [Table 4.3](#)

For patients with documented withdrawals, the reasons for withdrawal are shown in [Table 13](#). The most common reason for withdrawal was lack of effectiveness, followed by "other." Adverse drug reactions accounted for withdrawals in 4.2% of patients in the FAS.

Table 13. Reasons for Discontinuation from the FAS (N = 4466) by Visit

Patients, n (% of FAS)	Month After Inclusion							Total
	3	6	12	24	36	48	60	
Documented withdrawals ^a	380 (8.5)	417 (9.3)	422 (9.4)	334 (7.5)	181 (4.1)	92 (2.1)	63 (1.4)	1889 (42.3)
Adverse drug reaction	67 (1.6)	46 (1.2)	35 (1.2)	25 (1.1)	5 (0.3)	8 (0.7)	1 (0.1)	187 (4.2)
Lack of effectiveness	219 (5.1)	249 (6.7)	237 (7.8)	177 (8.1)	81 (5.4)	29 (2.7)	13 (1.6)	1005 (22.5)
Other reason	89 (2.1)	111 (3.0)	138 (4.5)	124 (5.7)	90 (6.0)	52 (4.9)	49 (6.2)	653 (14.6)
Unknown reason	5 (0.1)	11 (0.3)	12 (0.4)	8 (0.4)	5 (0.3)	3 (0.3)	0 (0.0)	44 (1.0)

a. There were no multiple answers; patients were asked to provide the most important reason for study discontinuation.

Reference: Appendix 7 [Table 4.1](#)

10.1.4 Safety Set

The database for this study included 7229 patients who received at least one dose of adalimumab; all patients were included in the safety set. At Month 60, there were 1210 ongoing patients (16.7%) ([Table 14](#)).

Table 14. Disposition of Patients in the Safety Set

Patients, n (% of Safety Set)	Month After Inclusion							
	0	3	6	12	24	36	48	60
Total safety set	7229	7229	7229	7229	7229	7229	7229	7229
Ongoing patients at the end of visit	7229 (100)	5886 (81.4)	5048 (69.8)	4107 (56.8)	2919 (40.4)	2137 (29.6)	1608 (22.2)	1210 (16.7)
Cumulative documented withdrawals (discontinuation rates)	-	746 (10.3)	1300 (18.0)	1871 (25.9)	2362 (32.7)	2617 (36.2)	2762 (38.2)	2868 (39.7)
Cumulative lost to follow up	-	318 (4.4)	670 (9.3)	1128 (15.6)	1810 (25.0)	2363 (32.7)	2765 (38.2)	3151 (43.6)
Single visit missing (a later visit is following)	-	279 (3.9)	211 (2.9)	123 (1.7)	138 (1.9)	112 (1.5)	94 (1.3)	0 (0.0)

Reference: Appendix 9 [Table 4.3](#)

For patients with documented withdrawals, the reasons for withdrawal are shown in [Table 15](#). As for the FAS, the most common reason for withdrawal was lack of effectiveness (19.7% of patients), followed by "other" (14.9%).

Table 15. Reasons for Discontinuation from the Safety Set (N = 7229) by Visit

Patients, n (% of Safety Set)	Month After Inclusion							Total
	3	6	12	24	36	48	60	
Documented withdrawals ^a	746 (10.3)	554 (7.7)	571 (7.9)	491 (6.8)	255 (3.5)	145 (2.0)	106 (1.5)	2868 (39.7)
Adverse drug reaction	132 (1.8)	61 (0.8)	50 (0.7)	33 (0.5)	9 (0.1)	12 (0.2)	2 (0.0)	299 (4.1)
Lack of effectiveness	354 (4.9)	337 (4.7)	308 (4.3)	251 (3.5)	110 (1.5)	39 (0.5)	24 (0.3)	1423 (19.7)
Other reason	253 (3.5)	142 (2.0)	196 (2.7)	192 (2.7)	124 (1.7)	88 (1.2)	80 (1.1)	1075 (14.9)
Unknown reason	7 (0.1)	14 (0.2)	17 (0.2)	15 (0.2)	12 (0.2)	6 (0.1)	0 (0.0)	71 (1.0)

a. There were no multiple answers; patients were asked to provide the most important reason for study discontinuation.

Reference: Appendix 9 [Table 4.1](#)

10.2 Descriptive Data

The following sections provide data for employed patients, the FAS, and the safety set. Relevant descriptive data for the subset of patients in AGIL-CV are presented in Section [10.4.3.2](#).

10.2.1 Reasons for Adalimumab Therapy

The most common reasons for receiving adalimumab therapy in this study were high disease activity and lack of effectiveness of previous therapy (more than one answer was possible) ([Table 16](#)).

Table 16. Reasons for Receiving Adalimumab Therapy

Indication ^a	Employed Patients N = 3285	FAS N = 4466	Safety N = 7229
	n (%)	n (%)	n (%)
High disease activity	2614 (79.6)	3728 (83.5)	5781 (80.0)
Lack of effectiveness of previous therapy	2232 (67.9)	3143 (70.4)	4901 (67.8)
Intolerance of previous therapy	890 (27.1)	1267 (28.4)	2027 (28.0)
Rapid radiologic progression	523 (15.9)	694 (15.5)	1162 (16.1)
Other	100 (3.0)	90 (2.0)	227 (3.1)

a. Multiple answers possible.

Reference: Appendices 6, 7 and 9 Table 1.10

10.2.2 Baseline Characteristics

As expected for populations of RA patients, all three populations had a higher proportion of women than men (Table 17). Slightly over half of the patients in the FAS and safety cohorts were not employed. The employed patient cohort tended to be younger and have a shorter duration of disease than the FAS and safety cohorts. The FAS had slightly higher disease severity, probably due to the fact that patients with low disease activity (DAS28 < 3.2) were excluded from the FAS.

Table 17. Baseline Characteristics^a

Characteristic	Employed Patients	FAS	Safety
N	3285	4464	7729
Age ^b	48.3 (9.4)	55.1 (13.0)	54.9 (13.2)
Female (% of patients)	69.8	74.1	73.4
BMI (kg/m ²) ^b	26.4 (5.2)	27.1 (5.6)	26.9 (5.5)
Current smoker (% of patients)	25.0	22.7	22.2
RF positive (% of patients)	63.6	65.8	65.0
Anti-CCP positive (% of patients)	64.3	66.0	65.6
Rheumatoid nodules (% of patients)	11.2	15.5	14.5
Morning stiffness (% of patients)	73.9	83.5	76.5
Duration (minutes) ^b	54.0 (70.7)	65.3 (72.8)	56.9 (71.0)
Duration of disease (years) ^b	7.9 (7.2)	9.2 (8.7)	9.6 (8.8)
HAQ-DI ^b	0.95 (0.68)	1.30 (0.70)	1.19 (0.74)
Joint status ^b			
TJC	6.9 (6.5)	8.8 (6.7)	7.4 (6.8)
SJC	4.7 (5.0)	6.0 (5.4)	5.0 (5.3)
ESR (mm/hour) ^b			
Male	23.5 (21.9)	31.0 (23.7)	27.0 (23.6)
Female	23.0 (18.6)	29.0 (21.2)	26.3 (20.9)
CRP (mg/L) ^b	15.8 (45.8)	19.3 (50.7)	17.3 (48.7)
DAS28 ^b	4.43 (1.49)	5.13 (1.14)	4.63 (1.51)
Patient global assessment of disease activity ^{b,c}	5.4 (2.5)	6.1 (2.2)	5.6 (2.5)
Physician global assessment of disease activity ^{b,c}	5.5 (2.3)	6.0 (1.9)	5.5 (2.2)
Fatigue ^{b,c}	5.4 (2.9)	5.8 (2.7)	5.4 (2.8)
Pain ^{b,c}	5.3 (2.6)	6.1 (2.3)	5.6 (2.5)
Concomitant medication (% of patients)			
MTX	55.2	53.4	51.8
Mean dose (mg/week) ^b	14.7 (5.0)	14.8 (7.0)	14.5 (6.4)
Leflunomide	11.6	12.0	10.8
Sulfasalazine	3.6	3.6	3.4

Characteristic	Employed Patients	FAS	Safety
NSAID or coxib	20.8	22.1	20.4
Analgesics	9.0	10.9	10.3
Systemic glucocorticoids	62.8	68.1	63.9
Prednisolone-equivalent dose (mg/d) ^b	7.6 (6.2)	7.7 (5.8)	7.5 (5.7)
Joint erosions (% of patients)	58.8	61.6	63.6
Prior joint surgery (% of patients)	16.6	22.3	23.2
In-patient hospitalizations in last 6 months			
Number of hospitalizations ^b	0.3 (1.4)	0.4 (1.5)	0.4 (1.5)
Days of hospitalization ^b	1.5 (5.3)	2.3 (7.3)	2.1 (6.8)
Participation in Abbott Care (AbbVie Care) service program (% of patients)	35.7	34.9	35.4
Employment status (% of patients)			
Part-time	34.4	16.0	16.3
Full-time	65.6	30.6	31.2
Not employed	-	53.4	52.5
Missed work days in last 6 months (% of patients)	53.9	51.1	49.2
Number of missed work days in last 6 months (employed patients only) ^b	19.2 (38.4)	22.0 (43.8)	19.9 (41.7)
Modified WPAI (employed patients only)			
Presenteeism, %	46.7 (26.9)	51.9 (25.9)	47.2 (27.3)
Absenteeism, % of hours	21.0 (36.6)	23.8 (38.2)	21.4 (36.9)
Total work productivity impairment, %	50.9 (28.9)	56.2 (27.7)	50.9 (29.2)
Total activity impairment, %	51.7 (25.9)	59.2 (22.8)	54.9 (25.0)
Modified WAI (employed patients only)	32.2 (7.7)	30.6 (7.5)	32.1 (7.8)

a. The complete set of parameters was not available for each patient.

b. Mean (SD).

c. Categorical scale ranging from 0 (best) to 10 (worst).

Reference: Appendices 6, 7, and 9 Tables 1.2, 1.3.1, 1.6.1, 1.7, 1.8.1, 1.9, 1.12, 1.13.1, 1.13.2, 1.14, 1.15, 1, 17.1, 1.17.2, 1.17.3, 1.17.4.2, 1.20, 1.24, 1.25.5, 1.25.6, 1.26, 1.27.1, 1.27.2, 1.27.3, 1.27.4, 1.28, 1.29, 1.30, 1.31, 1.33, 1.34, 3.2, 3.4, 3.5

An in-depth analysis of disease duration in the FAS showed that most patients had long-standing disease. More than one-third (34.6%) had a disease duration of 10 years or more, and fewer than 20% had a disease duration of under 2 years (Table 18).

Table 18. Analysis of Disease Duration in the FAS^a

Disease Duration (years)	n	%
< 2 years	834	18.9
2 to < 4 years	718	16.3
4 to < 6 years	524	11.9
6 to < 8 years	412	9.3
8 to < 10 years	406	9.2
10 to < 15 years	665	15.1
15 to < 20 years	360	8.2
20 to < 30 years	329	7.5
≥ 30 years	168	3.8

a. N = 4466; disease duration data available for 4416.

Reference: Appendix 7 Table 1.8.1

10.2.3 Baseline Comorbidities

Baseline reports of comorbid conditions were based on patient recall and review of ongoing medications; no diagnostic tests were performed. Clinicians asked patients whether they had any of eleven pre-specified comorbid conditions: arterial hypertension, coronary heart disease, hyperlipidemia, diabetes Type I or Type II, chronic inflammatory disease, chronic obstructive pulmonary disease, osteoporosis, degenerative joint disease, degenerative spinal disease, or mental illness (e.g., depression). There was also space to enter "other" comorbid diseases.

The majority of patients in the FAS and safety set reported having one of the pre-specified comorbid conditions at baseline (Table 19). Arterial hypertension was the most common pre-specified comorbid condition in all three cohorts. The employed patient cohort had

lower proportions of pre-specified comorbid conditions, probably due to the younger mean age and lower disease severity of this group.

Table 19. Pre-Specified Comorbid Conditions Reported by Patients

Comorbid Condition	Employed Patients	FAS	Safety
	N = 3285	N = 4466	N = 7229
Patients with pre-specified comorbid diseases (%)	55.1	69.3	66.7
Patients with specific comorbid diseases (%) ^a			
Arterial hypertension	22.7	35.5	33.8
Degenerative joint disease	10.9	18.7	17.5
Degenerative spinal disease	8.6	15.3	14.2
Osteoporosis	6.9	14.9	14.4
Diabetes type II	4.4	8.8	8.2
Hyperlipidemia	4.4	8.2	7.7
Mental illness (e.g., depression)	4.5	6.7	6.3
Coronary heart disease	1.6	5.5	5.5
Chronic obstructive pulmonary disease	3.1	5.0	4.6
Chronic inflammatory disease	1.8	2.0	2.0
Diabetes type I	1.2	1.4	1.4
Other comorbid disease	28.6	32.3	30.9

a. More than one answer was possible.

Reference: Appendices 6, 7, and 9 Table 2

10.2.4 Previous RA Therapy

Most patients in the study had received previous therapy with non-biologic DMARDs (Table 20). Methotrexate (MTX) was the most common non-biologic DMARD followed by leflunomide. The use of pain/anti-inflammatory medications, such as glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), coxibs (cyclo-oxygenase 2 inhibitors), and analgesics, was also common in this population.

Table 20. Previous DMARD and Pain/Anti-Inflammatory Therapy

Previous Therapy	Employed Patients N = 3285	FAS N = 4466	Safety N = 7229
DMARD therapy (% of patients) ^a			
MTX	60.4	63.9	62.1
Leflunomide	52.8	56.7	55.4
Sulfasalazine	30.5	31.1	31.2
Pain/anti-inflammatory therapy (% of patients) ^a			
Systemic glucocorticoids	43.8	42.9	43.9
NSAID or coxibs	34.5	35.0	35.0
Analgesics	19.3	23.2	22.3
Other	14.0	15.6	15.8

a. More than one answer was possible.

Reference: Appendices 6, 7, and 9 Table 3.1

Prior biologic therapy was reported by approximately 25% of patients in the FAS and safety set (Table 21). Etanercept was the most common prior biologic therapy.

Table 21. Previous Biologic Therapy

Previous Biologic Therapy	Employed Patients N = 3285	FAS N = 4466	Safety N = 7229
Patients with previous biologics (% of patients) ^a			
Etanercept	13.5	18.5	18.2
Infliximab	2.5	3.1	3.3
Tocilizumab	2.4	2.8	3.0
Certolizumab	2.1	2.1	2.2
Golimumab	1.7	2.1	1.8
Rituximab	0.9	1.3	1.2
Abatecept	1.1	1.3	1.3
Other	4.9	1.1	6.0
Duration of previous biologic therapy (months [SD])			
Etanercept	24.1 (28.7)	30.2 (34.4)	28.0 (32.5)
Infliximab	37.0 (41.2)	29.5 (33.3)	29.5 (33.3)
Tocilizumab	11.7 (14.4)	12.1 (12.5)	14.0 (18.6)
Certolizumab	9.4 (11.1)	9.9 (10.6)	10.6 (11.7)
Golimumab	15.5 (25.2)	15.2 (22.4)	14.9 (20.5)
Rituximab	12.9 (14.7)	20.9 (24.1)	19.6 (23.1)
Abatecept	10.2 (10.2)	11.1 (11.5)	10.9 (11.1)

a. More than one answer was possible.

Reference: Appendices 6, 7, and 9 Tables 3.6.1 and 3.6.2

10.3 Outcome Data

Safety evaluations were based on all patients who received at least one dose of adalimumab (N = 7229). Safety data were collected as cumulative reports; AE data are not available for each visit.

Table 22 shows the number of employed patients available for employment-related effectiveness outcomes at each visit. To be considered an employed patient, patients were required to be employed outside of the home on either a part-time or full-time basis.

Table 22. Employed Patient Numbers for Employment-Related Effectiveness Outcomes at Each Visit

Effectiveness Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
Sick leave days in past 6 months	3156	-	2326	1906	1321	890	613	426
Modified WPAI								
Absenteeism	2253	1892	1550	1256	847	557	371	261
Presenteeism	2758	2433	2093	1714	1209	804	539	370
Total work impairment	2026	1793	1458	1183	811	530	356	239
Total activity impairment	3248	2783	2444	2025	1434	977	691	514
Modified WAI	2110	-	2036	1573	1178	797	540	377

Reference: Appendix 6 [Table 5.2](#), [5.8](#), [5.9.1](#), [5.9.2](#), [5.9.3](#), [5.9.4](#)

[Table 23](#) shows the number of FAS patients available for major clinical outcomes at each visit. Most assessments were performed at each visit, although the numbers of patients were slightly lower for laboratory tests (CRP and ESR) and for DAS28, which includes ESR.

Table 23. FAS Numbers for Major Clinical Outcomes at Each Visit

Effectiveness Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
DAS28	4466	3749	3229	2621	1818	1250	912	650
TJC	4466	4280	3657	2969	2095	1456	1040	752
SJC	4466	4280	3657	2969	2095	1456	1040	752
Physician global assessment of disease activity	4459	4280	3660	2958	2088	1450	1041	747
ESR	4466	3893	3321	2705	1891	1299	953	673
CRP	4353	3928	3356	2744	1954	1348	973	690
HAQ-DI	4449	4143	3546	2881	2019	1403	994	728
EQ-5D	4400	4118	3524	2856	2020	1401	992	732
EQ-VAS	4405	4116	3522	2850	2013	1407	994	730
Morning stiffness	4411	4247	3632	2948	2079	1446	1035	746
Patient global assessment of disease activity	4407	4178	3582	2902	2042	1417	1013	737
Pain	4455	4178	3582	2901	2045	1415	1004	730
Fatigue	4449	4180	3580	2901	2046	1418	1005	732

Reference: Appendix 7 [Tables 5.1 to 5.11](#)

10.4 Main Results

10.4.1 Employment-Related Outcomes

Primary effectiveness outcomes related to employment were performed in patients who were employed part- or full-time at baseline. At baseline, 65.6% of patients in the employed patient cohort were employed full-time and 34.4% were employed part-time. This approximately 2:1 ratio of full-time to part-time employment was generally maintained throughout the study ([Table 24](#)). Modest changes that occurred in employment status were mostly due to patients retiring during the course of the 5-year study.

Table 24. Employment Status of Patients in the Employed Patient Cohort Over 60 Months

Patients, n (% of Ongoing Employed Patients)	Month After Inclusion						
	0	6	12	24	36	48	60
Ongoing employed patients	3285	2458	2072	1476	1024	717	531
Full-time employment ^a	2156 (65.6)	1560 (63.5)	1290 (62.3)	903 (61.2)	625 (61.0)	412 (57.5)	285 (53.7)
Part-time employment	1129 (34.4)	767 (31.2)	622 (30.0)	413 (28.0)	268 (26.2)	186 (25.9)	129 (24.3)
School/education	--	12 (0.5)	8 (0.4)	5 (0.3)	4 (0.4)	3 (0.4)	1 (0.2)
Home-making/ child-rearing	--	23 (0.9)	22 (1.1)	23 (1.6)	14 (1.4)	14 (2.0)	11 (2.1)
Unemployed	--	49 (2.0)	51 (2.5)	52 (3.5)	26 (2.5)	17 (2.4)	21 (4.0)
Retirement	--	47 (1.9)	79 (3.8)	80 (5.4)	87 (8.5)	85 (11.9)	84 (15.8)

a. Defined as working at least 35 hours per week.

Reference: Appendix 6 [Table 5.1](#)

10.4.1.1 Sick Leave Days

During 60 months of adalimumab therapy, the mean number of missed working days due to sick leave in the previous 6 months decreased from 19.2 at baseline to 7.9 at Month 60 in patients remaining on therapy ([Table 25](#)). Data analysis revealed that the distribution was skewed due to the large number of patients with 0 sick leave days in the previous 6 months (from 46.1% to 62.1% of patients during the study; see Appendix 6 [Table 5.7.1](#)). Median values decreased from 3 at Month 0 to 0 at Month 6 and stayed at 0 for the remainder of the study.

Change from baseline analyses were conducted on patients who had data for both time points. At 6 months, mean sick leave days in the prior 6 months had decreased by 4.3 days compared with baseline. The greatest decrease in sick leave days was observed at month 36 (6.7 days).

Table 25. Sick Leave Days in Previous 6 Months

	Month after inclusion						
	0	6	12	24	36	48	60
Sick leave days							
n	3156	2326	1906	1321	890	613	426
Mean (SD)	19.2 (38.4)	12.4 (33.9)	11.4 (31.8)	7.4 (19.7)	6.8 (18.7)	5.1 (13.0)	7.9 (21.8)
Median	3	0	0	0	0	0	0
Range	0 – 183	0 – 183	0 – 183	0 – 183	0 – 183	0 – 183	0 – 183
Change from baseline in sick leave days ^a							
n	--	2267	1855	1290	868	596	415
Mean (SD)	--	-4.3 (32.7)	-3.4 (37.3)	-5.6 (30.3)	-6.7 (32.2)	-6.4 (27.7)	-4.1 (32.0)

a. In patients with values for both time points.

Reference: Appendix 6 [Table 5.2](#)

10.4.1.2 Categorical Evaluations of Sick Leave Days

Because the asymmetric data distribution for sick leave days in the previous 6 months weakened the validity of analyses based on mean values, we used a categorical analysis to evaluate the impact of adalimumab treatment on sick leave days. The categorical analysis was based on the proportions of patients within or above the normal range for mean sick leave days in the German population (≤ 5 days or >5 days in the past 6 months),⁴¹ as described in Section [9.9.2.1](#).

At baseline, 44.7% of the employed patient cohort had a higher than normal number of sick leave days ([Table 26](#)). This proportion decreased to 29.5% at month 6 and was maintained at or slightly below that level through month 60 in patients who remained on therapy. The change from baseline in the proportion of patients with ≤ 5 sick leave days in the previous 6 months was highly significant at both Month 24 and Month 60 ($P < 0.0001$ and $P = 0.008$, respectively).

Table 26. Patients with ≤ 5 or > 5 Sick Leave Days in the Past 6 Months

	Month After Inclusion						
	0	6	12	24	36	48	60
n	3156	2326	1906	1321	890	613	426
0 to 5 sick leave days, n (%)	1744 (55.3)	1639 (70.5)	1363 (71.5)	953 (72.1) ^a	657 (73.8)	465 (75.9)	315 (73.9) ^b
>5 sick leave days, n (%)	1412 (44.7)	687 (29.5)	543 (28.5)	368 (27.9) ^a	233 (26.2)	148 (24.1)	111 (26.1) ^b

a. $P < 0.0001$ (McNemar test) for change from baseline in patients with data at both time points.

b. $P = 0.008$ (McNemar test) for change from baseline in patients with data at both time points.

Reference: Appendix 6 [Tables 5.7.2.1, 5.7.2.2, 5.7.2.3](#)

We also performed a subgroup analysis of the proportion of patients with normal or elevated numbers of sick leave days based on the number of sick leave days at baseline ([Table 27](#)). Of patients with higher than normal sick leave days at baseline (> 5 in the previous 6 months) who remained on therapy, 57.3% had a normal number of sick leave days (≤ 5) at Month 12 and 63.3% achieved normal levels at Month 60. Approximately 80% of patients with a normal number of sick leave days at baseline retained this status throughout the study.

Table 27. Proportion of Patients with Normal Sick Leave Duration (≤ 5 in Past 6 Months) by Baseline Sick Leave Days

Baseline Subgroup	Month After Inclusion						
	0	6	12	24	36	48	60
<i>0 to 5 sick leave days in past 6 months</i>							
n	1744	1310	1113	788	534	374	265
% of patients	100	83.4	80.5	81.2	83.0	82.9	79.6
<i>> 5 sick leave days in past 6 months</i>							
n	1412	957	742	502	334	222	150
% of patients	0	53.2	57.3	58.2	60.2	63.5	63.3

Reference: Appendix 6 [Table 6.7.2](#)

10.4.1.3 Modified WPAI

WPAI absenteeism data (Table 28), which was based on patient recall over the past 7 days, supported the decrease in missed working days due to illness in the previous 6 months. Absenteeism was decreased by about one-half during the first 3 months of adalimumab therapy, from a mean of 21% of hours at Month 0 to 10.4% of hours at Month 3, and stayed at approximately this level throughout the 60-month study in patients remaining on therapy. Change from baseline was statistically significant at Month 24 and Month 60. Significant improvements were also observed in presenteeism (productivity while at work), total work productivity impairment (a composite measure of absenteeism and presenteeism), and total activity impairment (effect of the disease on non-occupational activities) at both Month 24 and Month 60.

Table 28. Modified WPAI^a Outcomes (Past 7 Days)

	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>Absenteeism, % of hours</i>								
n	2253	1892	1550	1256	847	557	371	261
Mean (SD)	21.0 (36.6)	10.4 (26.6)	10.8 (27.4)	9.3 (25.6)	8.8 (24.0)	7.5 (23.1)	7.7 (23.2)	12.8 (30.6)
Median	0	0	0	0	0	0	0	0
<i>Change from baseline in absenteeism^b</i>								
n	--	1482	1220	969	660	424	287	200
Mean (SD)	--	-7.9 (34.6)	-8.0 (37.2)	-7.3 (38.3)	-6.5 (36.1) ^c	-8.0 (34.7)	-5.2 (34.6)	-5.2 (40.7) ^d
<i>Presenteeism, %</i>								
n	2758	2433	2093	1714	1209	804	539	370
Mean (SD)	46.7 (26.9)	34.8 (24.3)	33.9 (24.3)	31.8 (23.7)	31.1 (23.7)	28.6 (23.3)	27.0 (22.1)	25.1 (21.3)
Median	50	30	30	30	30	20	20	20

	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>Change from baseline in presenteeism^b</i>								
n	--	2157	1852	1513	1084	717	490	343
Mean (SD)	--	-11.3 (25.8)	-11.8 (26.7)	-12.7 (28.2)	-12.9 (28.6) ^c	-15.3 (28.8)	-16.4 (29.4)	-15.2 (27.8) ^c
<i>Total work productivity impairment, %</i>								
n	2026	1793	1458	1183	811	530	356	239
Mean (SD)	50.9 (28.9)	37.1 (26.5)	36.0 (26.7)	32.7 (25.4)	33.0 (26.0)	29.8 (24.8)	29.6 (24.3)	28.8 (24.9)
Median	50	30	30	30	30	20	20	20
<i>Change from baseline in total work productivity impairment^b</i>								
n	--	1313	1073	851	596	382	261	171
Mean (SD)	--	-13.0 (27.7)	-14.4 (28.8)	-16.4 (30.3)	-15.3 (30.6) ^c	-18.8 (29.3)	-16.7 (31.6)	-16.5 (33.8) ^c
<i>Total activity impairment, %</i>								
n	3248	2783	2444	2025	1434	977	691	514
Mean (SD)	51.7 (25.9)	39.5 (24.7)	37.6 (25.2)	35.3 (24.9)	33.9 (24.4)	31.5 (23.9)	31.3 (23.5)	30.4 (23.2)
Median	50	40	30	30	30	30	30	30
<i>Change from baseline in total activity impairment^b</i>								
n	--	2758	2420	2007	1424	970	687	509
Mean (SD)	--	-11.9 (26.5)	-12.8 (27.5)	-13.8 (28.6)	-14.3 (28.4) ^c	-15.4 (29.7)	-14.8 (29.4)	-14.8 (28.6) ^c

a. Lower percentages correspond to better outcomes.

b. In patients with values for both time points.

c. $P < 0.0001$ (Wilcoxon).

d. $P < 0.05$ (Wilcoxon).

Reference: Appendix 6 [Tables 5.9.1.1, 5.9.1.2, 5.9.2.1, 5.9.2.2, 5.9.3.1, 5.9.3.2, 5.9.4.1, 5.9.4.2](#)

10.4.1.4 Modified WAI

Improvements in employment-related outcomes were also evident in modified WAI scores ([Table 29](#)). At Month 0, the mean WAI value of 32.2 was within the range considered to be "medium" work ability (WAI of 28 to 36). From Month 36 through

Month 60, mean WAI values reflected "good" work ability (WAI of 37 to 43).²⁸ The change from baseline was statistically significant at Months 24 and 60 ($P < 0.0001$).

Table 29. Modified WAI Outcomes

	Month After Inclusion						
	0	6	12	24	36	48	60
<i>Modified WAI^a</i>							
n	2110	2036	1573	1178	797	540	377
Mean (SD)	32.2 (7.7)	34.9 (7.6)	36.1 (7.5)	36.7 (7.3)	37.2 (7.2)	38.0 (6.8)	37.7 (7.2)
Median	32.5	36.0	37.0	37.5	38.0	39.0	39.0
<i>Change from baseline in modified WAI^b</i>							
n		1908	1442	986	666	452	318
Mean (SD)	--	2.5 (5.9)	3.0 (6.7)	3.2 (6.8) ^c	3.6 (7.0)	3.3 (6.6)	3.0 (7.0) ^c

a. Higher scores correspond to better outcomes.

b. In patients with values for both time points.

c. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 6 [Tables 5.8.1, 5.8.2](#)

10.4.2 Clinical Outcomes

Clinical outcomes were assessed in the FAS (N = 4466).

10.4.2.1 Disease Activity

10.4.2.1.1 DAS28

During 60 months of adalimumab treatment, mean DAS28 values in the FAS decreased from 5.12, a level corresponding to high disease activity, to 2.93 at Month 60, a value representing low disease activity.³² Most of the decrease was observed in the first 6 months of therapy. Patients who remained on therapy showed sustained reductions in disease activity throughout 60 months in patients remaining on therapy ([Table 30](#)). Changes from baseline in DAS28 were statistically significant at both Month 24 and Month 60 ($P < 0.0001$).

Table 30. Changes in DAS28 in the FAS

Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>DAS28^a</i>								
n	4466	3749	3229	2621	1818	1250	912	650
Mean (SD)	5.13 (1.14)	3.81 (1.38)	3.55 (1.36)	3.38 (1.35)	3.21 (1.32)	3.10 (1.27)	3.01 (1.21)	2.93 (1.22)
<i>Change from baseline in DAS28^{b,c}</i>								
n	--	3749	3229	2621	1818	1250	912	650
Mean (SD)	--	-1.34 (1.39)	-1.56 (1.46)	-1.71 (1.55)	-1.84 (1.57) ^d	-1.94 (1.61)	-2.01 (1.59)	-2.15 (1.63) ^d

- a. Higher scores indicate greater disease activity.
b. Negative changes indicate reductions (improvement) in disease activity.
c. Because baseline DAS28 was an inclusion criterion, all patients with DAS28 at the given visit had data for both time points.
d. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 7 [Table 5.1.1](#), [5.1.2](#)

The proportion of patients achieving clinical remission ($\text{DAS28} < 2.6$)³² increased during 60 months of adalimumab therapy. At Month 6, more than one-quarter (26.1%) of patients had achieved clinical remission. At Month 60, approximately 45% of the patients remaining in the study had achieved clinical remission ([Table 31](#)).

Table 31. Percentages of FAS Patients Achieving Clinical Remission (DAS28 < 2.6) at Each Visit

	Month After Inclusion							
	0	3	6	12	24	36	48	60
n	4466	3749	3229	2621	1818	1250	912	650
% of patients	0.0	20.5	26.1	30.5	37.0	39.4	42.9	45.2

Reference: Appendix 7 [Table 5.1.3](#)

We also conducted a responder analysis using the DAS28 critical difference ($\text{DAS28}_{\text{crit}}$) response criterion, an individual assessment that represents a significant and clinically relevant change in disease activity as described by Behrens et al.³⁸ This criterion (DAS28

decrease of ≥ 1.8 from baseline) was used to evaluate the proportion of patients who achieved a therapeutic response at each visit. The percentage of patients with a DAS28_{crit} response increased from 42.9% at Month 6 to 59.7% at Month 60 in patients remaining on therapy (Table 32).

Table 32. Percentages of FAS Patients Achieving a DAS28_{crit} Response^a at Each Visit

	Month After Inclusion							
	0	3	6	12	24	36	48	60
n	--	3749	3229	2621	1818	1250	912	650
% of patients	--	35.8	42.9	46.3	50.1	53.9	55.6	59.7

a. DAS28 decrease of ≥ 1.8 from baseline.

Reference: Appendix 7 Table 5.1.3

10.4.2.1.2 Additional Disease Activity Parameters

Objective assessments of clinical symptoms (TJC, SJC, and physician global assessment of disease activity) were consistent with the reductions in DAS28 (Table 33). Changes in TJC and SJC from baseline to Month 24 and Month 60 were statistically significant. The physician global assessment of disease activity was not a primary clinical objective and so statistical tests were not performed on this variable.

Table 33. Changes in Disease Outcome Assessments in the FAS

Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>TJC</i>								
n	4466	4280	3657	2969	2095	1456	1040	752
Mean (SD)	8.8 (6.7)	4.6 (5.8)	3.8 (5.3)	3.3 (4.9)	2.8 (4.6)	2.5 (4.4)	2.2 (4.0)	2.2 (3.9)
<i>Change from baseline in TJC^a</i>								
n	--	4280	3657	2969	2095	1456	1040	752
Mean (SD)	--	-4.3 (6.2)	-4.9 (6.5)	-5.3 (6.7)	-5.6 (6.5) ^d	-5.9 (6.7)	-6.1 (6.7)	-6.4 (6.5) ^d
<i>SJC</i>								
n	4466	4280	3657	2969	2095	1456	1040	752
Mean (SD)	6.0 (5.4)	2.9 (4.1)	2.2 (3.5)	1.9 (3.4)	1.6 (3.0)	1.4 (2.6)	1.2 (2.4)	1.1 (2.7)
<i>Change from baseline in SJC^a</i>								
n	--	4280	3657	2969	2095	1456	1040	752
Mean (SD)	--	-3.2 (4.9)	-3.8 (5.2)	-4.1 (5.4)	-4.4 (5.6) ^d	-4.8 (5.7)	-5.0 (5.7)	-5.5 (6.1) ^d
<i>Physician global assessment of disease activity^b</i>								
n	4459	4280	3660	2958	2088	1450	1041	747
Mean (SD)	6.0 (1.9)	3.7 (2.1)	3.3 (2.1)	3.0 (2.1)	2.7 (2.0)	2.5 (1.9)	2.3 (1.8)	2.2 (1.7)
<i>Change from baseline in physician global assessment of disease activity^c</i>								
n	--	4274	3655	2954	2085	1448	1039	746
Mean (SD)	--	-2.3 (2.4)	-2.7 (2.5)	-2.9 (2.6)	-3.1 (2.6)	-3.3 (2.6)	-3.3 (2.5)	-3.4 (2.4)

- a. Because baseline DAS28 was an inclusion criterion, all patients with DAS28 (and its components) at the given visit had data for both time points.
- b. On a categorical scale ranging from 0 (inactive) to 10 (highly active).
- c. In patients with values for both time points.
- d. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 7 Tables 5.2.1, 5.2.2, 5.3.1, 5.3.2, to 5.4

10.4.2.2 Inflammatory Markers

Statistically significant reductions in inflammatory laboratory markers were observed during treatment with adalimumab (Table 34). Reduced levels of inflammatory markers

were observed at the earliest visit (3 months) and levels continued to decrease throughout the study in patients remaining on therapy.

Table 34. Changes in Inflammatory Markers in the FAS

Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>ESR (mm/hr)</i>								
n	4466	3893	3321	2705	1891	1299	653	673
Mean (SD)	29.5 (21.9)	22.7 (19.6)	21.5 (18.2)	20.8 (18.1)	20.0 (17.5)	19.6 (17.0)	19.5 (17.6)	18.9 (16.9)
<i>Change from baseline in ESR (mm/hr)^a</i>								
n	--	3893	3321	2705	1891	1299	953	673
Mean (SD)	--	-7.1 (20.5)	-7.9 (20.6)	-8.5 (21.6)	-9.0 (22.2) ^c	-8.9 (22.1)	-9.3 (22.7)	-9.9 (22.5) ^c
<i>CRP (mg/L)</i>								
n	4353	3928	3356	2744	1954	1348	973	690
Mean (SD)	19.3 (50.7)	12.4 (37.0)	11.9 (39.0)	11.9 (48.1)	12.8 (51.4)	11.6 (51.4)	8.4 (30.3)	5.5 (9.4)
<i>Change from baseline in CRP (mg/L)^a</i>								
n	--	3858	3296	2693	1918	1319	950	678
Mean (SD)	--	-7.1 (45.2)	-7.3 (49.1)	-7.5 (59.4)	-8.0 (64.0) ^c	-8.6 (65.9)	-5.8 (47.5)	-7.8 (39.3) ^c

a. Because baseline DAS28 was an inclusion criterion, all patients with DAS28 (and its components) at the given visit had data for both time points.

b. In patients with values for both time points.

c. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 7 Tables 5.9.1.1, 5.9.1.2, 5.9.2.1, 5.9.2.2

10.4.2.3 HAQ-DI

Functional improvements, as assessed by mean HAQ-DI scores, followed a similar pattern to improvements in disease activity assessments (Table 35), indicating that decreases in disease activity were accompanied by patient-reported functional improvements. Changes from baseline in HAQ-DI were statistically significant at Month 24 and Month 60.

Table 35. Changes in HAQ-DI Values in the FAS

Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>HAQ-DI^a</i>								
n	4449	4143	3546	2881	2019	1403	994	728
Mean (SD)	1.30 (0.70)	1.08 (0.73)	1.02 (0.74)	0.98 (0.74)	0.94 (0.74)	0.94 (0.73)	0.90 (0.72)	0.92 (0.71)
<i>Change from baseline in HAQ-DI^b</i>								
n	--	4130	3537	2873	2014	1400	992	727
Mean (SD)	--	-0.22 (0.51)	-0.24 (0.54)	-0.27 (0.58)	-0.28 (0.60) ^c	-0.30 (0.62)	-0.32 (0.61)	-0.28 (0.63) ^c

a. Higher scores indicate greater functional impairment.

b. In patients with values for both time points.

c. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 7 Table 5.10.1, 5.10.2

10.4.2.4 EQ-5D and VAS

The EQ-5D and VAS were used to assess patient-reported health-related quality of life. Improvements in all five EQ-5D domains (mobility, self-care, performance of usual activities, pain/discomfort, and anxiety/depression) were observed during treatment with adalimumab. The EQ VAS "health thermometer," which ranges from 0 (worst) to 100 (best), showed an improvement from a mean of 48.9 at Month 0 to 68.6 at Month 60 in patients remaining on therapy. As with objective clinical outcomes, most of the improvement occurred within the first 6 months after initiation of therapy and was maintained for the duration of treatment. Changes from baseline in the EQ-VAS were statistically significant at the two time points assessed, Month 24 and Month 60.

Table 36. EQ-5D Health State by Dimension in the FAS

Outcome, n (% of patients)	Month after inclusion							
	0	3	6	12	24	36	48	60
n	4400	4118	3524	2856	2020	1401	992	732
<i>Mobility</i>								
No problems	1662 (37.8)	2072 (50.3)	1937 (55.0)	1644 (57.6)	1190 (58.9)	843 (60.2)	614 (61.9)	447 (61.1)
Some problems	2728 (62.0)	2034 (49.4)	1575 (44.7)	1200 (42.0)	824 (40.8)	554 (39.5)	376 (37.9)	282 (38.5)
Confined to bed	8 (0.2)	12 (0.3)	12 (0.3)	12 (0.4)	6 (0.3)	4 (0.3)	2 (0.2)	3 (0.4)
<i>Self-care</i>								
No problems	2599 (59.1)	2792 (67.8)	2476 (70.3)	2088 (73.1)	1484 (73.5)	1038 (74.1)	729 (73.5)	506 (69.1)
Some problems	1680 (38.2)	1226 (29.8)	972 (27.6)	706 (24.7)	503 (24.9)	338 (24.1)	243 (24.5)	208 (28.4)
Unable to wash or dress myself	115 (2.6)	98 (2.4)	75 (2.1)	62 (2.2)	33 (1.6)	25 (1.8)	20 (2.0)	18 (2.5)
<i>Usual activities (e.g., work, study, housework, family or leisure activities)</i>								
No problems	953 (21.7)	1463 (35.5)	1431 (40.6)	1303 (45.6)	958 (47.4)	677 (48.3)	503 (50.7)	353 (48.2)
Some problems	3236 (73.6)	2511 (61.0)	1989 (56.5)	1455 (50.9)	1015 (50.2)	696 (49.7)	464 (46.8)	362 (49.5)
Unable to perform	206 (4.7)	142 (3.4)	103 (2.9)	98 (3.4)	47 (2.3)	28 (2.0)	25 (2.5)	17 (2.3)
<i>Pain/discomfort</i>								
None	147 (3.3)	585 (14.2)	587 (16.7)	582 (20.4)	478 (23.7)	383 (27.3)	298 (30.0)	225 (30.7)
Moderate	2965 (67.4)	2932 (71.2)	2508 (71.2)	1989 (69.6)	1381 (68.4)	917 (65.5)	631 (63.6)	461 (63.0)
Extreme	1288 (29.3)	601 (14.6)	429 (12.2)	285 (10.0)	161 (8.0)	101 (7.2)	63 (6.4)	46 (6.3)

Outcome, n (% of patients)	Month after inclusion							
	0	3	6	12	24	36	48	60
<i>Anxiety/depression</i>								
None	2159 (49.1)	2328 (56.6)	2141 (60.8)	1791 (62.8)	1349 (66.8)	977 (69.8)	705 (71.1)	526 (71.9)
Moderate	1961 (44.6)	1601 (38.9)	1238 (35.1)	956 (33.5)	607 (30.0)	395 (28.2)	265 (26.7)	190 (26.0)
Extreme	275 (6.3)	187 (4.5)	144 (4.1)	107 (3.7)	64 (3.2)	28 (2.0)	22 (2.2)	16 (2.2)

Reference: Appendix 7 [Table 5.11.1](#), [5.11.2](#), [5.11.3](#), [5.11.4](#), [5.11.5](#)

Table 37. Mean EQ VAS in the FAS

	Month after inclusion							
	0	3	6	12	24	36	48	60
<i>EQ VAS^a</i>								
n	4405	4116	3522	2850	2013	1407	994	730
Mean (SD)	48.9 (20.8)	58.9 (21.5)	61.2 (21.7)	63.4 (21.9)	65.6 (21.4)	67.2 (21.5)	68.4 (20.9)	68.6 (21.8)
<i>Change from baseline^b</i>								
n	--	4073	3480	2815	1990	1393	986	725
Mean (SD)	--	10.0 (24.0)	11.7 (24.9)	12.9 (25.8)	14.9 (25.4) ^c	16.2 (25.4)	15.8 (25.2)	14.9 (25.4) ^c

a. Higher scores indicate better health status.

b. In patients with values for both time points.

c. $P < 0.0001$ (Wilcoxon).

Reference: Appendix 7 [Table 5.11.6.1](#), [5.11.6.2](#)

10.4.2.5 Other Patient-Reported Outcomes

Other patient-reported outcomes (duration of morning stiffness, global disease activity, pain, and fatigue) were examined as secondary objectives. These patient-reported outcomes showed sustained improvements during the 60-month observation period in patients remaining on therapy ([Table 38](#)).

Table 38. Mean Values for Additional Patient-Reported Outcomes in the FAS

Outcome	Month After Inclusion							
	0	3	6	12	24	36	48	60
<i>Morning stiffness</i>								
n	4411	4247	3632	2948	2079	1446	1035	746
Percent of patients	83.5	62.9	57.4	52.0	47.6	44.8	41.4	39.7
Duration (min), mean (SD)	65.3 (72.8)	34.6 (55.6)	27.4 (44.3)	24.2 (43.5)	20.9 (39.8)	19.0 (41.0)	15.0 (29.8)	15.2 (32.7)
<i>Patient global assessment of disease activity^a</i>								
n	4407	4178	3582	2902	2042	1417	1013	737
Mean (SD)	6.1 (2.2)	4.5 (2.3)	4.2 (2.4)	4.0 (2.4)	3.7 (2.3)	3.6 (2.4)	3.4 (2.3)	3.4 (2.3)
<i>Pain^a</i>								
n	4455	4178	3582	2901	2045	1415	1004	730
Mean (SD)	6.1 (2.3)	4.4 (2.5)	4.2 (2.5)	3.9 (2.5)	3.7 (2.4)	3.5 (2.4)	3.3 (2.4)	3.3 (2.4)
<i>Fatigue^a</i>								
n	4449	4180	3580	2901	2046	1418	1005	732
Mean (SD)	5.8 (2.7)	4.4 (2.7)	4.2 (2.7)	4.0 (2.7)	3.8 (2.7)	3.5 (2.6)	3.5 (2.6)	3.4 (2.7)

a. On a categorical scale ranging from 0 (best) to 10 (worst).

Reference: Appendix 7 [Tables 5.5, 5.6, 5.7, 5.8.1](#)

10.4.2.6 Medical Care

Physician visits and hospitalizations were evaluated as secondary objectives. Decreases were observed in both parameters during adalimumab treatment. Visits to physicians decreased by approximately half during the 60-month study in patients remaining on therapy. Improvements were observed at Month 6, the earliest post-treatment visit with this assessment, and continued throughout the study. Marked decreases were also observed in the number and days of inpatient hospitalizations.

Table 39. Physician Visits and Inpatient Hospitalization in the FAS

	Month After Inclusion						
	0	6	12	24	36	48	60
Reporting Period	Prior 6 months	Prior 6 months	Prior 6 months	Prior 12 months divided by 2	Prior 12 months divided by 2	Prior 12 months divided by 2	Prior 12 months divided by 2
n	4344	3408	2774	1946	1357	960	703
<i>Number of physician visits, mean (SD)</i>							
Rheumatologist	3.3 (3.1)	2.5 (2.7)	2.2 (2.0)	1.9 (1.5)	1.8 (1.4)	1.9 (1.4)	1.8 (1.6)
General practitioner	4.0 (4.6)	2.9 (4.4)	2.6 (3.2)	2.1 (2.5)	2.1 (3.0)	1.9 (2.4)	1.8 (2.5)
Orthopedic specialist	0.9 (2.2)	0.6 (1.9)	0.7 (1.6)	0.5 (1.3)	0.5 (1.3)	0.5 (1.0)	0.5 (1.9)
Other specialists	1.2 (2.4)	0.9 (1.8)	0.9 (1.8)	0.8 (1.4)	0.8 (1.5)	0.8 (1.5)	0.8 (1.5)
<i>Inpatient hospitalization, mean (SD)</i>							
Number	0.4 (1.5)	0.2 (1.0)	0.2 (1.0)	0.1 (0.5)	0.1 (0.4)	0.1 (0.7)	0.1 (0.4)
Days	2.3 (7.3)	1.1 (4.4)	1.1 (4.8)	0.8 (3.5)	0.7 (3.1)	0.7 (3.5)	0.5 (2.4)

Reference: Appendix 7 [Table 5.12.1](#) to [5.12.6](#)

10.4.2.7 Non-Occupational Activity Impairment

During 60 months of adalimumab therapy, impairment of non-occupational activities was reduced both with respect to the proportion of patients impacted by impairment and the mean number of days affected ([Table 40](#)). The proportions of patients with impairment in child-rearing/parenting or educational activities dropped by about two-thirds between Month 0 and Month 12 and were maintained at this level throughout Month 60 in patients remaining in the study. Impairment of household and recreational activities was also reduced, but to a lesser extent. More than half of patients continued to report impairment in those areas throughout the study.

Table 40. Impairment of Non-Occupational Activities in the FAS

	Month After Inclusion						
	0	6	12	24	36	48	60
Reporting period	Prior 6 months	Prior 6 months	Prior 6 months	Prior 12 months divided by 2	Prior 12 months divided by 2	Prior 12 months divided by 2	Prior 12 months divided by 2
<i>Household</i>							
n ^a	4039	3103	2526	1803	1243	883	645
Patients, n (%) ^a	3335 (82.6)	1890 (60.9)	1411 (55.9)	1004 (55.7)	681 (54.8)	494 (55.9)	357 (55.3)
Days, mean (SD) ^b	56.9 (64.3)	27.7 (50.6)	22.4 (46.1)	20.6 (46.3)	18.2 (43.7)	19.2 (46.1)	16.1 (39.8)
<i>Child-rearing/parenting</i>							
n ^a	1295	1113	916	672	439	306	198
Patients, n (%) ^a	338 (26.1)	155 (13.9)	89 (9.7)	74 (11.0)	38 (8.7)	30 (9.8)	15 (7.6)
Days, mean (SD) ^b	15.1 (41.6)	4.7 (23.1)	3.1 (18.1)	2.8 (18.4)	1.9 (13.6)	3.0 (19.7)	1.6 (8.2)
<i>Educational</i>							
n ^a	1010	899	769	565	381	262	169
Patients, n (%) ^a	167 (16.5)	61 (6.8)	53 (6.9)	27 (4.8)	17 (4.5)	11 (4.2)	7 (4.1)
Days, mean (SD) ^b	8.3 (31.6)	2.5 (17.1)	1.6 (13.3)	1.1 (10.1)	1.0 (10.1)	0.9 (11.5)	1.4 (12.6)
<i>Recreational</i>							
n ^a	3697	2826	2272	1624	1148	814	594
Patients, n (%) ^a	3041 (82.3)	1699 (60.1)	1227 (54.0)	895 (55.1)	615 (53.6)	459 (56.4)	321 (54.0)
Days, mean (SD) ^b	59.1 (65.6)	28.3 (50.9)	23.0 (47.4)	19.5 (45.0)	18.5 (44.9)	19.1 (46.0)	16.3 (41.7)

a. n numbers and percentages based on applicable patients; patients with missing data were not included.

b. Patients with no impairment were considered to have 0 days. Patients who listed impairment but did not state the number of days were not included.

Reference: Appendix 7 Table 5.13.1 to 5.13.4

10.4.2.8 Concomitant Medications

Although one of the secondary objectives of the study was to evaluate changes in concomitant medications during adalimumab therapy, the CRF did not have a structured format for this information; medication changes were entered as free text. Accordingly, it was not possible to extract consistent information concerning changes in concomitant medication. [Table 41](#) shows concomitant medications reported at baseline and at any time point during the study. The proportion of patients taking concomitant RA medications stayed relatively constant throughout the course of the study.

Table 41. Concomitant DMARD and Pain/Anti-Inflammatory Medications in the FAS (N = 4466)

Concomitant Therapy	Baseline (Month 0)	Reported at Any Visit (From Month 0 to Month 60)
DMARD therapy (% of patients)		
MTX	53.4	58.6
Leflunomide	12.0	13.0
Sulfasalazine	3.6	4.1
Pain/anti-inflammatory therapy (% of patients)		
Analgesics	10.9	12.5
NSAIDs or coxibs	22.1	24.2
Systemic glucocorticoids	68.1	73.4
Equivalent dose of prednisolone (mg/day) ^a	7.7	9.2
Other	3.8	9.8

a. Mean (SD).

Reference: [Appendix 7 Table 3.2 to 3.5](#)

10.4.2.9 Patient Assessment of Adalimumab Therapy

At each visit, patients' were asked how therapy with adalimumab compared with previous RA therapies. The majority of patients considered adalimumab to be either better or considerably better than previous therapies ([Table 42](#)). Over the 60-month observation period, the proportion of patients who considered adalimumab to be considerably better

than other therapies increased, while those who considered it to be about the same, worse, or noticeably worse decreased. This shift in proportions probably reflects treatment discontinuations in patients who did not consider adalimumab to be better than other therapies.

Table 42. Patient Assessment of Adalimumab Therapy

	Month after inclusion						
	3	6	12	24	36	48	60
n	4007	3452	2814	1983	1366	971	716
% of patients							
Considerably better	35.6	39.6	46.3	51.6	51.5	55.5	53.6
Better	36.6	39.7	37.3	37.1	40.4	38.1	38.8
About the same	19.2	14.9	12.2	9.1	6.7	5.6	5.6
Worse	6.9	5.0	3.8	1.9	1.3	0.5	1.1
Noticeably worse	1.6	0.9	0.4	0.3	0.1	0.3	0.8

Reference: Appendix 7 [Table 5.14](#)

10.4.2.10 Participation in Abbott Care (AbbVie Care)

At Month 0, approximately 35% of patients participated in the Abbott Care (AbbVie Care) program. This proportion stayed fairly constant throughout the study, although it decreased somewhat after 36 months.

Table 43. Percentages of FAS Patients Participating in Abbott Care (AbbVie Care) at Each Visit

	Month After Inclusion							
	0	3	6	12	24	36	48	60
n	3951	3496	3302	2688	1889	1311	933	687
% of patients	34.9	35.1	37.4	36.5	33.7	32.5	31.2	28.8

Reference: Appendix 7 [Table 5.15](#)

10.4.3 CV Substudy Outcomes

10.4.3.1 Analyzed Population

The AGIL-CV substudy included a subset of patients in the AGIL study. A total of 260 patients enrolled in the study (3.4% of the safety set), which was lower than the target sample size of 300. None of the patients in this substudy had the opportunity to reach the Month 48 and Month 60 visits. Accordingly, those time points are not presented.

Approximately half of the patient cohort was available for analysis at Month 12, and approximately 30% at Month 24 (Table 44).

Table 44. Disposition of Patients in AGIL-CV

Patients, n (% AGIL-CV Patient Set)	Month After Inclusion					
	0	3	6	12	24	36
Total patient set	260	260	260	260	260	260
Ongoing patients at the end of visit	260 (100)	206 (79.2)	166 (63.8)	127 (48.8)	74 (28.5)	36 (13.8)
Cumulative documented withdrawals (discontinuation rates)	-	36 (13.8)	64 (24.6)	89 (34.2)	113 (43.5)	124 (47.7)
Cumulative lost to follow up	-	10 (3.8)	22 (8.5)	40 (15.4)	65 (25.0)	92 (35.4)
Single visit missing (a later visit is following)	-	8 (3.1)	8 (3.1)	4 (1.5)	8 (3.1)	8 (3.1)

Reference: Appendix 8 Table 4.3

For patients with documented withdrawals, the reasons for withdrawal are shown in Table 45. As with the other populations analyzed in this study (employed patients, FAS, and safety set), the most common reason for study withdrawal was lack of effectiveness (25.0% of patients).

Table 45. Reasons for Discontinuation from AGIL-CV (N = 260) by Visit

Patients, n (% of AGIL-CV Patient Set)	Month After Inclusion					Total
	3	6	12	24	36	
Documented withdrawals ^a	36 (13.8)	28 (10.8)	25 (9.6)	24 (9.2)	11 (4.2)	124 (47.7)
Adverse drug reaction	10 (3.8)	3 (1.2)	2 (0.8)	3 (1.2)	0 (0.0)	18 (6.9)
Lack of effectiveness	18 (6.9)	19 (7.3)	16 (6.2)	11 (4.2)	1 (0.4)	65 (25.0)
Other reason	8 (3.1)	5 (1.9)	7 (2.7)	10 (3.8)	9 (3.5)	39 (15.0)
Unknown reason	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.0)	2 (0.8)

a. There are no multiple answers; patients were asked to provide the most important reason for study discontinuation.

Reference: Appendix 8 [Table 4.2](#)

10.4.3.2 Descriptive Data for AGIL-CV

10.4.3.2.1 Baseline Characteristics

Baseline patient and disease characteristics in the AGIL-CV substudy indicated a typical RA population with a higher proportion of women than men, mean age of 53.6, and moderate disease activity (mean DAS28 of 4.85) ([Table 46](#)). The AGIL-CV patient cohort was generally similar to the AGIL FAS cohort (see [Table 17](#) for comparison), although disease duration and disease severity were both lower in AGIL-CV (6.9 versus 9.2 years and mean DAS28 of 4.85 versus 5.13).

Table 46. Key Baseline Characteristics in AGIL-CV

Characteristic	Number Assessed	Mean (SD) or Percent of Patients
Age	258	53.6 (8.6)
% female	260	71.5%
Weight (kg)	248	78.6 (17.2)
Height (cm)	246	168.8 (9.0)
BMI (kg/m ²)	246	27.5 (5.4)
RF positive (%)	246	56.5%
Anti-CCP positive (%)	239	56.9%
Duration of disease (years)	241	6.9 (7.0)
HAQ-DI	247	1.24 (0.74)
DAS28	224	4.85 (1.32)
ESR (mm/h)		
Male	69	30.7 (26.6)
Female	168	26.6 (20.0)
Joint erosions	172	46.5%
Abdominal girth (cm)	237	96.3 (15.5)
Hip circumference (cm)	237	107.2 (12.7)
Smoking status	244	29.9%
Alcohol consumption	253	27.3%
Units per week ^a	65	4.5 (5.2)
Concomitant medication		
MTX	246	62.3%
Leflunomide	246	9.2%
Sulfasalazine	246	3.1%
NSAID or coxib	246	25.4%
Analgesics	246	11.5%
Systemic glucocorticoids	246	73.5%
Prednisolone-equivalent dose (mg/day)	175	7.7 (5.3)

Characteristic	Number Assessed	Mean (SD) or Percent of Patients
Family history		
At least one parent with diabetes mellitus	245	27.3%
At least one parent with obesity	243	21.8%
At least one parent with a heart attack before age of 60	243	15.6%
Prior CV event		
Myocardial infarction	260	2.3%
Stroke	260	3.5%
Vital signs		
Systolic blood pressure (mmHg)	253	132.4 (18.1)
Diastolic blood pressure (mmHg)	253	83.5 (11.0)
Pulse (beats/min)	245	73.7 (10.5)
Blood chemistry values		
CRP (mg/L)	231	14.0 (34.7)
Fasting glucose (mg/dL) (corrected) ^b	137	96.9 (34.8)
Fasting HDL-C (mg/dL) (corrected) ^b	194	63.6 (27.3)
Fasting LDL-C (mg/dL) (corrected) ^b	191	138.8 (44.4)
Fasting Total-C (mg/dL) (corrected) ^b	203	213.4 (63.1)
Fasting triglycerides (mg/dL) (corrected) ^b	183	139.4 (83.1)

a. Includes only patients who reported alcohol consumption. 1 unit was defined as 10 g pure alcohol corresponding to 0.125 L wine or beer or 2.5 cL spirits.

b. Corrected values as described in Section 9.8.5.

Reference: Appendix 8 Tables 1.2, 1.3.1, 1.4.1, 1.5.1, 1.6.1, 1.7, 1.8.1, 1.9, 1.17.1, 1.17.2, 1.17.3, 1.17.4.2, 1.31, 1.33, 3.3, 3.4, 5.1.1, 5.1.2, 5.1.5.1, 5.1.5.2, 5.1.5.3, 5.1.6.1, 5.1.6.2, 5.1.7.1, 5.1.7.2, 5.1.7.3, 5.2.2, 5.2.4, 5.3.1, 5.3.2, 5.3.3, 5.3.4, 5.3.5, 5.3.6

10.4.3.2.2 Baseline Comorbidities

Baseline reports of comorbid conditions were based on patient recall and review of ongoing medications; no diagnostic tests were performed. Patients were asked about eleven pre-specified comorbid conditions (see Section 10.2.3 for a complete description). The majority of patients in AGIL-CV reported a comorbid condition at baseline (Table 47). Arterial hypertension and degenerative joint disease were the most common comorbid conditions. The AGIL-CV cohort generally reported similar proportions of

comorbid conditions as the other patient cohorts (see [Table 19](#) for comparison), but degenerative joint disease, mental illness, and diabetes type 1 were reported at higher rates in AGIL-CV.

Table 47. Pre-Specified Comorbid Conditions in AGIL-CV

Comorbid Condition	AGIL-CV Patient Set
	N = 260
Patients with any comorbid disease (%)	74.6
Patients with specific comorbid diseases (%) ^a	
Arterial hypertension	37.7
Degenerative joint disease	30.4
Degenerative spinal disease	16.2
Mental illness (e.g., depression)	12.3
Osteoporosis	11.2
Hyperlipidemia	10.0
Diabetes type II	9.2
Chronic obstructive pulmonary disease	8.1
Coronary heart disease	4.2
Diabetes type I	3.5
Chronic inflammatory disease	3.1
Other comorbid disease	47.3

a. More than one answer was possible.

Reference: Appendix 8 [Table 2](#)

10.4.3.2.3 Previous RA Therapy

The patterns of previous RA treatment for patients in AGIL-CV ([Table 48](#) and [Table 49](#)) were similar to patterns seen for the other patient populations (see [Table 20](#) and [Table 21](#) for comparison).

Table 48. Previous DMARD and Pain/Anti-Inflammatory Therapy in AGIL-CV

Previous Therapy	AGIL-CV Patients N = 260
DMARD therapy (% of patients) ^a	
MTX	55.4
Leflunomide	52.3
Sulfasalazine	23.8
Pain/anti-inflammatory therapy (% of patients) ^a	
Systemic glucocorticoids	36.2
NSAIDs or coxibs	35.4
Analgesics	23.5
Other	12.7

a. More than one answer was possible.

Reference: Appendix 8 [Table 3.1](#)

Table 49. Previous Biologic Therapy in AGIL-CV

Previous Biologic Therapy	AGIL-CV Patients N = 260
Patients with previous biologics (%) ^a	
Etanercept	12.3
Infliximab	0.8
Tocilizumab	3.1
Certolizumab	6.5
Golimumab	1.5
Rituximab	1.2
Abatecept	1.5
Other	3.1
Duration of previous biologic therapy (months ± SD)	
Etanercept	33.4 (40.1)
Infliximab	13.0 (0.0)
Tocilizumab	25.6 (23.0)
Certolizumab	8.2 (5.5)
Golimumab	14.8 (17.6)
Rituximab	13.0 (6.6)
Abatecept	10.0 (7.4)

a. More than one answer was possible.

Reference: Appendix 8 [Tables 3.6.1, 3.6.2](#)

10.4.3.3 Outcome Data for AGIL-CV

[Table 50](#) shows the number of AGIL-CV patients available for CV and metabolic outcomes at each visit.

Table 50. AGIL-CV Patient Numbers for Major CV and Metabolic Outcomes at Each Visit

Effectiveness Outcome	Month After Inclusion					
	0	3	6	12	24	36
Weight	248	223	181	143	86	42
BMI	246	210	170	134	80	41
Abdominal girth	237	212	174	134	84	41
Hip circumference	237	211	173	134	84	41
Blood pressure	253	218	181	139	84	41
Pulse	245	212	174	132	83	41
CRP	231	189	156	115	69	36
Fasting glucose	137	127	101	79	45	17
Fasting HDL-C	194	139	121	89	56	24
Fasting LDL-C	191	134	116	88	55	25
Fasting Total-C	203	150	128	92	56	26
Fasting triglycerides	183	130	115	88	57	23
CV events	251	234	188	147	89	45

Reference: Appendix 8 Tables 5.2.1, 6.1.1.1, 6.1.2.1, 6.1.3.1, 6.1.4.1, 6.1.5.1.1, 6.1.5.3.1, 6.2.1.1, 6.2.2.1, 6.2.3.1, 6.2.4.1, 6.2.5.1, 6.2.6.1

10.4.3.4 Main Results for AGIL-CV

As shown in Table 50, patient numbers were quite low throughout the study. At Month 24, less than one-third of the baseline population was available for key analyses, particularly lipid profiles. Statistical significance tests were performed on change from baseline to month 24 for primary objectives, but interpretation of the data is difficult due to the limited patient numbers.

10.4.3.4.1 Body Measurements

Change from baseline in body measurements was one of the primary research questions of AGIL-CV; these outcomes were calculated for patients who had data for both time points (baseline and the indicated subsequent visit). During 36 months of adalimumab

treatment, mean and median values for body measurements showed slight fluctuations but remained relatively constant (Table 51). At Month 24, there were no significant changes from baseline in body measurements.

Table 51. Body Measurements in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>Weight (kg)</i>						
n	248	223	181	143	86	42
Mean (SD)	78.6 (17.2)	79.0 (17.2)	78.6 (17.3)	79.2 (18.0)	80.6 (19.1)	82.1 (19.3)
Median	77	77	77	78	78	80.5
Range	43 – 125	44 – 130	46 – 133	44 – 135	48 – 133	56 – 134
<i>Change from baseline in weight (kg)^a</i>						
n	--	212	172	135	80	41
Mean (SD)	--	0.2 (3.3)	0.3 (3.5)	0.9 (4.5)	-0.1 (5.9) ^b	1.0 (5.2)
<i>BMI (kg/m²)</i>						
n	246	210	170	134	80	41
Mean (SD)	27.5 (5.4)	27.5 (5.3)	27.4 (5.4)	27.7 (5.5)	27.9 (5.8)	27.8 (5.8)
Median	26.8	26.8	26.9	27.1	27.0	26.7
Range	17 – 46	18 – 46	19 – 46	19 – 45	17 – 47	19 – 49
<i>Change from baseline in BMI (kgm/m²)^a</i>						
n	--	210	170	134	80	41
Mean (SD)	--	0.1 (1.2)	0.1 (1.2)	0.3 (1.6)	0.0 (2.1) ^b	0.3 (1.8)
<i>Abdominal girth (cm)</i>						
n	237	212	174	134	84	41
Mean (SD)	96.3 (15.5)	96.1 (16.0)	96.1 (15.8)	97.2 (15.8)	98.3 (18.9)	101.9 (14.8)
Median	96	96	96	97.5	99	104
Range	62 – 145	62 – 166	62 – 150	66 – 132	43 – 173	68 – 130
<i>Change from baseline in abdominal girth (cm)^a</i>						
n	--	198	165	126	79	38
Mean (SD)	--	0.6 (7.7)	0.7 (6.0)	1.6 (6.4)	1.2 (11.6) ^b	3.7 (7.8)

Outcome	Month					
	0	3	6	12	24	36
<i>Hip circumference (cm)</i>						
n	237	211	173	134	84	41
Mean (SD)	107.2 (12.7)	106.9 (12.1)	107.8 (13.2)	107.9 (13.0)	108.5 (14.3)	109.1 (16.4)
Median	106	106	105	105.5	106	109
Range	80 – 160	82 – 144	82 – 165	73 – 144	84 – 146	70 – 144
Change from baseline in hip circumference (cm)^a						
n	--	197	164	126	79	38
Mean (SD)	--	0.0 (6.6)	1.2 (9.0)	1.1 (8.0)	0.2 (7.2) ^b	0.3 (8.0)

a. In patients with values for both time points.

b. $P =$ not significant (> 0.05).

Reference: Appendix 8 [Tables 6.1.1.1, 6.1.1.2, 6.1.2.1, 6.1.2.2, 6.1.3.1, 6.1.3.2, 6.1.4.1, 6.1.4.2](#)

10.4.3.4.2 Vital Signs

Vital signs showed slight decreases (improvements) in mean values during treatment with adalimumab ([Table 52](#)), but the small patient numbers and large data ranges make it difficult to interpret the effects of treatment. Median values stayed relatively constant throughout the study. Changes from baseline to Month 24 were not statistically significant.

Table 52. Vital Signs in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>Systolic blood pressure (mmHg)</i>						
n	253	218	181	139	84	41
Mean (SD)	132.4 (18.1)	131.8 (17.4)	131.6 (18.3)	129.8 (15.5)	130.7 (13.7)	130.4 (11.9)
Median	130	130	130	130	130	130
Range	90 – 215	90 – 217	90 – 215	80 – 187	100 – 179	97 – 158
<i>Change from baseline in systolic blood pressure (mmHg)^a</i>						
n	-	211	176	134	81	40
Mean (SD)	-	-0.6 (15.0)	-0.4 (18.0)	-1.7 (16.5)	-1.3 (16.7) ^b	2.4 (15.4)
<i>Diastolic blood pressure (mmHg)</i>						
n	253	217	181	139	84	41
Mean (SD)	83.5 (11.0)	82.0 (10.9)	81.7 (10.5)	80.6 (9.4)	81.3 (9.3)	79.9 (7.6)
Median	81	80	80	80	80	80
Range	57 – 140	60 – 134	51 – 113	60 – 104	60 – 115	67 – 101
<i>Change from baseline in diastolic blood pressure (mmHg)^a</i>						
n	-	210	176	134	81	40
Mean (SD)	-	-1.1 (10.0)	-0.9 (10.0)	-2.5 (10.2)	-1.6 (11.1) ^b	-3.2 (9.0)
<i>Pulse (beats/min)</i>						
n	245	212	174	132	83	41
Mean (SD)	73.7 (10.5)	73.2 (10.7)	74.8 (11.4)	73.0 (9.2)	73.9 (8.8)	73.5 (10.9)
Median	72	72	74.5	72	72	72
Range	49 – 106	50 – 110	47 – 131	48 – 100	60 – 98	55 – 103
<i>Change from baseline in pulse (beats/min)^a</i>						
n	-	202	168	125	79	39
Mean (SD)	-	-0.3 (10.0)	0.5 (10.3)	-0.3 (11.4)	0.7 (9.1) ^b	-1.4 (11.0)

a. In patients with values for both time points.

b. $P =$ not significant (> 0.05).

Reference: Appendix 8 Tables 6.1.5.1.1, 6.1.5.1.2, 6.1.5.2.1, 6.1.5.2.2, 6.1.5.3.1, 6.1.5.3.2

10.4.3.4.3 Blood Chemistry Values

With the exception of the inflammatory marker CRP, blood chemistry values showed random variability during adalimumab treatment. As in the FAS, CRP values significantly decreased from baseline to Month 24. None of the other blood chemistry values showed a significant change from baseline to Month 24.

Table 53. Blood Chemistry Values in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>CRP (mg/L)</i>						
n	231	189	156	115	69	36
Mean (SD)	14.0 (34.7)	10.4 (20.3)	7.6 (16.4)	6.6 (14.4)	5.1 (9.9)	4.6 (3.5)
Median	6	4	3	3	3	3.6
Range	0 – 430	0 – 156	0 – 130	0 – 111	0 – 80	1 – 16
<i>Change from baseline in CRP (mg/L)^a</i>						
n	-	169	141	107	63	33
Mean (SD)	-	-5.9 (38.8)	-8.3 (41.9)	-11.1 (47.9)	-7.5 (16.0) ^b	-10.6 (24.9)
<i>Fasting glucose (mg/dL)(corrected)^c</i>						
n	137	127	101	79	45	17
Mean (SD)	96.9 (34.8)	93.9 (28.2)	101.4 (41.0)	93.6 (19.1)	97.0 (23.9)	99.9 (34.9)
Median	91.9	88.3	90.1	90.0	92.0	96.0
Range	27 – 293	20 – 270	54 – 405	61 – 153	64 – 162	89 – 185
<i>Change from baseline in fasting glucose (mg/dL)^a</i>						
n	-	94	78	61	36	15
Mean (SD)	-	-4.4 (29.3)	1.1 (32.8)	-7.0 (26.8)	-0.3 (30.4) ^d	1.0 (41.0)

Outcome	Month					
	0	3	6	12	24	36
<i>Fasting HDL-C (mg/dL)(corrected)^c</i>						
n	194	139	121	89	56	24
Mean (SD)	63.6 (27.3)	65.1 (22.8)	69.3 (35.4)	72.2 (61.9)	64.5 (19.5)	71.5 (25.3)
Median	60	63	67	66	62	75
Range	23 – 262	25 – 175	25 – 361	18 – 519	32 – 133	36 – 127
<i>Change from baseline in fasting HDL-C (mg/dL)^a</i>						
n	-	109	99	72	48	19
Mean (SD)	-	2.4 (27.1)	1.9 (27.4)	5.0 (60.8)	-1.9 (33.9) ^d	-7.5 (46.6)
<i>Fasting LDL-C (mg/dL)(corrected)^c</i>						
n	191	134	116	88	55	25
Mean (SD)	138.8 (44.4)	135.9 (40.6)	137.7 (45.5)	135.1 (38.1)	138.0 (41.8)	146.2 (58.9)
Median	133	132.2	129.6	134.5	143	136
Range	41 – 271	31 – 277	27 – 302	40 – 276	32 – 273	78 – 374
<i>Change from baseline in fasting LDL-C (mg/dL)^a</i>						
n	-	103	93	69	46	18
Mean (SD)	-	-3.5 (39.2)	-1.4 (36.4)	0.7 (34.1)	5.1 (40.4) ^d	0.9 (24.5)
<i>Fasting Total-C (mg/dL)(corrected)^c</i>						
n	203	150	128	92	56	26
Mean (SD)	223.0 (60.4)	223.3 (52.7)	220.0 (50.6)	218.2 (42.2)	218.3 (49.1)	229.8 (61.7)
Median	215	216.3	215.6	219	219	222.5
Range	60 – 701	85 – 537	50 – 387	76 – 344	78 – 362	146 – 446
<i>Change from baseline in Total-C (mg/dL)^a</i>						
n	-	122	109	78	50	22
Mean (SD)	-	4.5 (35.6)	-0.2 (64.1)	7.3 (37.1)	13.0 (47.7) ^d	19.2 (68.0)
<i>Fasting triglycerides (mg/dL) (corrected)^c</i>						
n	183	130	115	88	57	23
Mean (SD)	139.4 (83.1)	137.8 (84.3)	132.2 (81.9)	141.1 (93.8)	126.4 (63.2)	144.0 (71.1)
Median	115	119.5	111	123.5	111	141
Range	18 – 463	14 – 519	27 – 515	16 – 751	23 – 333	44 – 319

Outcome	Month					
	0	3	6	12	24	36
<i>Change from baseline in fasting triglycerides (mg/dL)^a</i>						
n	-	97	90	68	45	17
Mean (SD)	-	-5.3 (67.4)	3.3 (60.1)	16.3 (82.3)	-2.6 (81.3) ^d	-2.9 (101.8)

a. In patients with values for both time points.

b. $P < 0.0001$.

c. Corrected values as described in Section 9.8.5.

d. $P =$ not significant (> 0.05).

Reference: Appendix 8 Tables 6.2.1.1, 6.2.1.2, 6.2.2.1, 6.2.2.2, 6.2.3.1, 6.2.3.2, 6.2.4.1, 6.2.4.2, 6.2.5.1, 6.2.5.2, 6.2.6.1, 6.2.6.2

10.4.3.4.4 Vital Signs in Responders Versus Non-Responders

A primary research question of AGIL-CV was to compare changes in vital signs between DAS28 responders and DAS28 non-responders. Responder analyses were based on the response category at Month 12. Analysis of data on the basis of EULAR response, as described in Table 4, was limited by the small patient numbers in each category. The available data did not show any clear patterns of change in vital signs based on therapeutic response (Table 54).

Table 54. Vital Signs by EULAR Response at Month 12 in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>Systolic blood pressure (mmHg)</i>						
Good response						
n	48	45	45	46	35	19
Mean (SD)	131.2 (13.1)	129.7 (12.1)	128.2 (15.2)	125.7 (12.7)	129.3 (13.3)	130.4 (13.8)
Moderate response						
n	26	23	21	24	17	10
Mean (SD)	138.8 (15.7)	135.3 (17.1)	129.0 (11.7)	133.1 (16.2)	136.1 (11.8)	137.2 (10.4)
No response						
n	32	29	29	29	9	2
Mean (SD)	131.7 (15.3)	129.9 (13.0)	130.1 (15.1)	132.7 (12.2)	127.0 (14.9)	125.5 (3.5)
<i>Diastolic blood pressure (mmHg)</i>						
Good response						
n	48	45	45	46	35	19
Mean (SD)	83.1 (8.6)	81.3 (8.0)	81.6 (7.7)	80.0 (8.5)	82.0 (8.5)	80.9 (9.7)
Moderate response						
n	26	23	21	24	17	10
Mean (SD)	85.3 (6.0)	85.7 (15.4)	84.0 (11.3)	82.5 (9.4)	83.3 (12.3)	80.1 (4.8)
No response						
n	32	29	29	29	9	2
Mean (SD)	83.6 (11.5)	80.8 (10.7)	80.0 (10.0)	81.3 (9.9)	78.9 (9.4)	75.0 (2.8)

Outcome	Month					
	0	3	6	12	24	36
<i>Pulse (beats/min)</i>						
Good response						
n	48	44	44	45	35	19
Mean (SD)	74.2 (9.9)	70.9 (9.2)	74.9 (10.8)	74.1 (10.6)	74.5 (9.0)	74.4 (13.2)
Moderate response						
n	26	23	21	24	17	10
Mean (SD)	75.4 (10.1)	75.0 (11.0)	72.2 (9.0)	73.2 (8.7)	72.8 (9.8)	71.3 (10.0)
No response						
n	29	26	25	26	9	2
Mean (SD)	72.9 (13.2)	73.3 (10.6)	72.5 (11.8)	71.4 (9.8)	73.0 (9.3)	78.0 (1.4)

Reference: Appendix 8 [Tables 6.1.5.1.3, 6.1.5.2.3, 6.1.5.3.3](#)

We also conducted a responder analysis using the DAS28_{crit} response criterion at Month 12 (DAS28 decrease of ≥ 1.8 from baseline).³⁸ As with the EULAR response analysis, there was no clear pattern of differences in vital signs between DAS28_{crit} responders and non-responders ([Table 55](#)).

Table 55. Vital Signs by DAS28_{dcrit} Response at Month 12 in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>Systolic blood pressure (mmHg)</i>						
Responders						
n	52	48	47	49	41	22
Mean (SD)	134.0 (14.4)	130.4 (13.3)	128.1 (15.1)	128.6 (14.8)	131.1 (13.3)	132.2 (13.9)
Non-responders						
n	54	49	48	50	20	9
Mean (SD)	132.4 (15.0)	131.8 (14.3)	129.8 (13.7)	130.5 (12.8)	130.3 (13.7)	132.4 (9.6)
<i>Diastolic blood pressure (mmHg)</i>						
Responders						
n	52	48	47	49	41	22
Mean (SD)	84.0 (8.2)	81.9 (9.0)	82.0 (8.3)	81.5 (9.0)	81.6 (7.7)	81.2 (8.9)
Non-responders						
n	54	49	48	50	20	9
Mean (SD)	83.6 (9.8)	82.5 (12.7)	81.3 (10.3)	80.4 (9.2)	82.6 (13.2)	78.0 (5.8)
<i>Pulse (beats/min)</i>						
Responders						
n	52	47	46	48	41	22
Mean (SD)	75.2 (10.0)	72.3 (9.3)	74.5 (10.6)	74.3 (10.2)	74.5 (9.4)	74.7 (12.8)
Non-responders						
n	51	46	44	47	20	9
Mean (SD)	73.0 (11.7)	72.9 (11.0)	72.6 (10.9)	71.9 (9.5)	72.3 (8.7)	70.9 (8.8)

Reference: Appendix 8 [Tables 6.1.5.1.4, 6.1.5.2.4, 6.1.5.3.4](#)

10.4.3.4.5 Blood Chemistry Parameters in Responders Versus Non-Responders

Responder analyses were also performed for lab chemistry blood parameters for glucose and lipid metabolism ([Table 56](#) and [Table 57](#)). As for vital signs, the low numbers of patients in each group limit interpretation of the data. CRP levels tended to be lower in

patients with a good EULAR response compared with those with a moderate response or no response, but fasting glucose and lipid levels did not appear to be associated with therapeutic response. There were no clear patterns for DAS28dcrtr responders versus non-responders.

Table 56. Blood Chemistry Values by EULAR Response at Month 12 in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>CRP (mg/L)</i>						
Good response						
n	47	41	40	41	29	17
Mean (SD)	11.2 (17.1)	5.3 (10.1)	3.9 (4.3)	3.6 (8.3)	3.0 (2.1)	3.9 (3.4)
Moderate response						
n	24	18	19	20	15	7
Mean (SD)	27.8 (35.3)	12.6 (29.2)	12.9 (26.6)	7.3 (10.0)	10.7 (19.9)	6.2 (4.3)
No response						
n	29	30	25	26	8	4
Mean (SD)	13.9 (34.2)	13.9 (32.5)	10.9 (25.9)	12.1 (26.0)	3.7 (3.2)	5.4 (2.1)
<i>Fasting glucose (mg/dL) (corrected)^a</i>						
Good response						
n	33	29	27	28	18	9
Mean (SD)	91.5 (19.6)	93.4 (25.3)	91.3 (19.0)	91.1 (19.6)	90.1 (20.7)	99.6 (35.0)
Moderate response						
n	12	12	8	12	8	3
Mean (SD)	110.2 (48.6)	99.8 (34.6)	110.4 (44.3)	94.7 (23.0)	97.4 (16.8)	77.2 (23.6)
No response						
n	17	20	17	19	8	1
Mean (SD)	99.7 (24.2)	91.3 (13.0)	92.3 (21.6)	97.5 (17.6)	98.5 (31.2)	102.0

Outcome	Month					
	0	3	6	12	24	36
<i>HDL-C (mg/dL) (corrected)^a</i>						
Good response						
n	36	32	33	32	25	10
Mean (SD)	63.0 (39.1)	64.4 (26.7)	67.4 (27.8)	62.8 (19.1)	63.3 (16.7)	75.5 (27.6)
Moderate response						
n	20	14	12	16	10	5
Mean (SD)	64.7 (18.6)	71.4 (22.3)	77.5 (25.7)	63.2 (18.4)	70.2 (25.9)	67.2 (17.2)
No response						
n	24	21	21	19	9	3
Mean (SD)	60.4 (19.0)	65.2 (22.8)	59.0 (19.3)	59.2 (17.3)	64.9 (14.6)	96.3 (20.6)
<i>LDL-C (mg/dL) (corrected)^a</i>						
Good response						
n	36	29	31	32	25	10
Mean (SD)	133.1 (47.6)	128.3 (30.6)	143.0 (38.5)	134.0 (35.9)	133.6 (32.5)	137.8 (46.5)
Moderate response						
n	19	14	11	16	10	6
Mean (SD)	132.4 (34.8)	149.1 (43.7)	134.5 (38.2)	151.2 (47.1)	165.4 (57.6)	175.7 (100.6)
No response						
n	23	20	21	18	9	3
Mean (SD)	137.7 (49.0)	135.0 (42.6)	122.9 (37.8)	126.2 (35.2)	124.8 (35.9)	143.0 (31.1)

Outcome	Month					
	0	3	6	12	24	36
<i>Total C (mg/dL) (corrected)^a</i>						
Good response						
n	38	34	35	33	25	11
Mean (SD)	207.8 (53.8)	210.8 (33.9)	217.1 (50.2)	209.9 (40.5)	210.6 (31.0)	227.9 (80.2)
Moderate response						
n	21	14	12	17	10	6
Mean (SD)	221.7 (32.8)	242.4 (51.1)	226.4 (49.7)	242.7 (48.1)	239.0 (80.2)	239.7 (56.5)
No response						
n	23	23	22	17	9	3
Mean (SD)	216.0 (60.4)	209.3 (44.0)	205.4 (47.2)	203.4 (44.8)	216.0 (50.7)	256.7 (27.5)
<i>Triglycerides (mg/dL) (corrected)^a</i>						
Good response						
n	36	29	30	31	25	10
Mean (SD)	135.4 (89.2)	123.8 (66.7)	130.2 (75.8)	142.4 (81.7)	114.1 (58.4)	127.7 (68.4)
Moderate response						
n	18	13	10	17	10	5
Mean (SD)	152.5 (99.3)	159.0 (117.1)	112.4 (39.9)	189.5 (156.4)	159.6 (54.9)	154.6 (31.7)
No response						
n	21	20	21	19	9	3
Mean SD	124.3 (75.5)	138.2 (59.8)	132.9 (60.6)	115.9 (51.6)	133.7 (77.8)	142.0 (118.8)

a. Corrected values as described in Section 9.8.5.

Reference: Appendix 8 Tables 6.2.1.3, 6.2.2.3, 6.2.3.3, 6.2.4.3, 6.2.5.3, 6.2.6.3

Table 57. Blood Chemistry Values by DAS28_{crit} Response at Month 12 in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
<i>CRP (mg/L)</i>						
Responders						
n	50	42	42	43	32	19
Mean (SD)	15.8 (26.8)	5.5 (9.9)	4.2 (4.5)	4.7 (8.7)	6.5 (14.0)	4.9 (4.1)
Non-responders						
n	50	47	42	44	20	9
Mean (SD)	16.2 (30.0)	13.4 (31.4)	11.8 (26.6)	9.2 (21.0)	3.4 (2.5)	4.2 (2.4)
<i>Fasting glucose (mg/dL) (corrected)^a</i>						
Responders						
n	33	30	27	32	20	11
Mean (SD)	93.8 (26.1)	93.9 (24.9)	91.6 (20.9)	91.5 (19.5)	91.1 (20.6)	96.3 (33.6)
Non-responders						
n	29	31	25	27	14	2
Mean (SD)	101.4 (31.7)	94.0 (23.7)	97.8 (29.7)	96.8 (19.6)	97.6 (25.2)	85.0 (24.0)
<i>HDL-C (mg/dL) (corrected)^a</i>						
Responders						
n	40	33	36	35	27	12
Mean (SD)	66.0 (37.7)	69.2 (28.3)	72.7 (28.7)	65.0 (19.5)	65.8 (16.3)	75.9 (25.6)
Non-responders						
n	40	34	30	32	17	6
Mean (SD)	59.3 (17.8)	63.1 (20.1)	59.1 (18.8)	58.5 (16.4)	64.4 (22.1)	78.2 (25.6)

Outcome	Month					
	0	3	6	12	24	36
<i>LDL-C (mg/dL) (corrected)^a</i>						
Responders						
n	39	30	32	35	27	13
Mean (SD)	132.9 (44.2)	132.2 (32.1)	143.0 (39.4)	136.0 (36.1)	138.9 (36.3)	155.2 (78.8)
Non-responders						
n	39	33	31	31	17	6
Mean (SD)	135.4 (45.8)	137.6 (43.0)	126.3 (36.6)	136.1 (43.0)	139.2 (50.5)	140.5 (21.2)
<i>Total C (mg/dL) (corrected)^a</i>						
Responders						
n	42	35	37	36	27	14
Mean (SD)	214.5 (46.0)	221.1 (38.3)	223.4 (51.8)	219.8 (43.2)	214.8 (47.8)	237.5 (74.8)
Non-responders						
n	40	36	32	31	17	6
Mean (SD)	212.8 (56.6)	212.1 (46.2)	205.3 (44.4)	212.8 (48.8)	223.4 (54.3)	231.7 (46.9)
<i>Triglycerides (mg/dL) (corrected)^a</i>						
Responders						
n	39	29	30	34	27	12
Mean (SD)	145.1 (94.6)	142.3 (96.5)	133.0 (73.0)	168.8 (126.6)	125.6 (55.0)	141.1 (58.9)
Non-responders						
n	36	33	31	33	17	6
Mean (SD)	127.0 (79.5)	130.1 (57.4)	123.6 (58.3)	124.2 (63.1)	133.0 (76.4)	130.5 (87.4)

a. Corrected values as described in Section 9.8.5.

Reference: Appendix 8 Tables 6.2.1.4, 6.2.2.4, 6.2.3.4, 6.2.4.4, 6.2.5.4, 6.2.6.4

10.4.3.4.6 CV Events

Patients in AGIL-CV were asked whether they had experienced a myocardial infarction or stroke since the past visit. At Month 0, 6 patients (2.4%) reported a previous myocardial infarction and 9 (3.6%) reported a previous stroke. During the 36-month documentation, no new cases of myocardial infarction and 3 cases of stroke were reported in this patient cohort. There was no obvious association between duration of treatment and incidence of these rare CV events.

Table 58. CV Events in AGIL-CV

Outcome	Month					
	0	3	6	12	24	36
n	251	234	188	147	89	45
Myocardial infarction, n (%)	6 (2.4)	0	0	0	0	0
Stroke, n (%)	9 (3.6)	0	1 (0.5)	0	1 (1.1)	1 (2.2)

Reference: Appendix 8 [Tables 5.2.1, 5.2.3](#)

10.5 Other Analyses

In exploratory analyses, multiple fixed regression models were used to evaluate predictors of change in employment-related outcomes (sick leave days, modified WPAI outcomes, modified WAI scores) from baseline to Month 24 in order to examine the effect of long-term adalimumab treatment on work ability. For disease activity (DAS28) and patient-reported function (HAQ-DI), multiple regression models examined factors that influenced changes from baseline to Month 6, the visit that is considered by expert rheumatologists to be the most important for determining whether therapy should be continued, switched, or modified with concomitant therapy.

10.5.1 Parameters Influencing Change in Sick Leave Days from Month 0 to Month 24

Regression models were used to evaluate predictors of change in sick leave days from Month 0 to Month 24 of adalimumab therapy. The model encompassed 41 variables,

including baseline demographic and disease characteristics, concomitant treatment and comorbidities, and educational level (see Appendix 6 [Table 7.1](#)). The only variable with a significant influence on change in sick leave days over the first 24 months of treatment was the number of sick leave days at baseline: patients with a greater number of sick leave days in the prior 6 months at baseline experienced more improvement in sick leave days than patients with fewer baseline sick leave days ([Table 59](#)). This single variable described most of the variance observed (cumulated $r^2 = 0.6002$). None of the other variables evaluated had a significant effect on change in sick leave days.

Table 59. Predictors of Change in Sick Leave Days at Month 24

Variable	Model Values (N = 1290)	
	Beta-Weight ^a	P value
Intercept	5.03803	< 0.0001
Positive predictor for decrease in sick leave days		
Sick leave days in the past 6 months at baseline	-0.81548	< 0.0001

a. The beta-weight shows the influence for each unit of the predictor's scale.

Reference: Appendix 6 [Table 7.1](#)

10.5.2 Parameters Influencing Change in Modified WPAI from Month 0 to Month 24

Similar to the regression model for sick leave days, the regression model for modified WPAI absenteeism identified baseline absenteeism as the most important predictor of change in absenteeism from Month 0 to Month 24 ([Table 60](#)). Higher baseline HAQ-DI scores (greater functional impairment) were a negative predictor of decreased absenteeism.

Table 60. Predictors of Change in Modified WPAI Absenteeism at Month 24

Variable	Model Values (N = 660)	
	Beta-Weight ^a	P value
Intercept	3.00060	0.0422
Positive predictor for improvement in absenteeism		
Baseline absenteeism (%)	-090618	< 0.0001
Negative predictor for improvement in absenteeism		
Baseline HAQ-DI ^b	5.04378	0.0005

a. The beta-weight shows the influence for each unit of the predictor's scale.

b. Higher values indicate worse function.

Reference: Appendix 6 [Table 7.2](#)

Unlike sick leave days and absenteeism, there were a number of baseline variables that predicted changes in presenteeism from Month 0 to Month 24. The most important was baseline presenteeism, but modified WAI scores, higher educational level and morning stiffness also predicted improvements in presenteeism. Negative predictors of improvements in presenteeism included greater functional impairment and fatigue at baseline.

Table 61. Predictors of Change in Modified WPAI Presenteeism at Month 24

Variable	Model Values (N = 1046)	
	Beta-Weight ^a	P value
Intercept	44.28477	< 0.0001
Positive predictors for improvement in presenteeism		
Baseline presenteeism (%)	-0.95390	< 0.0001
Modified WAI ^b	-0.69550	< 0.0001
Diploma qualifying for matriculation	-6.90256	< 0.0001
Morning stiffness (min)	-0.03493	< 0.0001
Negative predictors for improvement in presenteeism		
Baseline HAQ-DI ^c	6.19186	< 0.0001
Fatigue ^c	1.34736	0.0010

a. The beta-weight shows the influence for each unit of the predictor's scale.

b. Higher scores correspond to better outcomes.

c. Higher values indicate worse outcomes.

Reference: Appendix 6 [Table 7.3](#)

10.5.3 Parameters Influencing Change in Modified WAI from Month 0 to Month 24

Regression models for change in modified WAI from Month 0 to Month 24 identified the baseline score as the most important variable: higher baseline scores, which correspond to better employment outcomes, were a negative predictor of improvement. Age was also a negative predictor of improvement, whereas positive RF serostatus was a positive predictor.

Table 62. Predictors of Change in Modified WAI at Month 24

Variable	Model Values (N = 906)	
	Beta-Weight ^a	P value
Intercept	27.72471	< 0.0001
Positive predictor for improvement in WAI		
RF positive serostatus	1.67854	< 0.001
Negative predictors for improvement in WAI		
Modified WAI	-0.50224	< 0.0001
Age	-0.18091	< 0.0001

a. The beta-weight shows the influence for each unit of the predictor's scale.

Reference: Appendix 6 [Table 7.4](#)

10.5.4 Parameters Influencing Change in DAS28 from Month 0 to Month 6

Regression models included 35 variables reflecting baseline demographic characteristics, disease characteristics, medications, and comorbidities (see Appendix 7 [Table 7](#) for complete list). The final fixed model was based on 3196 patients with appropriate data and had a final cumulated r^2 of 0.2874. Significant predictors ($P < 0.01$) for change in DAS28 at month are shown in [Table 63](#). In agreement with Kleinert et al,⁴⁵ the strongest positive predictor for DAS28 improvement was baseline DAS28; patients with higher baseline disease activity had a greater DAS28 reduction at Month 6 than those with lower baseline scores. MTX treatment at baseline was also a positive predictor of reduced disease activity at Month 6. Negative predictors of decreased DAS28 at Month 6 were higher baseline HAQ-DI scores (more severe functional impairment), a greater number of prior biologic therapies, higher BMI, older age, and use of analgesics at baseline. These negative predictors are associated with a reduced therapeutic effect at Month 6.

Table 63. Predictors of Decrease (Improvement) in DAS28 at Month 6

Variable	Model Values (N = 3196)	
	Beta-Weight ^a	P value
Intercept	0.68622	< 0.0001
Positive predictors for decrease in disease activity		
Baseline DAS28 ^b	-0.68831	< 0.0001
MTX	-0.28603	< 0.0001
Negative predictors for decrease in disease activity		
Baseline HAQ-DI ^c	0.27091	< 0.0001
Number of previous biologics	0.19937	< 0.0001
BMI	0.02076	< 0.0001
Age	0.00797	< 0.0001
Analgesics	0.24520	0.0007

a. The beta-weight shows the influence for each unit of the predictor's scale.

b. Higher values indicate higher disease activity.

c. Higher values indicate worse function.

Reference: Appendix 7 [Table 6](#)

10.5.5 Parameters Influencing Change in HAQ-DI from Month 0 to Month 6

We also used regression models to evaluate predictors of change in function during the first 6 months of adalimumab therapy. The quality of the regression was suboptimal and variability was not well explained by the predictors (cumulated r^2 of 0.1782). However, the model did identify several of the same predictors as for DAS28 (MTX as a positive predictor of improvement and age, BMI, and number of previous biologics as negative predictors), suggesting that the model may be of some relevance ([Table 64](#)).

Table 64. Predictors of Decrease (Improvement) in HAQ-DI at Month 6

Variable	Model Values (N = 3395)	
	Beta-Weight ^a	P value
Intercept	-0.51382	< 0.0001
Positive predictors for improvement in function		
Baseline HAQ-DI ^b	-0.30656	< 0.0001
Morning stiffness (minutes)	-0.00061523	< 0.0001
Male gender	-0.07893	< 0.0001
MTX	-0.05563	< 0.0001
Negative predictors for improvement in function		
Age	0.00558	< 0.0001
BMI	0.01312	< 0.0001
Duration of disease (years)	0.00452	< 0.0001
Number of previous biologics	0.06971	< 0.0001
Chronic obstructive pulmonary disease	0.14404	0.0003
Prior joint surgery	0.07634	0.0011

a. The beta-weight shows the influence for each unit of the predictor's scale.

b. Higher values indicate worse function.

Reference: Appendix7 [Table 7](#)

10.6 Adverse Events and Adverse Reactions

10.6.1 Adalimumab Exposure

During this non-interventional study, clinicians were asked to report AEs considered to be related to the study medication for all patients who received at least one dose of adalimumab (safety set; N = 7229). AEs were collected throughout the 60-month period. Data on duration of exposure to adalimumab were based on observation time and derived from the dates for study initiation and study withdrawal. If the patient did not have a date for study withdrawal, the date of the last visit was used. This method of calculation allowed most patients to be included (7131/7229; 98.6%), but may have overestimated the duration of adalimumab exposure. The mean exposure to adalimumab was calculated as

approximately 2 years (Table 65). However, as indicated by the large standard deviation, the duration of exposure varied widely among patients.

Table 65. Duration of Adalimumab Exposure in the Safety Set

n	Mean Years (SD)
7131	2.06 (1.77)

Reference: Appendix 9 Table 1.11.2

10.6.2 Adverse Event Rates

Data on safety were based on patient and clinician reports. Most patients in this study had comorbid conditions and were receiving concomitant medications. Accordingly, it is not possible to make a causality assessment at the individual case level for reported AEs. Doctors associated with the adalimumab non-interventional study were asked to provide details and outcomes for SAEs, including deaths n most cases additional information was not supplied, possibly because these events were treated by other specialists and therefore the rheumatologist did not have access to this information.

Despite these issues, AEs reported in this study were consistent with the known safety profile of adalimumab.^{23,46} During the 60 months of observation, 32.1% of patients in the safety set reported an AE. As specified by the reporting requirements of clinicaltrials.gov, Table 66 shows AEs not including SAEs (see Appendix 9, Table 5.3 for all documented AEs, including SAEs). The most common AE by SOC was infections and infestations (14.8%), and the most common AE by PT was influenza-like illness (2.9%).

Table 66. Adverse Events^a Occurring in > 1% of the Safety Set

System Organ Class	Preferred Term	Safety Set N = 7229 n (%)
Any AE		2324 (32.1)
Infections and infestations	Any	1071 (14.8)
	Bronchitis	177 (2.4)
	Nasopharyngitis	137 (1.9)
	Upper respiratory tract infection	130 (1.8)
	Respiratory tract infection	106 (1.5)
	Infection	88 (1.2)
	Herpes zoster	79 (1.1)
General disorders and administration site conditions	Any	523 (7.2)
	Influenza like illness	213 (2.9)
Skin and subcutaneous tissue disorders	Any	391 (5.4)
Surgical and medical procedures	Any	362 (5.0)
	Therapy cessation	78 (1.1)
Musculoskeletal and connective tissue disorders	Any	324 (4.5)
Gastrointestinal disorders	Any	247 (3.4)
Nervous system disorders	Any	207 (2.9)
Respiratory, thoracic and mediastinal disorders	Any	204 (2.8)
Investigations	Any	200 (2.8)
Injury, poisoning and procedural complications	Any	121 (1.7)
Vascular disorders	Any	93 (1.3)

a. Excluding SAEs.

Reference: Appendix 9 [Table 5.7 – 5.9](#)

10.6.3 Serious Adverse Events and Death

An AE was considered to be serious if any of the following criteria were met:

- Death of patient
- Life-threatening event
- Hospitalization
- Prolongation of hospitalization
- Congenital anomaly
- Persistent or significant disability or incapacity
- Important medical event requiring medical or surgical intervention to prevent serious outcome
- Spontaneous or elective abortion

SAEs were reported in 932/7729 (12.9%) patients. The most common SAEs by SOC were surgical and medical procedures (Table 67), primarily involving hospitalizations and joint surgeries, followed by infections and infestations. The only SAE PT reported by > 1% of patients was hospitalization (n = 110; 1.5%). A complete listing of SAEs by SOC and PT can be found in Appendix 9 Table 5.6.

Table 67. Serious Adverse Events Occurring in Any Patient by SOC

System Organ Class	Safety Set N = 7229 n (%)
Any SAE	932 (12.9)
SAE by SOC	
Surgical and medical procedures	405 (5.6)
Infections and infestations	267 (3.7)
Musculoskeletal and connective tissue disorders	163 (2.3)
General disorders and administration site conditions	110 (1.5)
Injury, poisoning, and procedural complications	96 (1.3)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	90 (1.2)
Cardiac disorders	80 (1.1)

System Organ Class	Safety Set N = 7229 n (%)
SAE by SOC (continued)	
Nervous system disorders	70 (1.0)
Gastrointestinal disorders	60 (0.8)
Respiratory, thoracic, and mediastinal disorders	59 (0.8)
Investigations	57 (0.8)
Skin and subcutaneous tissue disorders	49 (0.7)
Vascular disorders	45 (0.6)
Renal and urinary disorders	29 (0.4)
Hepatobiliary disorders	23 (0.3)
Blood and lymphatic system disorders	21 (0.3)
Psychiatric disorders	17 (0.2)
Metabolism and nutrition disorders	12 (0.2)
Reproductive system and breast disorders	11 (0.2)
Ear and labyrinth disorders	8 (0.1)
Endocrine disorders	8 (0.1)
Eye disorders	7 (0.1)
Immune system disorders	4 (0.1)
Product issues	4 (0.1)
Pregnancy, puerperium, and perinatal conditions	3 (< 0.1)
Social circumstances	3 (< 0.1)
Congenital, familial, and genetic disorders	2 (< 0.1)

Reference: Appendix 9 [Table 5.4](#)

Deaths, as reported on the AE reporting form, occurred in 23 patients during the study. The age of these patients ranged from 57 to 87. The causes of death were malignancies (n = 4; pancreatic carcinoma, recurrence of plasmacytoma, brain tumor, and metastases to liver and lung), cerebrovascular accident (n = 3), myocardial infarction (n = 3; 1 was accompanied by thoracic vertebral fracture), septic shock (n = 3; two were associated with multiple organ failure, one of which was accompanied by pneumonia subsequent to a lung transplant, and one involved peritonitis and perforation of the sigmoid colon); decubitus

ulcer (n = 1), accidental death (n = 1), pneumonia/heart failure (n = 1), and jaundice due to decompensated alcoholic cirrhosis (n = 1). The cause of death was listed as a "natural death" for one patient and not listed for the 5 remaining patients. One case of septic shock (due to peritonitis) and the case of jaundice/cirrhosis were considered to have a "possible" causality to treatment. For the patient with jaundice/cirrhosis, the clinician noted that the "possible" causality referred to the potential association of decompensation with cytomegalovirus infection, but that causality for cirrhosis was "unlikely." For all other deaths, causality was listed as "unlikely" (n = 11) or "not related" (n = 9). For one patient, the causality was not listed.

10.6.4 Adverse Events in Patients with Pre-Specified Comorbidities

Analysis of AEs by baseline comorbidities did not identify any unexpected safety signals. Rates of AEs tended to be somewhat higher in patients with pre-specified baseline comorbidities, particularly in those with chronic inflammatory disease or hyperlipidemia (Table 68). However, many of these AEs could be explained by the underlying comorbidity, such as a higher frequency of the SOC "investigations" in patients with hyperlipidemia, a higher frequency of the SOC "gastrointestinal disorders" in patients with chronic inflammatory disease, and a higher frequency of the SOC "cardiac disorders" in patients with coronary heart disease. These data should be interpreted with caution for comorbidities affecting a small numbers of patients, such as diabetes type I.

Table 68. Adverse Events by SOC in > 5% of Patients by Pre-Specified Baseline Comorbidities

Comorbidity	AE by SOC	With Comorbidity n (%)	Without Comorbidity n (%)
Arterial hypertension	n	2447 (100)	4782 (100)
	Any AE	1102 (45.0)	1662 (34.8)
	Infections and infestations	506 (20.7)	746 (15.6)
	Surgical and medical procedures	312 (12.8)	386 (8.1)
	General disorders and administration site conditions	244 (10.0)	376 (7.9)
	Musculoskeletal and connective tissue disorders	197 (8.1)	262 (5.5)
	Skin and subcutaneous disorders	154 (6.3)	272 (5.7)
Coronary heart disease	n	395 (100)	6834 (100)
	Any AE	184 (46.6)	2580 (37.8)
	Infections and infestations	83 (21.0)	1169 (17.1)
	Surgical and medical procedures	53 (13.4)	645 (9.4)
	General disorders and administration site conditions	44 (11.1)	576 (8.4)
	Musculoskeletal and connective tissue disorders	30 (7.6)	429 (6.3)
	Gastrointestinal disorders	30 (7.6)	429 (6.3)
	Skin and subcutaneous disorders	27 (6.8)	399 (5.8)
	Cardiac disorders	27 (6.8)	112 (1.6)
	Respiratory, thoracic, and mediastinal disorders	25 (6.3)	230 (3.4)
	Nervous system disorders	22 (5.6)	250 (3.7)
	Investigations	20 (5.1)	230 (3.4)

Comorbidity	AE by SOC	With Comorbidity n (%)	Without Comorbidity n (%)
Hyperlipidemia	n	559 (100)	6670 (100)
	Any AE	281 (50.3)	2483 (37.2)
	Infections and infestations	127 (22.7)	1125 (16.9)
	Surgical and medical procedures	78 (14.0)	620 (9.3)
	General disorders and administration site conditions	59 (10.6)	561 (8.4)
	Musculoskeletal and connective tissue disorders	60 (10.7)	399 (6.0)
	Skin and subcutaneous disorders	46 (8.2)	380 (5.7)
	Investigations	37 (6.6)	213 (3.2)
	Gastrointestinal disorders	32 (5.7)	256 (4.0)
	Nervous system disorders	31 (5.5)	241 (3.6)
Diabetes type I	n	101 (100)	7128 (100)
	Any AE	41 (40.6)	2723 (38.2)
	Infections and infestations	16 (15.8)	1236 (17.3)
	Skin and subcutaneous disorders	9 (8.9)	417 (5.9)
	General disorders and administration site conditions	8 (7.9)	612 (8.6)
	Respiratory, thoracic, and mediastinal disorders	7 (6.9)	248 (3.5)
	Investigations	7 (6.9)	243 (3.4)
Diabetes type II	n	596 (100)	6633 (100)
	Any AE	266 (44.6)	2498 (37.7)
	Infections and infestations	123 (20.6)	1129 (17.0)
	Surgical and medical procedures	76 (12.8)	622 (9.4)
	General disorders and administration site conditions	55 (9.2)	565 (8.5)
	Musculoskeletal and connective tissue disorders	41 (6.9)	418 (6.3)
	Skin and subcutaneous disorders	34 (5.7)	392 (5.9)

Comorbidity	AE by SOC	With Comorbidity n (%)	Without Comorbidity n (%)
Chronic inflammatory disease	n	145 (100)	7084 (100)
	Any AE	78 (53.8)	2686 (37.9)
	Infections and infestations	38 (26.2)	1214 (17.1)
	Surgical and medical procedures	27 (18.6)	671 (9.5)
	General disorders and administration site conditions	21 (14.5)	599 (8.5)
	Gastrointestinal disorders	201 (13.8)	277 (3.9)
	Musculoskeletal and connective tissue disorders	14 (9.7)	445 (6.3)
	Skin and subcutaneous disorders	11 (7.6)	415 (5.9)
	Investigations	11 (7.6)	239 (3.4)
	Injury, poisoning, and procedural complications	11 (7.6)	197 (2.8)
Chronic obstructive pulmonary disease	n	329 (100)	6900 (100)
	Any AE	163 (49.5)	2601 (37.7)
	Infections and infestations	80 (24.3)	1172 (17.0)
	General disorders and administration site conditions	44 (13.4)	576 (8.3)
	Surgical and medical procedures	42 (12.8)	656 (9.5)
	Musculoskeletal and connective tissue disorders	25 (7.6)	434 (6.3)
	Skin and subcutaneous tissue disorders	22 (6.7)	404 (5.9)
	Respiratory, thoracic and mediastinal disorders	22 (6.7)	233 (3.4)
Osteoporosis	n	1042 (100)	6187 (100)
	Any AE	447 (42.9)	2317 (37.4)
	Infections and infestations	205 (19.7)	1047 (16.9)
	Surgical and medical procedures	151 (14.5)	547 (8.8)
	General disorders and administration site conditions	86 (8.3)	534 (8.6)
	Musculoskeletal and connective tissue disorders	83 (8.0)	376 (6.1)
	Skin and subcutaneous tissue disorders	62 (6.0)	364 (5.9)
	Nervous system disorders	58 (5.6)	214 (3.5)

Comorbidity	AE by SOC	With Comorbidity n (%)	Without Comorbidity n (%)
Degenerative joint disease	n	1265 (100)	5964 (100)
	Any AE	536 (42.4)	2228 (37.4)
	Infections and infestations	229 (18.1)	1023 (17.2)
	Surgical and medical procedures	167 (13.2)	531 (8.9)
	Musculoskeletal and connective tissue disorders	120 (9.5)	339 (5.7)
	General disorders and administration site conditions	119 (9.4)	501 (8.4)
	Skin and subcutaneous tissue disorders	73 (5.8)	353 (5.9)
	Nervous system disorders	64 (5.1)	208 (3.5)
Degenerative spinal disease	n	1023 (100)	6206 (100)
	Any AE	428 (41.8)	2336 (37.6)
	Infections and infestations	192 (18.8)	1060 (17.1)
	Surgical and medical procedures	137 (13.4)	561 (9.0)
	Musculoskeletal and connective tissue disorders	87 (8.5)	371 (6.0)
	General disorders and administration site conditions	83 (8.1)	537 (8.7)
	Skin and subcutaneous tissue disorders	61 (6.0)	365 (5.9)
	Nervous system disorders	52 (5.1)	220 (3.5)
Mental illness (e.g., depression)	n	457 (100)	6772 (100)
	Any AE	199 (43.5)	2565 (37.9)
	Infections and infestations	90 (19.7)	1162 (17.2)
	Surgical and medical procedures	46 (10.1)	652 (9.6)
	General disorders and administration site conditions	41 (9.0)	579 (8.5)
	Musculoskeletal and connective tissue disorders	33 (7.2)	426 (6.3)
	Skin and subcutaneous tissue disorders	31 (6.8)	395 (5.8)
	Gastrointestinal disorders	31 (6.8)	266 (3.9)

Reference: Appendix 9 [Tables 2, 6.1 – 6.11](#)

10.6.5 Pregnancies

During this 60-month study, 38 pregnancies were reported in 36 patients. There were 10 live births (9 complication-free, 1 Caesarean section), 3 spontaneous abortions, 3 terminations, and 1 ectopic pregnancy. No outcome was provided for 19 pregnancies and the outcome was listed as "unknown" for 2 pregnancies.

Physician reports indicate that adalimumab therapy was stopped in 25 pregnancies; no therapeutic modifications were reported for the remaining 13 cases. Therapy was later resumed in 10 of the 25 pregnancies that reported stopping adalimumab. There was no information on resumption of therapy for the other 15 cases.

10.6.6 Safety in Pediatric Patients

Three patients enrolled in this study while under 18 years of age; their demographic information and study disposition data are summarized in [Table 69](#).

Table 69. Demographic and Study Disposition Data for Patients < 18 Years of Age at Treatment Initiation in AGIL

Patient #	Age at Study Entry	Sex	Study Initiation Date	Last Visit	Reason for Study Discontinuation
██████████	15	Male	██████████ 2009	Month 24	Loss of effectiveness
██████████	16	Male	██████████ 2010	Month 24	Lost to follow-up
██████████	16	Female	██████████ 2010	Month 6	Lost to follow-up

Patient ██████ did not report any adverse events. Patient ██████ was diagnosed with iritis approximately 18 months after initiation of adalimumab. Patient ██████ underwent arthroscopy of the right knee approximately 8 months after initiation of adalimumab. Neither AE was considered serious.

The small number of pediatric patients enrolled limits interpretation, but adalimumab did not appear to result in any new safety signals in these patients.

11.0 Discussion

11.1 Key Results

In this 60-month observational study, adalimumab demonstrated improvement of employment-related outcomes, long-term effectiveness, and a safety profile consistent with previous observations.^{4,5,23,46}

The impact of adalimumab therapy on employment-related outcomes was a primary objective of this study. Effective RA therapy has been shown to improve work-related outcomes, including sick leave absences and productivity.¹⁰ We found that treatment with adalimumab resulted in decreased missed work days, as assessed by patient recall of the previous 6 months. Mean sick leave days decreased from 19.2 at baseline to 7.9 at Month 60 in patients remaining on therapy. Mean values were somewhat misleading because of the asymmetrical data distribution driven by the high proportion of patients with no sick leave days. We therefore performed categorical analyses of patients with a normal or higher-than-normal number of sick leave days in the past 6 months (≤ 5 or > 5). Adalimumab therapy resulted in a significant increase in patients within the normal range at Month 24 and Month 60. Among patients with higher than normal sick leave days at baseline, approximately 60% returned to normal sick leave levels by Month 12, and this level was maintained throughout 5 years of treatment in patients remaining on therapy. Significant improvements at Month 24 and Month 60 were also observed in WPAI and WAI assessments of employment-related outcomes, including absenteeism and presenteeism in the past 7 days.

Other studies of adalimumab have also supported the positive effect of this therapy on reducing work loss in patients with RA, including a study on sick leave days in German patients treated with adalimumab for 12 months based on a previous non-interventional study (Study P10-448).⁴⁷ A post hoc analysis from a randomized trial of adalimumab plus methotrexate versus placebo plus methotrexate in patients with early RA found significant improvements in WPAI presenteeism and overall work impairment in the adalimumab arm over 26 weeks.⁶ Additional short-term (24- to 48-week) studies have documented the

effect of adalimumab on reducing missed work days and improving work productivity in Saudi Arabia⁴⁸ and Japan.⁴⁹ This body of literature consistently supports the impact of adalimumab therapy on improving employment-related outcomes in patients with RA.

Regression models for change in employment-related outcomes from Month 0 to Month 24 during adalimumab therapy identified the corresponding baseline employment-related variable as the most important predictor. Other predictors included functional ability, morning stiffness, educational status, fatigue, age and positive RF serostatus. Our data are consistent with predictors of employment-related outcomes in other studies.⁵⁰⁻⁵²

As expected, adalimumab therapy also resulted in significant improvements in clinical symptoms. Disease activity, as assessed by DAS28, improved from a mean of 5.12 at baseline, a level corresponding to high disease activity, to 2.93 at Month 60, a value representing low disease activity.³² Corresponding improvements were observed in joint counts and inflammatory markers. Patient-reported outcomes, including the HAQ-DI, an assessment of function, and the EQ-VAS, an assessment of health-related quality of life, also showed significant improvements during therapy. The number of physician visits and hospitalizations decreased during adalimumab treatment, and patients reported reduced impairment in non-occupational activities.

Regression models identified higher baseline DAS28 and MTX at baseline as positive predictors of improvement in disease activity at Month 6, and reduced function, more previous biologics, higher BMI and age, and use of analgesics at baseline as negative predictors. These findings are generally in line with other studies of predictors of therapeutic response in RA. In particular, DAS28 and MTX have been identified as important predictors of therapeutic response to TNF inhibitors in other studies,^{45,53} and previous biologic therapy has been identified as a negative predictor.^{45,54} Regression models for change in HAQ-DI at 6 months were less robust, but identified several of the same predictors as for DAS28, including MTX as a positive predictor and age, BMI, and previous biologics as negative predictors. As observed in other studies,⁴⁵ DAS28 was not a significant predictor of changes in HAQ-DI.

Approximately 35% of the patients in this study participated in the Abbot Care (AbbVie Care) patient support program at baseline; this level decreased to under 30% in the final study visits, perhaps due to a diminished need for support in patients on long-term adalimumab therapy.

The AGIL-CV patient cohort was 260 at baseline, which was smaller than the planned target size of 300. Accordingly, findings from these data must be interpreted with caution. During adalimumab therapy, no clear trends were observed in body measurements, vital signs, or blood chemistry values other than CRP. There are two possible explanations for this lack of effect: (1) adalimumab does not have a significant influence on these parameters during long-term treatment; or (2) the sample size was too small to detect significant results. The fact that significant changes were observed in CRP levels suggests that the first option may be the most likely explanation for the observed lack of changes. Analyses of body measurements, vital signs, and blood chemistry outcomes based on therapeutic response also failed to reveal any clear trends. Recorded CV events were very rare during the 36-month documentation in AGIL-CV (3 cases of stroke).

It should be noted that other studies have found that adalimumab therapy is associated with small increases in lipid levels. A retrospective study based on a medical claims and pharmacy database in the US (OptumInsight Impact) found that initiation of anti-TNF therapy in patients with RA resulted in a modest increase in lipid levels in patients not receiving concomitant therapy with lipid-lowering agents.⁵⁵ Similar findings have been reported for adalimumab therapy in analysis of clinical trial data of patients with early RA. During 6 months of therapy, treatment with adalimumab plus MTX resulted in modest elevations in HDL-C, LDL-C, and Total-C in MTX-naïve patients with early RA (n = 783); increases in LDL-C and Total-C were significantly higher ($P < 0.05$) than increases from baseline with MTX + placebo (n = 774).⁵⁶ In contrast to these findings, we did not observe a consistent increase in lipid values during adalimumab therapy, perhaps due to the small number of patients evaluated.

In a meta-analysis of data from randomized clinical trials, anti-TNF therapy was associated with an increased risk of developing hypertension.⁵⁷ However, in agreement with our data, in-depth studies of individual patients,^{58,59} one of which employed 24-hour ambulatory blood pressure measurements,⁵⁸ reported that anti-TNF therapy for periods of 3 months and 1 year did not significantly affect either systolic or diastolic blood pressure.

The AE profile was consistent with previously reported findings.^{4,5,23,46} During the 60-month study, 32.1% of patients reported an AE and 12.9% had an SAE. The most common category of AE by SOC was infections and infestations, and the most common category of SAE was surgical and medical procedures, primarily involving hospitalizations and joint operations. Twenty-three deaths occurred during the study. A review of AEs and deaths did not reveal any patterns of concern. AE rates occurring in patients with pre-specified baseline comorbidities showed some elevations compared with patients who did not have that comorbidity, but most of the AEs could be explained by the underlying comorbidity and no safety signals were observed.

11.2 Limitations

Interpretation of these results is somewhat compromised by the rate of discontinuation in this study. Later time points were affected by the decision to terminate the study in June 2017. Although most patients had the opportunity to reach the Month 24 visit, patients who enrolled between 2013 and 2017 (n = 2352; 35.0% of the safety set) could not reach the Month 60 visit. The employed patient cohort target sample size of 850 was available up to the Month 36 visit, but not at later time points. However, this sample size was based on mean values; sufficient patients for categorical analyses were available at all time points. The target sample size for AGIL-CV was not achieved.

The changing RA therapy environment may also have influenced discontinuation rates. Recent studies of therapy discontinuation rates in patients with RA, including one based on a cohort of patients treated with adalimumab, have found that drug discontinuation rates increased after 2005, probably due to the availability of a greater number of biologic therapies.^{60,61}

At 24 months, 40.4% of patients in the safety set continued in the study, which is slightly lower than the 48% 24-month continuation rate reported for biologic-naïve patients initiating adalimumab in a large US Registry, the Corrona database.⁶² At 60 months, 16.7% of patients in the safety set continued on adalimumab treatment. The cumulative documented withdrawal rate at 60 months was 39.7%, but another 43.6% of patients were lost to follow-up for unknown reasons.

Effectiveness outcomes at later time points may have been influenced by responder bias (see Section 9.6.4). Patients with favorable responses are more likely to continue therapy than those experiencing a suboptimal response, which may have accounted for the continued reductions in disease activity parameters.

Both socioeconomic outcomes and AE reports may have been affected by recall bias (see Section 9.6.3). It is thus possible that these parameters were underreported to some extent.

Confounding factors, including age, comorbid conditions, and concomitant medications, complicate the interpretation of post-hoc subgroup analyses, including the subgroup analysis by baseline sick leave days. These results should therefore be interpreted with caution.

Interpretation of data from the AGIL-CV cohort is complicated by the fact that this cohort did not reach the target sample size.

AE reports may have been influenced by underreporting by clinicians, as the observed AE rates were considered low for this population cohort by expert reviewers. A study conducted in Germany found that 68% of a random sample of doctors had suspected an adverse drug reaction without reporting it, usually because they considered it too well known, too trivial, or of uncertain causality.⁶³ These findings suggest that underreporting of AEs is widespread. In addition, adverse events treated by a different specialist, such as a cardiologist, may never have been reported to the rheumatologist who provided documentation for this study. This may also have contributed to a lack of detailed reports

on deaths, SAEs, and pregnancies. In addition, as is usual in non-interventional studies in Germany, doctors did not receive specific training on potential adverse drug reactions, so they may have not been aware that certain AEs should have been reported as a potential adverse drug reaction, thus contributing to underreporting.

11.3 Interpretation

This observational study included a large number of adult RA patients treated in daily clinical practice for up to 60 months. At 24 months, the sample sizes for the employed patient, FAS, and safety set cohorts remained sufficiently large for robust analyses. During the first 24 months of this study, adalimumab treatment was associated with strong and significant improvements in employment-related outcomes and clinical symptoms. These changes were maintained throughout the study, but the fewer patients available at later time points and the potential for responder bias make data from later visits more difficult to interpret.

The AGIL-CV cohort did not meet its target sample size. Analyses of data from this substudy did not identify significant changes in body measurements, vital signs, or lipid profiles during the first 24 months of adalimumab treatment. A significant change in CRP levels was observed; this finding suggests that, even with the reduced sample size, a large effect on lipid parameters or vital signs would have been detected.

Adalimumab was generally safe and well-tolerated during up to 60 months of therapy. The AE profile observed in our study was consistent with other reports. There were no indications of unexpected AEs.

11.4 Generalisability

Because of the large number of patients enrolled in this study at sites throughout Germany, the results are likely to be representative of other adult RA patients in Germany. Data on ethnic groups was not collected, but over 90% of the population in Germany is of German ethnicity.⁶⁴ The limited ethnic diversity of this population may

thus limit the generalisability of these findings to populations with primarily white European ancestry.

12.0 Other Information

None.

13.0 Conclusion

The findings of this observational study support the conclusion that long-term treatment with adalimumab has a favorable impact on employment-related outcomes in adult patients with RA. In this study, adalimumab was highly effective by both objective and subjective measures of disease activity in RA patients remaining on therapy. Because of a limited sample size, the AGIL-CV substudy was unable to provide a robust assessment of the impact of therapy on metabolic and CV risk. No unexpected adverse events occurred during 60 months of adalimumab therapy. This study provides further support for the favorable effect of adalimumab on employment-related outcomes and for the long-term safety and effectiveness of this therapy in adult patients with RA during routine daily clinical care.

14.0 References

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. 2016;388(10055):2023-38.
2. Fuchs J, Rabenberg M, Scheidt-Nave C. Prevalence of selected musculoskeletal conditions in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1). [English translation] *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56(5-6):678-86.
3. Schett G, Stach C, Zwerina J, et al. How antirheumatic drugs protect joints from damage in rheumatoid arthritis. *Arthritis Rheum*. 2008;58(10):2936-48.
4. Breedveld FC, Weisman MH, Kavanaugh AF, et al. The PREMIER study: a multicenter, randomized, double-blind clinical trial of combination therapy with

- adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early, aggressive rheumatoid arthritis who had not had previous methotrexate treatment. *Arthritis Rheum.* 2006;54(1):26-37.
5. Burmester GR, Mariette X, Montecucco C, et al. Adalimumab alone and in combination with disease-modifying antirheumatic drugs for the treatment of rheumatoid arthritis in clinical practice: the Research in Active Rheumatoid Arthritis (ReAct) trial. *Ann Rheum Dis.* 2007;66(6):732-9.
 6. Emery P, Smolen JS, Ganguli A, et al. Effect of adalimumab on work-related outcomes scores in patients with early rheumatoid arthritis receiving methotrexate. *Rheumatology (Oxford).* 2016;55(8):1458-65.
 7. van Vilsteren M, Boot CR, Knol DL, et al. Productivity at work and quality of life in patients with rheumatoid arthritis. *BMC Musculoskeletal Disord.* 2015;16:107.
 8. Merkesdal S, Ruof J, Huelsemann JL, et al. Indirect cost assessment in patients with rheumatoid arthritis (RA): comparison of data from the health-economic patient questionnaire HEQ-RA and insurance claims data. *Arthritis Rheum.* 2005;53(2):234-40.
 9. Braakman-Jansen LMA, Taal E, Kuper IH, et al. Productivity loss due to absenteeism and presenteeism by different instruments in patients with RA and subjects without RA. *Rheumatology (Oxford).* 2012;51(2):354-61.
 10. Verstappen SMM. Rheumatoid arthritis and work: the impact of rheumatoid arthritis on absenteeism and presenteeism. *Best Pract Res Clin Rheumatol.* 2015;29(3):495-511.
 11. Silverman SL. From randomized controlled trials to observational studies. *Am J Med.* 2009;122(2):114-20.
 12. Barbhaiya M, Solomon DH. Rheumatoid arthritis and cardiovascular disease: an update on treatment issues. *Curr Opin Rheumatol.* 2018;25(3):317-24.
 13. Agca R, Heslinga SC, Rollefstad S, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and
-

- other forms of inflammatory joint disorders: 2015/2016 update. *Ann Rheum Dis.* 2017;76(1):17-28.
14. Crowson CS, Rollefstad S, Ikdahl E, et al. Impact of risk factors associated with cardiovascular outcomes in patients with rheumatoid arthritis. *Ann Rheum Dis.* 2018;77(1):48-54.
 15. Roubille C, Richer V, Starnino T, et al. The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis, and psoriatic arthritis: a systematic review and meta-analysis. *Ann Rheum Dis.* 2015;74(3):480-9.
 16. Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J.* 2003;24(11):987-1003.
 17. Greenberg JD, Kremer JM, Curtis JR, et al. Tumour necrosis factor antagonist use and associated risk reduction of cardiovascular events among patients with rheumatoid arthritis. *Ann Rheum Dis.* 2011;70(4):576-82.
 18. Gonzalez-Juanatey C, Vazquez-Rodriguez TR, Miranda-Filloo JA, et al. Anti-TNF-alpha-adalimumab therapy is associated with persistent improvement of endothelial function without progression of carotid intima-media wall thickness in patients with rheumatoid arthritis refractory to conventional therapy. *Mediators Inflamm.* 2012;2012:674265.
 19. Vassilopoulos D, Gravos A, Viachopoulos C, et al. Adalimumab decreases aortic stiffness independently of its effect in disease activity in patients with rheumatoid arthritis. *Clin Rheumatol.* 2015;34(2):359-64.
 20. Popa C, Netea MG, Radstake T, et al. Influence of anti-tumour necrosis factor therapy on cardiovascular risk factors in patients with active rheumatoid arthritis. *Ann Rheum Dis.* 2005;64(2):303-5.
 21. Wijbrandts CA, van Leuven SI, Boom HD, et al. Sustained changes in lipid profile and macrophage migration inhibitory factor levels after anti-tumour necrosis factor therapy in rheumatoid arthritis. *Ann Rheum Dis.* 2009;68(8):1316-21.
-

22. Bundesministerium der Justiz. Medicinal Products Act (English translation). [Internet]. Juris GmbH. 2013. Available from: http://www.gesetze-im-internet.de/englisch_amg/englisch_amg.html#p0599. Accessed on: January 17, 2018.
 23. European Medicines Agency. Humira[®] (adalimumab) [Summary of Product Characteristics] [Internet]. Abbvie Ltd. 2009 December 11 [updated 2017 December 15]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000481/WC500050870.pdf. Accessed on: January 19, 2018.
 24. Zhang W, Bansback N, Boonen A, et al. Validity of the Work Productivity and Activity Impairment Questionnaire – general health version in patients with rheumatoid arthritis. *Arthritis Res Ther.* 2010;12:R177.
 25. Reilly Associates. Work Productivity and Impairment Questionnaire: General Health v2.0 (WPAI:GH) [Internet]. Available from: http://www.reillyassociates.net/WPAI_GH.html. Accessed on: January 27, 2018.
 26. Amler N, Felder S, Mau W, et al. Instruments for measuring the effects of early intervention on maintaining and restoring ability to work in Germany: opinion of an interdisciplinary working group [article in German]. *Gesundheitswesen.* 2018;80(1):79-86.
 27. Reilly Associates. WPAI scoring [Internet]. Available from: http://www.reillyassociates.net/WPAI_Scoring.html. Accessed on: October 30, 2017.
 28. Morschhäuser M, Sochert R. Healthy work in an ageing Europe. Strategies and instruments for prolonging working life. European Network for Workplace Health Promotion [Internet]. 2006. Available from: <http://www.ageingatwork.eu/resources/health-work-in-an-ageing-europe-enwhp-3.pdf>. Accessed on: January 17, 2018.
-

29. Hoving JL, Bartelds GM, Sluiter JK, et al. Perceived work ability, quality of life, and fatigue in patients with rheumatoid arthritis after a 6-month course of TNF inhibitors: prospective intervention study and partial economic evaluation. *Scan J Rheumatol*. 2009;38(4):246-50.
 30. Prevoo ML, van't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum*. 1995;38(1):44-8.
 31. Vander Cruyssen B, Van Looy S, Wyns B, et al. DAS28 best reflects the physician's clinical judgment of response to infliximab therapy in rheumatoid arthritis patients: validation of the DAS28 score in patients under infliximab treatment. *Arthritis Res Ther*. 2005;7(5):R1063-71.
 32. Fransen J, van Riel PLCM. The Disease Activity Score and the EULAR response criteria. *Clin Exp Rheumatol*. 2005;23 (Suppl 39):S93-9.
 33. Anderson J, Caplan L, Yazdany J, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. *Arthritis Care Res (Hoboken)*. 2012;64(5):640-7.
 34. Bruce B, Fries JF. The Health Assessment Questionnaire (HAQ). *Clin Exp Rheumatol*. 2005;23 (Suppl 39):S14-8.
 35. Maska L, Anderson J, Michaud K. Measures of functional status and quality of life in rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2011;63 (Suppl 11):S4-13.
 36. Harrison MJ, Davies LM, Bansback NJ, et al. The validity and responsiveness of generic utility measures in rheumatoid arthritis: a review. *J Rheumatol*. 2008;35(4):592-602.
 37. van Reenen M, Oppe M. EQ-5D-3L user guide. Basic information on how to use the EQ-5D-5L instrument [Internet]. Version 2.1, April 2015. Available from: https://euroqol.org/wp-content/uploads/2016/09/EQ-5D-3L_UserGuide_2015.pdf. Accessed on: January 18, 2018.
-

38. Behrens F, Tony HP, Alten R, et al. Development and validation of a new disease activity score in 28 joints-based treatment response criterion for rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2013;65(10):1608-16.
 39. Mok CC, Ko GT, Ho LY, et al. Prevalence of atherosclerotic risk factors and the metabolic syndrome in patients with chronic inflammatory arthritis. *Arthritis Care Res (Hoboken)*. 2011;63(2):195-202.
 40. Fleischmann RM, van der Heijde D, Gardiner PV, et al. DAS28-CRP and DASE28-ESR cut-offs for high disease activity in rheumatoid arthritis are not interchangeable. *RMD Open*. 2017;3(1):e000382.
 41. Federal Statistical Office (Destatis). Quality of employment. Dimension 2: income and indirect benefits from employment. Staff on sick leave [Internet]. 2017. Available from: https://www.destatis.de/EN/FactsFigures/Indicators/QualityEmployment/Dimension2/2_3_StaffSickLeave.html;jsessionid=835DD2CB2C5FD25E5621982FF991ADC4.InternetLive1. Accessed on: October 30, 2017.
 42. Woolson RF. Multiple linear regression. In: Woolson RF (ed). *Statistical Methods for the Analysis of Biomedical Data*. New York:John Wiley & Sons, Inc.; 1987. p. 295-300.
 43. Bortz J. Partialkorrelation und multiple Korrelation [Partial correlation and multiple correlation]. In: Bortz J (ed). *Statistik für Human- und Sozialwissenschaftler [Statistics for Human and Social Scientists]*, 6th edition. Heidelberg: Springer; 2005. p. 439-81.
 44. Rawling JO, Pantula SG, Dickey DA. *Applied regression analysis. A research tool*. 2nd ed. New York: Springer; 1998.
 45. Kleinert S, Tony HP, Krause A, et al. Impact of patient and disease characteristics on therapeutic success during adalimumab treatment of patients with rheumatoid arthritis: data from a German noninterventional observational study. *Rheumatol Int*. 2012;32(9):2759-67.
-

46. Burmester GR, Landewe R, Genovese MC, et al. Adalimumab long-term safety: infections, vaccination response and pregnancy outcomes in patients with rheumatoid arthritis. *Ann Rheum Dis*. 2017;76(2):414-7.
 47. Krüger K, Wollenhaupt J, Lorenz HM, et al. Reduction in sickness absence in patients with rheumatoid arthritis receiving adalimumab: data from a German noninterventional study. *Rheumatol Int*. 2012;32(12):3977-83.
 48. Hussain W, Janoudi N, Noorwali A, et al. Effect of adalimumab on work ability assessed in rheumatoid arthritis disease patients in Saudi Arabia (AWARDS). *Open Rheumatol J*. 2015;9:46-50.
 49. Takeuchi T, Nakajima R, Komatsu S, et al. Impact of adalimumab on work productivity and activity impairment in Japanese patients with rheumatoid arthritis: large-scale, prospective, single-cohort ANOUVEAU study. *Adv Ther*. 2017;34(3):686-702.
 50. Lenssinck MLB, Burdorf A, Boonen A, et al. Consequences of inflammatory arthritis for workplace productivity loss and sick leave: a systematic review. *Ann Rheum Dis*. 2013;72(4):493-505.
 51. Mattila K, Buttgerit F, Tuominen R. Influence of rheumatoid arthritis-related morning stiffness on productivity at work: results from a survey in 11 European countries. *Rheumatol Int*. 2015;35:1791-7.
 52. de Croon EM, Sluiter JK, Nijssen TF, et al. Predictive factors of work disability in rheumatoid arthritis: a systematic literature review. *Ann Rheum Dis*. 2004;63(11):1362-7.
 53. Kristensen LE, Kapetanovic MC, Gülfe A, et al. Predictors of response to anti TNF therapy according to ACR and EULAR criteria in patients with established RA: results from the South Swedish Arthritis Treatment Group Register. *Rheumatology (Oxford)*. 2008;47(4):495-9.
 54. Feuchtenberger M, Kleinert S, Scharbatke E-C, et al. The impact of prior biologic therapy on adalimumab response in patients with rheumatoid arthritis. *Clin Exp Rheumatol*. 2015;33(3):321-9.
-

55. Curtis JR, Baser JA. Dyslipidemia and changes in lipid profiles associated with rheumatoid arthritis and initiation of anti-tumor necrosis factor therapy. *Arthritis Care Res (Hoboken)*. 2012;64(9):1282-91.
 56. Furst D, Lacerda AP, Andhivarothai N, et al. Impact of adalimumab therapy on laboratory parameters of interest in patients with early or long-standing rheumatoid arthritis [abstract]. *Arthritis Rheum*. 2012;64 (Suppl):486.
 57. Zhao Q, Hong D, Zhang Y, et al. Association between anti-TNF therapy for rheumatoid arthritis and hypertension. A meta-analysis of randomized controlled trials. *Medicine*. 2015;94(14):e731.
 58. Grossman C, Bornstein G, Leibowitz A, et al. Effect of tumor necrosis factor- α inhibitors on ambulatory 24-h blood. *Blood Press*. 2017;26(1):24-9.
 59. Angel K, Provan SA, Fagerhol MK, et al. Effect of 1-year anti-TNF- α therapy on aortic stiffness, carotid atherosclerosis, and calprotectin in inflammatory arthropathies: a controlled study. *Am J Hypertens*. 2012;25(6):644-50.
 60. Iannone F, Sinigaglia L, Favalli EG, et al. Drug survival of adalimumab in patients with rheumatoid arthritis over 10 years in the real-world settings: high rate remission together with normal function ability. *Clin Rheumatol*. 2016;35(11):2649-56.
 61. Ramiro S, Landewe R, van der Heijde D, et al. Discontinuation rates of biologics in patients with rheumatoid arthritis: are TNF inhibitors different from non-TNF inhibitors? *RMD Open*. 2015;1(1):e000155.
 62. Pappas DA, Kremer JM, Griffith J, et al. Long-term effectiveness of adalimumab in patients with rheumatoid arthritis: an observational analysis from the CORRONA rheumatoid arthritis registry. *Rheumatol Ther*. 2017;4(2):375-89.
 63. Hasford J, Goettler M, Munter KH, et al. Physicians' knowledge and attitudes regarding the spontaneous reporting system for adverse drug reactions. *J Clin Epidemiol*. 2002;55(9):945-50.
-

64. The World Factbook 2017. Germany: people and society [Internet]. Washington DC: Central Intelligence Agency. Available from: <https://www.cia.gov/library/publications/the-world-factbook/geos/gm.html>. Accessed on: January 19, 2018.

Annexes and Appendices

Annex 1. List of Attached Stand-Alone Documents

Number	Document Reference Number	Date	Title
1	Appendix 1	28 October 2008	AGIL Protocol (English translation)
2	Appendix 2	06 March 2012	AGIL-CV Amendment (English translation)
3	Appendix 3	01 March 2009	Case Report Form (English translation excerpt) ^a
4	Appendix 4	10 May 2012	Complete Case Report Form (AGIL and AGIL-CV; German)
5	Appendix 5	26 May 2010	Ethics approval letter (German) ^b
6	Appendix 6	05 March 2018	Statistical Tables for Employed Patients (English)
7	Appendix 7	05 March 2018	Statistical Tables for Clinical Outcomes (FAS) (English)
8	Appendix 8	06 March 2018	Statistical Tables for CV Substudy (AGIL-CV) (English)
9	Appendix 9	05 March 2018	Statistical Tables for Safety Set (English)

a. Includes baseline (Month 0) and Month 3 visits. Subsequent visits were identical to Month 3 with minor differences.

b. Update to original approval dated 18 May 2009.

Annex 2. List of Documents Available on Request

Number	Document Reference Number	Date	Title
10	Appendix 10	17 May 2010	AGIL Protocol (German)
11	Appendix 11	17 May 2010	AGIL-CV Amendment (German)
12	Appendix 12	17 May 2010	Case Report Form (AGIL only; German)
13	Appendix 13	03 November 2017	Statistical Analysis Plan (German)
14	Appendix 14	29 September 2016	Data Validation Plan for Full Study (German)
15	Appendix 15	19 July 2017	Data Validation Plan for CV Substudy (German)

Annex 3. WPAI Questionnaire

The English version of the WPAI is shown below.²⁵ The modified WPAI used in this study omitted Question 1 (current employment) because this topic was covered elsewhere in the CRF.

Work Productivity and Activity Impairment Questionnaire: General Health V2.0 (WPAI:GH)

The following questions ask about the effect of your health problems on your ability to work and perform regular activities. By health problems we mean any physical or emotional problem or symptom. *Please fill in the blanks or circle a number, as indicated.*

1. Are you currently employed (working for pay)? ____ NO ____ YES
If NO, check "NO" and skip to question 6.

The next questions are about the **past seven days**, not including today.

2. During the past seven days, how many hours did you miss from work because of your health problems? *Include hours you missed on sick days, times you went in late, left early, etc., because of your health problems. Do not include time you missed to participate in this study.*

____ HOURS

3. During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?

____ HOURS

4. During the past seven days, how many hours did you actually work?

____ HOURS *(If "0", skip to question 6.)*

5. During the past seven days, how much did your health problems affect your productivity while you were working?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If health problems affected your work only a little, choose a low number. Choose a high number if health problems affected your work a great deal.

Consider only how much health problems affected productivity while you were working.

Health problems had no effect on my work _____ Health problems completely prevented me from working

0 1 2 3 4 5 6 7 8 9 10

CIRCLE A NUMBER

6. During the past seven days, how much did your health problems affect your ability to do your regular daily activities, other than work at a job?

By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If health problems affected your activities only a little, choose a low number. Choose a high number if health problems affected your activities a great deal.

Consider only how much health problems affected your ability to do your regular daily activities, other than work at a job.

Health problems had no effect on my daily activities _____ Health problems completely prevented me from doing my daily activities

0 1 2 3 4 5 6 7 8 9 10

CIRCLE A NUMBER

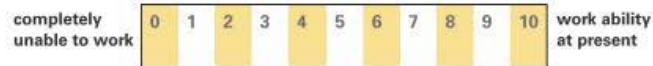
Annex 4. WAI Questionnaire

The English version of the WAI is shown below.²⁸ The modified WAI used in this study included Questions 1, 2, 4, 6, and 7 of the WAI. Question 3, which involves the number of current diseases diagnosed by a physician, was omitted because this parameter was unlikely to reflect change during treatment. Question 5 (sick leave during the past year) was replaced with a separate question concerning sick leave days located at an earlier position in the CRF.

Work Ability Index

1. Current work ability compared with the lifetime best

Assume that your work ability at its best has a value of 10 points.
How many points would you give your current work ability?
(0 means that you cannot currently work at all)



2. Work ability in relation to the demands of the job

How do you rate your current work ability with respect to the physical demands of your work?

very good	5
rather good	4
amoderate	3
rather poor	2
very poor	1

How do you rate your current work ability with respect to the mental demands of your work?

very good	5
rather good	4
amoderate	3
rather poor	2
very poor	1

3. Number of current diseases diagnosed by a physician

In the following list, mark your diseases or injuries. Also indicate whether a physician has diagnosed or treated these diseases. For each disease, therefore, there can be 2, 1, or no alternatives circled.

	Yes, own opinion	Yes, physician's diagnosis
Injury from accidents		
01 back	2	1
02 arm/hand	2	1
03 leg/foot	2	1
04 other part of body, where and what kind of of injury?	2	1
...		
Musculoskeletal disease		
05 disorder of the upper back or cervical spine, repeated instances of pain	2	1
06 disorder of the lower back, repeated instances of pain	2	1
07 (sciatica) pain radiating from the back into the leg	2	1
08 Musculoskeletal disorder affecting the limbs (hands, feet), repeated instances of pain	2	1
09 rheumatoid arthritis	2	1
10 other musculoskeletal disorder, what?	2	1
...		

	Yes, own opinion	Yes, physician's diagnosis
Cardiovascular diseases		
11 hypertension (high blood pressure)	2	1
12 Coronary heart disease, chest pains during exercise (angina pectoris)	2	1
13 coronary thrombosis, myocardial infarction	2	1
14 cardiac insufficiency	2	1
15 other cardiovascular disease, what?	2	1
...		
Respiratory disease		
16 repeated infections of the respiratory tract (also tonsillitis, acute sinusitis, acute bronchitis)	2	1
17 chronic bronchitis	2	1
18 chronic sinusitis	2	1
19 bronchial asthma	2	1
20 emphysema	2	1
21 pulmonary tuberculosis	2	1
22 other respiratory disease, what	2	1
...		
Mental disorder		
23 mental disease or severe mental health problem (for example, severe depression, mental disturbance)	2	1
24 slight mental disorder or problem (for example, slight depression, tension, anxiety, insomnia)	2	1
Neurological and sensory disease		
25 problems or injury to hearing	2	1
26 visual disease or injury (other than refractive error)	2	1
27 neurological disease (for example stroke, neuralgia, migraine, epilepsy)	2	1
28 other neurological or sensory disease, what?	2	1
...		
Digestive disease		
29 gall stones or disease	2	1
30 liver or pancreatic disease	2	1
31 gastric or duodenal ulcer	2	1
32 gastritis or duodenal irritation	2	1
33 colonic irritation, colitis	2	1
34 other digestive disease, what?	2	1
...		

	Yes, own opinion	Yes, physician's diagnosis
Genitourinary disease		
35 urinary tract infection	2	1
36 kidney disease	2	1
37 genitals disease (for example fallopian tube infection in women or prostatic infection in men)	2	1
38 Other genitourinary disease, what?	2	1
...		
Skin diseases		
39 allergic rash, eczema	2	1
40 other rash, what	2	1
...		
41 other skin disease, what?	2	1
...		
Tumour		
42 benign tumour	2	1
43 malignant tumour (cancer), where?	2	1
...		
Endocrine and metabolic diseases		
44 obesity	2	1
45 diabetes	2	1
46 goiter or others thyroid disease	2	1
47 other endocrine or metabolic disease, what?	2	1
...		
Blood diseases		
48 anemia	2	1
49 other blood disorder, what?	2	1
...		
Birth defects		
50 birth defect, what?	2	1
...		
Other disorder or disease		
51 What?	2	1
...		

4. Estimated work impairment due to diseases

Is your illness or injury a hindrance to your current job?
Circle more than one alternative if needed.

There is no hindrance/I have no diseases	6
I am able to do my job, but it causes some symptoms	5
I must sometimes slow down my work pace or change my work methods	4
I must often slow down my work pace or change my work methods	3
Because of my disease, I feel I am able to do only part-time work	2
In my opinion, I am entirely unable to work	1

5. Sick leave during the past year (12 months)

How many whole days have you been off work because of a health problem (disease or health care or for examination) during the past year (12 months)?

none at all	5
at the most 9 days	4
10 - 24 days	3
25 - 99 days	2
100 - 365 days	1

6. Own prognosis of work ability two years from now

Do you believe that – from the standpoint of your health – you will be able to do your current job two years from now?

unlikely	1
no certain	4
relatively certain	7

7. Mental resources

Have you recently been able to enjoy your regular daily activities?

often	4
rather often	3
sometimes	2
rather seldom	1
never	0

Have you recently been active and alert?

often	4
rather often	3
sometimes	2
rather seldom	1
never	0

Have you recently felt yourself to be full of hope for the future?

continuously	4
rather often	3
sometimes	2
rather seldom	1
never	0

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Appendix 1 AGIL Protocol (English Translation)

1 Title Page

Abbott GmbH & Co. KG

Documentation Plan AGIL (GER 08-05)

Long term Documentation of the Safety and Efficacy as well as the Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis under HUMIRA[®] (Adalimumab) in Routine Clinical Practice (AGIL)

Product Name: HUMIRA[®]

Type of Study: Non-interventional Study (NIS)

Date: 28-10-2008

Principal Investigator:



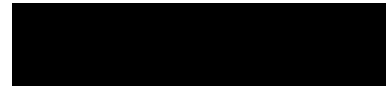
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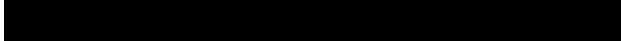
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Sponsor:

Abbott GmbH & Co. KG
Max-Planck-Ring 2
65205 Wiesbaden



This study will be conducted in compliance with this protocol and other applicable regulatory and legal requirements. 


2 Synopsis

Sponsor	Abbott GmbH & Co. KG Max-Planck-Ring 2 65205 Wiesbaden
Title	Long term Documentation of the Safety and Efficacy as well as the Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis under HUMIRA® (Adalimumab) in Routine Clinical Practice
Short title	AGIL
Type of study	Non-interventional study
Product, dose, and administration form	Adalimumab (HUMIRA®): 40 mg subcutan (s.c.) every other week
Project code	GER 08-05
Indication	Moderate to severe active rheumatoid arthritis (RA) and/or severe, active and progressive RA
Study objectives	<p><u>The primary objective</u> of the NIS is to explore the therapeutic success, measured by improvements in the following target variables (with regard to the respective baseline value):</p> <ul style="list-style-type: none">• The number of missed working days• The self-assessed work ability (WPAI)• The severity of clinical symptoms (number of tender and swollen joints, CRP and ESR, respectively; total score DAS28)• The severity of functional impairment (HAQ)• The health-related quality of life (EQ-5D) <p>All of the patient and disease characteristics which are documented at baseline will be evaluated for their additional impact on the target variables (therapeutic success). Particularly the impact of previous biologic therapies on clinical target variables will be evaluated.</p> <p><u>The secondary objective</u> is to document the therapeutic success by the following variables:</p> <ul style="list-style-type: none">• The number of physician visits• The number and duration of hospitalization• The number of days of impairment in non-occupational activities• The duration of morning stiffness, pain, exhaustion/fatigue• The reduction of number and dose of concomitant medication• Patient's assessment of adalimumab therapy compared to previous therapies.

	Target parameters for safety evaluation of adalimumab are:
	<ul style="list-style-type: none">• The evaluation of safety and tolerability by the documentation and analysis of serious adverse events (SAEs) and adverse events (AEs)• Evaluation of safety and tolerability for subgroups of patients with common frequent concomitant diseases, especially diabetes type II, cardiovascular, liver, and renal insufficiencies, and related concomitant medications.
Study population	Adult patients (≥ 18 years) with moderate to severe active RA and/or severe, active and progressive RA
Study design	Single-arm, multi-center format, prospective cohort study
Treatment duration	5 years
Methodology	Disease Activity Score (DAS28), Health Assessment Questionnaire (HAQ), Health Questionnaire Short Form (EQ-5D), WPAI
Total number of patients	2500 Patients
Adverse Events	As reported by patients and diagnosed at visits
Data analysis plan	The general biometric approach consists of evaluation of changes by descriptive statistical methods, as well as of regression analysis of parameters influencing the therapeutic success and additional subgroup analysis. By forward and backward stepwise regression, those patient and disease characteristics (baseline values of all target parameters, disease duration, previous therapies, demographic and anthropometric data, health-related quality of life etc.) will be selected which show a statistically significant partial correlation with the parameters of therapeutic success at month 3 (improvements in the number of affected joints [DAS28], HAQ, number of missed working days, and WPAI). Due to the clear temporal relation between the baseline values and the treatment effects at month 3, the selected predictors can be interpreted both as causal explanation and as prognosing factors concerning therapy-modifying influencing variables (since an reactive influence of the 3-month values on the baseline values can be ruled out). Additionally, the strength of the relationship between the predictors and the parameters of therapeutic success will be determined. The impact of the variables determined by regression analysis on the therapeutic success will be illustrated by subgroup analysis. The impact of adalimumab therapy on health-related quality of life (EQ-5D), the number of physician visits and hospitalization, the days of impairment in non-occupational activities, and the subjective symptoms (morning stiffness, pain, exhaustion/fatigue) will be descriptively evaluated and additionally analyzed by between-group comparison. Two interim analyses are planned.
Planned recruitment phase	March 2009 - March 2012
Planned study duration	March 2009 – March 2018
Product manufacturer	Abbott

3 Abkürzungen und Definitionen

AE	Adverse event
AMG	Arzneimittelgesetz
BMI	Body Mass Index
CCP	Cyclic citrullinated peptide
CRF	Case Report Form
CRO	Clinical Research Organization
CRP	C-reactive protein
DAS28	Disease Activity Score 28
DMARD	Disease Modifying Anti-Rheumatic Drug
EQ-5D	EuroQol Questionnaire 5 Dimensions
ESR	Erythrocyte sedimentation rate
FAS	Full analysis set
HAQ	Health Assessment Questionnaire
Hb	Hemoglobin
MedDRA	Medical Dictionary for Regulatory Activities
NIS	Non-interventional study
RF	Rheumatoid factor
SAE	Serious adverse event
SAP	Statistical analysis plan
SDV	Source Data Verification
WPAI-GH	Work Productivity and Activity Impairment-General Health version



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5 Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints that often results in progressing joint destruction and lead to substantial functional losses, impairment, and reduced quality of life. On the social level, disease-related costs (due to lack of functionality) to be paid by social security systems are increasingly gaining priority (1), (2).

An important cytokine that activates and intensifies inflammation in RA is the tumor necrosis factor α (TNF- α). Introduction of TNF- α inhibitors 10 years ago revolutionized RA treatment options and led to the development of further recombinant antibodies and fusion products, respectively, which are called biologics. Adalimumab is one of these biologics, a human monoclonal antibody against TNF- α , which has been approved in Germany for RA treatment under the trade name HUMIRA® since 2003. Adalimumab inhibits the interaction of TNF- α with its receptors and thus suppresses the biological effect of this proinflammatory cytokine. HUMIRA® is administered as a subcutaneous (sc) injection at a recommended dose of 40 mg every other week.

Several clinical trials have shown that adalimumab both reduces the clinical symptoms of RA and decelerates the structural destruction of the joints, thus significantly improving health-related quality of life.

Patients who had been included in a non-interventional long term study and had been treated with adalimumab under conditions of routine rheumatology practice had been suffering from RA for many years (mean disease duration 12 years) and showed a high disease activity (DAS28 = 5.8). These patients experienced a significant reduction in clinical signs and symptoms of RA after 24 months of adalimumab therapy (interim analysis July 2007). 20 % of patients were in clinical remission and over 40 % had improved in their physical functionality.

Unlike the previous RA documentation, this NIS will put added emphasis on data concerning work productivity and work ability as well as data concerning health-related quality of life. This will result in an according large-scale patient documentation form.

In order to improve quality, all filled questionnaires will be checked for completeness and missing data will be added by written query. A defined percentage of participating physicians will be audited. An independent CRO will perform double data entry, perform plausibility checks and statistically evaluate the data according to criteria determined in the protocol. The results will be published after finalization of the evaluation.

The planned documentation is a non-interventional study (NIS) according to § 4 section 23, point 3, Arzneimittelgesetz (AMG) and will be conducted in compliance with the recommendations of the Verband der forschenden Arzneimittelhersteller (Association of Research-based Pharmaceutical Companies).

6 Rationale

This NIS is designed to provide additional data on treatment effects of adalimumab in the long term treatment in patients with moderate to severe active RA under conditions of routine rheumatology care. In contrast to clinical trials, all patients treated in clinical routine will be included in the NIS, independent of comorbidities, concomitant medication, severity of their illness, or features such as age and gender.

Course of work productivity and work ability, the course of health-related quality of life, and changes in functionality under long term treatment with adalimumab will be documented. The numbers of patients included in the NIS allow identifying and quantifying the impact of disease and patient characteristics on the therapeutic success.

7 Study Objectives

In this NIS, a long term documentation of treatment with adalimumab in RA patients over 60 months with 8 data collection points (visits) is planned. The documentation will be performed by the physician as well as by patient's self-assessment.

The primary objective is to explore the therapeutic success by interim analyses after 12 and 24 months of treatment as well as by the final analysis after 60 months of treatment. Improvements concerning the following target variables will be evaluated (with regard to the respective baseline value):

- the number of missed working days
- the self-assessed work ability (WPAI)
- the severity of clinical symptoms (number of tender and swollen joints, CRP and ESR, respectively; total score DAS28)
- Severity of functional impairment (HAQ)
- The health-related quality of life (EQ-5D)

At month 3, patient and disease characteristics will be evaluated with regard to their additional impact on changes in the number of affected joints (DAS28), in the HAQ, and in the WPAI. The impact on the number of missed working days will be evaluated at month 6.

The secondary objective is to document the therapeutic success by interim analyses at month 12 and 24 months as well as by the final analysis after 60 months. The therapeutic success will be evaluated by the following variables:

- The number of physician visits
- The number and duration of hospitalizations
- The number of days of impairment in non-occupational activities
- The duration of morning stiffness, pain, exhaustion/fatigue

-
- The reduction of number and dose of concomitant medication
 - Patient's assessment of adalimumab therapy compared to previous therapies

Target parameters for safety evaluation of adalimumab are:

- The evaluation of safety and tolerability by the documentation and analysis of serious adverse events (SAEs) and adverse events (AEs).
- Evaluation of safety and tolerability for subgroups of patients with common frequent concomitant diseases, especially diabetes type II, cardiovascular, liver, and renal insufficiencies, and related concomitant medications.

8 Investigational Plan

8.1 Selection of Study Population

This study population will consist of adult patients (≥ 18 years) with moderate to severe active rheumatoid arthritis (RA) who have failed other anti-rheumatic drugs including Methotrexat (MTX) and patients with a severe, active and progressive rheumatoid arthritis (with or without prior MTX).

Patients who have been previously treated with other biologics (including TNF inhibitors) can be included in the NIS.

The inclusion and exclusion criteria adhere to the approved label as stated in the German Summary of Product Characteristics (SPC) “Fachinformation” for HUMIRA®. No additional inclusion and exclusion criteria are applicable since this project is non-interventional.

Patients to be included will be informed about the NIS and the use of their anonymous data. Patients willing to participate must provide their written informed consent to the investigator before entry into the NIS. The signed informed consent form will be added to the patient’s file.

8.2 Number of Patients to be Enrolled

The NIS will include about 2500 patients in order to provide for the final evaluation of missed working days a sample size of $n = 850$ employed patients who are temporarily on sick leave during the study (see also Section 12.1 “Sample Size Calculation”).

8.3 Investigator Selection Criteria

The data for his NIS will be collected from rheumatology outpatient departments and office-based rheumatologists in Germany routinely treating patients with RA. Physicians from about 200 sites which are spread across all of Germany will participate in this NIS.

Principal Investigator:

[REDACTED]

[REDACTED]

8.4 Study Duration

The duration of the whole NIS is estimated to be about 9 years.

Study start: March 2009

Recruiting phase: March 2009 – March 2012

Data completion: March 2017

Data analysis and final report: March 2017 – March 2018

For each individual patient, the NIS starts with the enrollment in the long term documentation at the beginning of the treatment with adalimumab and ends either after 5 years or with the termination of the adalimumab therapy.

8.5 Study Conduct

8.5.1 Schedule of Observations

This NIS will be a single-arm, multi-center, prospective cohort study.

Non-interventional studies are one of several methodical instruments to collect information on drugs available on the market. Their defining characteristic is the lack of influence on the relationship between individual physicians and patients in respect to determining indication as well as choice and conduct of the treatment, while at the same time allowing for the structured and systematic collection of treatment data (see also Section 6). Adalimumab must not be prescribed for the purpose of including a patient in this NIS.

Patients will be informed about the type of therapy, alternate therapies, and risks, and they have to provide a written informed consent to the data collection on the documentation forms before the start of therapy. The presence of the written informed consent is documented on the base documentation form. Before enrollment in the NIS, the patients will be made anonymous. Abbott will only receive access to anonymous data. Abbott can only identify the patients via their patient number.

The visits are scheduled according to the recommendations of the Deutsche Gesellschaft für Rheumatologie (German Society for Rheumatology): The documentation consists of patient self-assessments as well as assessments by the physician. The following tables provide an overview of the observations to be documented by the physician ([Table 1](#)) and the patient ([Table 2](#)).

Due to long time intervals between the scheduled visits (one year after month 12), interim documentation forms will be provided for non-scheduled visits in order to document clinically significant events.



Table 1. Physician Schedule

	Month							
	0	3	6	12	24	36	48	60 ¹
Demographic data	X							
Inclusion criteria	X							
Indication HUMIRA®	X							
Medical history / change history	X	X	X	X	X	X	X	X
Radiologic findings ²	X			X	X	X	X	X
Previous RA therapies	X							
Concomitant diseases and therapies ³	X	X	X	X	X	X	X	X
Current HUMIRA® therapy ⁴	X	X	X	X	X	X	X	X
RA-related concomitant medication ⁴	X	X	X	X	X	X	X	X
Disease activity ⁵	X	X	X	X	X	X	X	X
Current joint status ⁵	X	X	X	X	X	X	X	X
Morning stiffness	X	X	X	X	X	X	X	X
Rheumatoid nodules	X							
Joint (replacement) surgery	X			X	X	X	X	X
Laboratory values: CRP, ESG, Hb-value, ⁶	X	X	X	X	X	X	X	X
Laboratory values: RF, CCP ⁶	X							
Laboratory values: Hepatitis B, Hepatitis C, tuberculosis screening, TB prophylaxis (if necessary) ⁶	X	X ⁷	X ⁷	X ⁷				
Adverse events		X	X	X	X	X	X	X
Patient's compliance		X	X	X	X	X	X	X

¹ Month 60 or last visit

² after baseline visit (month 0) only if current radiograph is available or if indicated

³ after baseline visit (month 0) only for newly developed diseases or changed therapy

⁴ after baseline visit only for changes in therapy or dose

⁵ Data are part of the DAS28 (Disease Activity Score)

⁶ after baseline visit (month 0) only if data is available or if indicated

⁷ only TB prophylaxis documented

Table 2. Patient Schedule

	Month							
	0	3	6	12	24	36	48	60
Personal data	X							
Education	X							
Professional status	X		X	X	X	X	X	X
Missed working days (last 6 months)	X		X	X	X	X	X	X
Physician visits and hospitalization (last 6 months)	X		X	X	X	X	X	X
Days of impairment in non-occupational activities	X		X		X	X	X	X
Work ability (WPAI)	X	X	X	X	X	X	X	X
Exhaustion/fatigue (last 7 days)	X	X	X	X	X	X	X	X
Pain (last 7 days)	X	X	X	X	X	X	X	X
Functionality (HAQ)	X	X	X	X	X	X	X	X
Health-related quality of life (EQ-5D)	X	X	X	X	X	X	X	X
Patient's assessment of adalimumab therapy compared to previous therapies		X	X	X	X	X	X	X
Participation Abbott Care service program	X	X	X	X	X	X	X	X

8.5.2 Description of Activities

The following data will be documented (if assessed in routine care):

Physician:

Baseline Visit (Month 0)

Demographics and History

Demographic Data (age, gender, height, weight)

Inclusion criteria (moderate to severe active RA and/or severe, active, and progressive RA, signed informed consent)

Exclusion criteria according to Fachinformation (hypersensitivity, active tuberculosis, other severe infections [e.g. sepsis, opportunistic infections], moderate to severe heart insufficiency [NYHA class III/IV])



Indication for the current HUMIRA® therapy

Radiological findings of affected joints

History (including initial diagnosis of RA and tobacco use)

Previous therapies: DMARD (MTX, SASP, leflunomid), glucocorticoids, biologics (infliximab, etanercept, rituximab, tocilizumab, abatacept), date of biologic discontinuation

Concomitant diseases and concomitant medication

Current RA therapy

Current HUMIRA® therapy

Additional DMARD, systemic glucocorticoids, analgetics, NSAID, COX inhibitors

Current status

Disease activity, joint status (28 joints, tender, swollen), morning stiffness, rheumatoid nodules, previous joint surgery

Laboratory values (RF, CCP, CRP, ESR, Hb-value, hepatitis B, hepatitis C, tuberculosis screening, TB prophylaxis, pregnancy test in women with childbearing potential)

Follow-up Visits (Month 3, 6, 12, 24, 36, 48, 60)

Change history

Current therapy (RA therapy and concomitant medication)

Disease activity

Joint status

Morning stiffness

Joint (replacement) surgery (beginning month 12)

Radiographic findings (beginning month 12)

Laboratory values (CRP, ESR, Hb-value, other laboratory values if indicated)

(S)AE

Patient's compliance

Patient:

Baseline Visit (Month 0)

Personal data

Education

Professional status

Missed working days, days of impairment in non-occupational activities

Physician visit, hospitalization

WPAI, HAQ, and EQ-5D

Exhaustion/Fatigue, pain
Participation in the Abbott Care service program

Follow-up Visits (Month 3, 6, 12, 24, 36, 48, 60)

WPAI, HAQ, and EQ-5D
Exhaustion/Fatigue, pain
Patient's assessment of adalimumab therapy
Participation in the Abbott Care service program

Follow-up Visits (Month 6, 12, 24, 36, 48, 60)

As above, additionally:
Missed working days, days of impairment in non-occupational activities
Physician visits, hospitalization
Changes in the professional status

8.5.3 Scales and Scores

The following scores will be derived from the documented data:

Disease Activity Score (DAS28): The DAS28 indicates the severity of the RA. The score varies between 0 and 10, with 10 indicating the highest degree of severity. The DAS28 is calculated from the following data documented on the physician form:

- Joint status: Number of swollen and tender joints (each with a maximum of 28)
- ESR (mm/1. h) or CRP (mg/l)
- Patient's assessment of current disease activity (from 0 = inactive to 10 = highly active)

The DAS28 is calculated by means of a validated algorithm (4), (5).

Health Assessment Questionnaire (HAQ): The HAQ is the internationally most-used instrument for assessing RA-related functional impairment. The patient has to answer 20 questions concerning impairment in daily activities within the following 8 areas:

- Dressing & Grooming
- Arising

-
- Eating
 - Walking
 - Hygiene
 - Reach
 - Grip
 - Activities

Patients assess their functionality over the past week by means of a 4-level scale ranging from 0 (without any difficulty) to 3 (unable to do). The highest (worst) values will be calculated into a mean value which indicates the degree of functional impairment (HAQ Disability Index: 0-3) (8).

WPAI: The WPAI is a questionnaire for the self-assessment of work productivity and activity impairment. In this observational study, the WPAI-GH is used which measures work productivity and activity impairment with reference to general health problems. All dimensions relate to the past seven days. The following dimensions are measured:

- Assessment of employment status
- Assessment of hours missed from work due to health problems and other reasons such as vacation or holidays (total number of hours to be indicated)
- Assessment of hours the patient has actually worked (total number of hours to be indicated)
- Assessment of impairment in work productivity and in regular daily activities (2 assessments with 10 levels each)

The WPAI yields four types of scores:

- ‘activity impairment’
- ‘absenteeism’ (work time missed)
- ‘presenteeism’ (impairment at work/reduced on-the-job effectiveness) and
- ‘work productivity loss’ (overall work impairment/absenteeism plus presenteeism).

Scores were transformed into percentages. Higher scores indicate greater impairment.

EuroQol-5 Dimensions (EQ-5D): The EQ-5D is a generic (not disease specific) instrument for measuring health-related quality of life. The patient questionnaire consists of two parts. The first part includes statements for the following five areas (dimensions):

- agility/mobility
- self-care
- usual activities
- pain, bodily discomfort
- anxiety, depression

For each dimension the patient is asked for a three-level assessment of his health on the current day: “no problems” (1), “some problems” (2), “extreme problems” (3). From the possible combinations of the five three-level areas result 241 different health-statuses.

The second part is a thermometer-scale (EQ-VAS) on which the patients rate their health on the current day between the endpoints “best health imaginable” (100) and “worst health imaginable” (0).

8.5.4 Study Medication

This is a non-interventional observational study with HUMIRA[®]. HUMIRA[®] is used according to the approved label for rheumatoid arthritis and is prescribed by the attending physician. Abbott does not provide any study medication.

HUMIRA[®]-injection is available as ready-to-use syringes and as pre-filled pen (injector, pre-filled/FertigPEN) and includes 40 mg adalimumab.

The recommended dose of HUMIRA[®] for adult patients with RA is 40 mg sc every other week.

9 Adverse Events

9.1 Adverse Event Definition and Serious Adverse Event Categories

An adverse event (AE) is defined as any untoward medical occurrence in a patient which does not necessarily have a causal relationship with their treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the labeling, as well as from accidental or intentional overdose, drug abuse, or drug withdrawal. Any worsening of a pre-existing condition or illness is considered an adverse event.

If an adverse event meets any of the following criteria, it is considered a **serious adverse event (SAE)**:

Death of Subject: An event that results in the death of a subject.

Life-Threatening: An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form

Hospitalization: An event that results in the admission to the hospital for any length of time. This does not include an emergency room visit or admission to an outpatient facility.

Prolongation of Hospitalization: An event that occurs while the study subject is hospitalized and prolongs the subject's hospital stay.

Congenital Anomaly: An anomaly detected at or after birth that results in fetal loss.

Persistent or Significant Disability/Incapacity: An event that results in a condition that substantially interferes with the activities of daily living of a study subject. Disability is not intended to include experiences of relatively minor medical

significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).

Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome: An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of subject, life-threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency of drug abuse.

Spontaneous Abortion: Miscarriage experienced by study subject.

Elective Abortion: Elective abortion performed on study subject.

9.2 Severity

The physician will use the following definitions to rate the severity for any adverse event being collected as an endpoint/data point in the study and for all serious adverse events:

Mild: The adverse event is transient and easily tolerated by the subject.

Moderate: The adverse event causes the subject discomfort and interrupts the subject's usual activities.

Severe: The adverse event causes considerable interference with the subject's usual activities and may be incapacitating or life-threatening.

9.3 Relationship to Pharmaceutical Product

The physician will use the following definitions for any adverse event being collected as an endpoint/data point the study and for all serious adverse events, to assess the relationship of the adverse event to the use of the pharmaceutical product:

Probably related: An adverse event has a strong temporal relationship to the study drug or recurs on re-challenge, and another etiology is unlikely or significantly less likely.

Possibly related: An adverse event has a strong temporal relationship to the study drug, and an alternative etiology is equally or less likely compared to the potential relationship to study drug.

Probably not related: An adverse event has little or no temporal relationship to the study drug, and/or a more likely alternative etiology exists,

Not related: An adverse event is due to an underlying or concurrent illness or effect of another drug and is not related to the study drug (e.g., has no temporal relationship to study drug or has a much more likely alternative etiology).

If an investigator's opinion of possibly, probably not, or not related to pharmaceutical product is given, **an alternate etiology must be provided by the investigator.**

9.4 Serious Adverse Event Collection Period

Serious adverse events will be reported to Abbott from the time the physician obtains the patient's authorization to use and disclose information (or the patient's informed consent) until 30 days or 5 half-lives following the intake of the last dose of physician-prescribed treatment.

9.5 Serious Adverse Event Reporting

In the event of a serious adverse event – whether or not related to Abbott product or comparator, if applicable – the physician will notify the Abbott drug safety identified below within 24 hours of the physician becoming aware of the event. The notification will be performed via fax on the form labeled “Bericht über Schwerwiegende Unerwünschte Arzneimittelwirkungen”:

**Arzneimittelsicherheit, Abbott GmbH & Co. KG,
Max-Planck-Ring 2
65205 Wiesbaden
Telephone ++ 49 6122 58 0**

9.6 Pregnancy Reporting

In the event of a pregnancy, the physician will notify the Abbott drug safety identified below within 24 hours of the physician becoming aware of the pregnancy. The notification will be performed via fax on the base documentation form:

**Arzneimittelsicherheit, Abbott GmbH & Co. KG,
Max-Planck-Ring 2
65205 Wiesbaden
Telephone ++ 49 6122 58 0**



Reported pregnancies will be reported like SAEs.

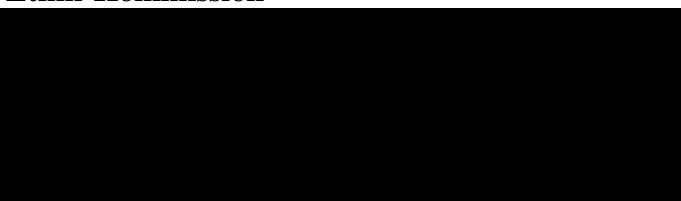
10 Ethics and Quality

In accordance to the code of conduct of the German pharmaceutical industry, the German principal coordinating investigator [REDACTED] will forward the NIS study protocol to the ethics committee for approval:

Ethik-Kommission bei der Med. Fakultät Universität Würzburg

Geschäftsstelle und Korrespondenzadresse:

Ethik-Kommission



The patient has to provide a written informed consent to use and/or disclose personal and/or health data before enrollment in the study. This written informed consent will be archived with the patient's file and documented on the report forms. According to § 67 section 6 AMG, the NIS will also be reported to the Kassenärztliche Bundesvereinigung (federal association of physicians), the umbrella organization of health insurance providers, and the responsible federal authority.

All patient data entered in the patient's CRF will be forwarded to Abbott GmbH & Co KG for evaluation - without naming the patient. Each CRF bears a pre-printed patient identification number, which replaces the patient's initials. The date of birth will be replaced by the patient's age at the start of the study. Accordingly, the patient's identity will not be disclosed to Abbott GmbH & Co. KG.

In-house monitoring of incoming CRF pages with respect to completeness and plausibility will be done by the CRO responsible for data management and statistics. Queries to the study centers will be handled by the sponsor.

Source data verification by the sponsor's monitor at the physician's site is planned for 5% of the documented patients. Informed consent, in- and exclusion criteria, and all available source data will be inspected.

This NIS will be sponsored by Abbott GmbH & Co. KG, Max-Planck-Ring 2, 65205 Wiesbaden, medizinische Abteilung.

11 Case Report Form

All data specified in Section 8.5 will be collected on paper forms (CRF). For each visit, the CRF includes forms to be completed by the physician as well as forms to be completed by the patient. Each center receives a folder with all documents and forms necessary for the baseline and follow-up documentation of five patients.

Any observation of an adverse event in the time period up to 60 months, beginning with the initiation of HUMIRA[®] therapy, is to be documented on the "Adverse Event" form labeled 'Bericht über unerwünschte Ereignisse' and checked for severity. If the event fulfills the serious criterion (Serious Adverse Event), the "Adverse Drug Reaction Report" form labeled 'Bericht über Schwerwiegende Unerwünschte Arzneimittelwirkungen' is to be completed additionally.

12 Data Analysis Plan

All statistical analysis procedures will be described in detail in a Statistical Analysis Plan (SAP). This plan will be developed by the responsible biometrician in collaboration with the sponsor. The SAP will be finalized and approved by the responsible biometrician, the sponsor, and the principle investigator before the database will be opened for the first interim analysis.

12.1 Sample Size Calculation

The primary parameter of this documentation is work productivity, which is captured by the number of missed working days. The sample size calculation is based on the results of an interim analysis of a documentation of adalimumab in RA with 4640 patients, of whom 1417 patients had been employed part time or full time. The mean number of missed working days was 26 days (standard deviation of 55 days) during the last 12 month prior to adalimumab therapy. The correlation between baseline and follow-up report is estimated with $r = 0.5$. According to these numbers, 850 employed patients are required to detect a mean difference of 5 days within 12 months at the 0.05 significance level (two-sided) with a power of 0.80. Since 30 % of patients are employed, a total number of about 2500 employed and non-employed patients are required in order to detect the specified difference in missed working days.

12.2 Analysis Population(s)

The data of all documented patients will be used in the statistical analysis of tolerability and safety of adalimuab. The data of patients whose RA had been treated with adalimuab previously will be excluded from the analysis of efficacy.

12.3 Missing Values

Missing observations will be documented as missing values. Instructions for the minimum documentation required for a patient to be evaluable will be established in the SAP.

All data will be analyzed on the basis of “observed cases”. For the statistical analysis of data concerning the course of disease, the health-related economic parameters and

the health-related quality of life (if related to changes from baseline values), an additional approach will be followed considering only patients with complete data at all visits.

12.4 Level of Significance

Inferential statistics will be performed at a nominal level of significance of 0.05 (two-sided). Due to the exploratory character of the analyses, the resulting p-values will not be adjusted for multiple testing.

12.5 Biometric Concept

The general biometric approach consists of the realization of the analyses described in section 7 “Study Objectives”. The analysis principally uses descriptive statistical methods, supported by regression statistical methods and subgroup analysis.

By forward and backward stepwise regression, those patient and disease characteristics (baseline values of all target parameters, disease duration, previous therapies, demographic and anthropometric data, health-related quality of life etc.) will be selected which show a statistically significant partial correlation with the parameters of therapeutic success at month 3 (improvements in the number of affected joints [DAS28], HAQ, number of missed working days, and WPAI). Due to the clear temporal relation between the baseline values and the treatment effects at month 3, the selected predictors can be interpreted both as causal explanation and as prognosing factors concerning therapy-modifying influencing variables (since an reactive influence of the 3-month values on the baseline values can be ruled out). Additionally, the strength of the relationship between the predictors and the parameters of therapeutic success will be determined.

The impact of the features determined by regression analysis on the therapeutic success will be illustrated by subgroup analysis. Subgrouping will be done according to content-related considerations: Regarding disease activity, patients will be classified into groups with high or low DAS28 values (lower and higher 5.1 units, respectively). Regarding age, patients will be classified into groups with high or low age (lower and higher 40 years, respectively).

The impact of adalimumab therapy on health-related quality of life (EQ-5D), the number of physician visits and hospitalizations, the days of impairment in non-occupational activities, and the subjective symptoms (morning stiffness, pain, exhaustion/fatigue) will be descriptively evaluated and additionally analyzed by between-group comparison.

The tolerability analysis will be based on MedDRA coded AEs and SAEs. Incidence rates will be reported on the “Preferred Term” and “System Organ Class” levels for all patients as well as for subgroups of patients with different degrees of disease activity as well as with different previous and concomitant therapies and diseases.

12.6 Times of Statistical Analyses

Interim analyses are planned after 3 and 5 years after the inclusion of the first patients, so that at month 12 and 24 sufficiently large groups of about 800 patients are available. The general analysis will be performed after closure of the follow-up of the last patient (8 years after starting the study).

13 Final Report and Publications

After the end of the NIS, an Integrated Final Report is generated in cooperation with the Principal Investigator, who also signs the report. The report includes a description of the objectives of the NIS, the employed methods, the results, as well as the conclusions. As the property of Abbott GmbH & Co. KG, the completed CRFs and the report are to be treated as confidential and may not be made accessible to unauthorized persons in any form (publication or presentation) without the explicit approval of Abbott GmbH & Co. KG. The results of this NIS may be published by Abbott GmbH & Co. KG or any of the participating investigators after approval by Abbott GmbH & Co. KG.



14 Literature

- (1) Lee, D.M., Weinblatt, M-E. (2001). Rheumatoid arthritis. *Lancet*; 358, 903-911.
- (2) Backman, C.L. (2004). Employment and work disability in rheumatoid arthritis. *Current Opinion in Rheumatology*; 16, 148-152.
- (3) Tony H.-P., Hein G., Richter C. et al. (2007). Adalimumab: Wirksamkeit und Sicherheit bei Patienten mit rheumatoider Arthritis in Deutschland: Zwischenauswertung der Langzeitdokumentation HUM03-1 im Alltag der rheumatologischen Praxis mit 4600 Patienten nach 24 Monaten Behandlung. *Zeitschrift für Rheumatology*, 60, Suppl. 1, S42.05.
- (4) Van der Cruyssen, B., Van Looy, S., Wyns, B. et.al. (2005). DAS28 best reflects the physician's clinical judgment of response to infliximab therapy in rheumatoid patients: validation of the DAS28 score in patients under infliximab treatment. *Arthritis Research & Therapy*; 7, R1063-R1071.
- (5) Van der Heijde, D.M.F.M., van 't Hof, M.A., van Riel, P.L.C.M. et al. (1990). Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. *Annals of the Rheumatic Diseases*; 49, 916-920.
- (6) Fries, J.F., Spitz, P., Kraines, R.G., Holman, H.R. (1980). Measurement of patient outcome in arthritis. *Arthritis Rheum*; 23, 137-145

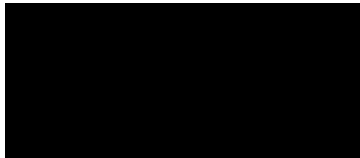


Documentation Plan AGIL
(GER-08-05)

Long term Documentation of the Safety and Efficacy as well as the Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis under HUMIRA® (Adalimumab) in Routine Clinical Practice (AGIL)

Responsibilities:

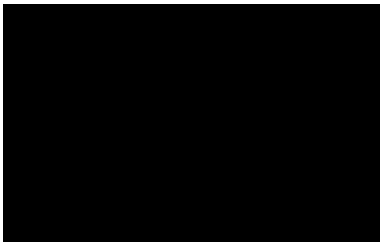
Protocol author:



Date

Signature

Study-designated physician:



Date

Signature

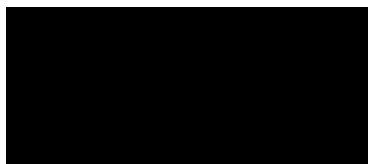
Representative from Statistics:

N.N.

Date

Signature

Affiliate Medical/Scientific Director:



Date

Signature

I hereby confirm that I have read and agreed this protocol and that I will conduct the study in compliance with this protocol.

Investigator:

N.N.

Date


Signature


(Original – 2 copies)

Appendix 2 AGIL-CV Amendment (English Translation)

Supplementary documentation AGIL-CV to record cardiovascular and metabolic risk factors in RA patients treated with adalimumab in routine clinical practice

Amendment I (dated 06-Mar-2012) of the observational plan AGIL GER 08-05 (17-May-2010)

This non-interventional study is to be conducted according to this observational plan. 






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Abbreviations and Definitions

Extension of the list of AGIL abbreviations:

dcrit	Critical difference
ESCCA	EULAR Standing Committee for Clinical Affairs
EULAR	European League Against Rheumatism
HDL cholesterol	High-density lipoprotein cholesterol
LDL cholesterol	Low-density lipoprotein cholesterol
LOCF	Last observation carried forward
SCORE	Systematic Coronary Risk Evaluation

1 Changes to the observational plan

1.1 Introduction

Introduction: AGIL-CV as a supplement to AGIL:

Amendment I describes the collection and analysis of cardiovascular and metabolic risk parameters in patients with rheumatoid arthritis (RA) determined in the course of additional documentation to NIS AGIL.

RA patients have increased cardiovascular morbidity and mortality as compared to the overall population. Furthermore, the majority of premature deaths in RA patients are attributable to cardiovascular disease (1), (2). RA patients show a higher cardiovascular risk, which can be put down to a higher prevalence of traditional risk factors (e.g. hypertension, dyslipidemia, smoking (3) as well as the underlying systemic inflammation, which play a key role in the development and progression of arteriosclerosis (4). Markers of inflammation are independent predictors of cardiovascular death (5). The systemic inflammation may even be the key process leading to myocardial infarction and premature death (6). RA is also associated with a pro-atherogenic lipid profile: Low HDL cholesterol levels are observed, which lead to an unfavorable cholesterol ratio (total cholesterol/HDL cholesterol) (7), (8). The prevalence of cardiovascular disease in RA is increased to an extent that is comparable to that of type 2 diabetes (9). Accordingly, RA should be regarded as an independent cardiovascular risk factor, and regular cardiovascular risk screening and management is therefore needed (1).

As TNF plays a significant role in the development of inflammatory processes, the inflammatory process of arteriosclerosis may be interrupted by inhibiting this cytokine. Studies show that early initiation of effective therapy is associated with a decreased cardiovascular risk (6), (10), (11).

The Standing Committee for Clinical Affairs of the European League Against Rheumatism ([EULAR], ESCCA) thus issued evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis that stress the implication of adequate control of disease activity and annual examinations to assess the cardiovascular risk (1).

Rheumatologists implementing these recommendations in everyday practice can routinely record their RA patients' cardiovascular and metabolic risks using this documentation.

1.2 Rationale

Rationale and considerations regarding objectives of AGIL-CV in addition to AGIL:

This supplementary documentation serves to record cardiovascular and metabolic risk factors in RA patients prior to starting adalimumab treatment in a routine clinical setting. In addition, the course of these risk factors and the impact of the disease activity on this course are to be documented during the 60-month adalimumab treatment.

1.3 Research question

Description of study aims AGIL-CV as a supplement to AGIL:

The **primary research questions of AGIL-CV** are

- To determine baseline changes in Months 12, 24 and 60 after starting adalimumab treatment with regard to the following primary cardiovascular and metabolic parameters:
 - Lab chemistry blood parameters for glucose and lipid metabolism
 - Vital signs
 - Body measurements
- The comparison between DAS28 responders and DAS28 nonresponders in terms of the primary parameters "lab chemistry blood parameters for glucose and lipid metabolism" and "vital signs"
- Determination of the time point and frequency of cardiovascular events in the course of the entire documentation

The secondary **research question** addresses the investigation of the impact of the

personal data and familial medical history recorded at baseline on the previously specified cardiovascular and metabolic parameters. The Systematic Coronary Risk Evaluation (SCORE) risk model is applied to determine the individual risk and changes thereof over time.

1.4 Number of patients to be included in AGIL-CV

Patient number required for the AGIL-CV research question in addition to AGIL

At least N=300 RA patients are required for the study to evaluate the cardiovascular and metabolic changes. This number takes premature therapy discontinuation by 50% of patients up to Month 60 into account (see Section 1.9).

1.5 Physician's selection criteria AGIL-CL

Additional selection criteria for the conduct of AGIL-CV:

The data for additional documentation of cardiovascular and metabolic risk factors are collected at selected sites that determine the cardiovascular risk profile as a routine measure for monitoring RA patients. All of these sites participate in NIS AGIL.

1.6 Course of long-term AGIL-CV documentation

Additional supplement of AGIL-CV:

This non-interventional study (**including Amendment I**) is conducted as a single-arm, multi-center, prospective cohort study.

Table 1 "Physician's overview" is supplemented by the following sub-table that shows the process of medical documentation for AGIL-CV.

Table 1 Physician's overview – collection of cardiovascular and metabolic risk factors

	Month							
	0	3	6	12	24	36	48	60 ¹
Body measurements (weight, height, waist and hip circumference) ²	X	X	X	X	X	X	X	X
Familial medical history (diabetes, obesity, premature cardiovascular disease)	X							
Tobacco use	X	X	X	X	X	X	X	X
Alcohol consumption	X	X	X	X	X	X	X	X
Vital signs ³	X	X	X	X	X	X	X	X
Documentation of cardiovascular events (myocardial infarction, stroke)	X	X	X	X	X	X	X	X
Laboratory parameters (fasted) ^{3,4}	X	X	X	X	X	X	X	X

¹ Month 60 or last visit

² Height is only determined at Month 0.

³ Data are incorporated into the SCORE risk model.

⁴ Glucose (serum or plasma), lipid profile (HDL cholesterol, LDL cholesterol, total cholesterol, triglycerides, CRP)

1.7 Description of study activities

Description of data to be documented for AGIL-CV as a supplement to AGIL:

Baseline examination (Month 0) to determine cardiovascular risk factors

Body measurements

Weight, height

Waist and hip circumference (waist measured 5 cm above anterior superior iliac spine)

Familial medical history

Parents' medical history: Diabetes mellitus and obesity
Premature cardiovascular disease in the family

Tobacco and alcohol

Tobacco use

Alcohol consumption

Vital signs

Blood pressure (in a sitting position, after 3-minute rest period)

Pulse (in a sitting position, after 3-minute rest period)

Laboratory parameters

Glucose after fasting (serum or plasma)

Lipid profile after fasting (HDL cholesterol, LDL cholesterol, total cholesterol, triglycerides)

CRP

Documentation of cardiovascular events

Myocardial infarction

Stroke

Examinations over the course of the study (Month 3, 6, 12, 24, 36, 48, 60) to determine cardiovascular risk factors

Body measurements (except height)

Vital signs

Laboratory parameters

Tobacco use

Documentation of cardiovascular events

1.8 Calculation of CV risk model

In addition to the documentation tools described in AGIL:

SCORE (Systematic Coronary Risk Evaluation): The SCORE risk model is routinely used in European clinical practice to manage cardiovascular diseases. It permits a direct estimate of the absolute ten-year risk of fatal cardiovascular disease events. This ten-year risk calculation is based on the conditional probability of cardiovascular mortality within the next ten years, provided that the patient survives up to the index age (13).

The estimate is based on the absolute cardiovascular disease risk rather than just on the risk of coronary heart disease. The following parameters are used to calculate the score:

- Age
- Sex
- Currently smoker/non-smoker
- Systolic/diastolic blood pressure (in a sitting position, after 3-minute rest period)
- Cholesterol ratio (total cholesterol/HDL cholesterol)

The overall risk of fatal cardiovascular disease is calculated by combining two different risk estimates:

- Coronary heart disease
- Non-coronary atherosclerotic vascular disease

This calculation determines a probability score of fatal cardiovascular disease within the next ten years ranging from "< 1%" to "15% and over".

Risk models are to be modified for RA patients by applying a multiplication factor of 1.5 if a patient meets at least two of the following three criteria (1):

- Disease duration of over ten years
- Positive RF or positive anti-CCP antibody result
- Presence of certain extra-articular manifestations

1.9 Sample size estimation

Sample size estimation for AGIL-CV as a supplement to AGIL:

The sample size estimation is based on published data concerning the blood pressure of RA patients (14):

Assuming an alpha and beta error of 5% each, the following minimum number of RA patients is required at the evaluation time points of Months 12, 24 and 60:

- N=128 patients are required in order to detect a mean systolic blood pressure difference of 10 mmHg (given a mean systolic blood pressure of 128 mmHg with a standard deviation of 18 mmHg).
- N=136 patients are required in order to detect a mean diastolic blood pressure difference of 5 mmHg (given a mean diastolic blood pressure of 74 mmHg with a standard deviation of 11 mmHg).

In documentations with adalimumab, premature discontinuation has been observed for approx. 50% of patients in the course of a 60-month documentation duration. If this rate is taken into account; an overall number of N=300 patients is sufficient to address the primary research questions given the above-named estimations.

1.10 Biometrics concept of AGIL-CV

Biometrics concept as an addition to AGIL-CV:

Using stepwise regression analyses with forward and backward techniques, all partial correlations between the primary parameters and the other disease and patient characteristics are determined at baseline. The impact of disease and patient characteristics on the changes in each of the primary parameters is established by means of these regression analyses at Months 12, 24 and 60. In particular, the DAS28 response (defined as the critical difference [dcrit] of ≤ -1.8 points, constituting an improvement of 1.8 points in DAS28) or DAS28 nonresponse was used as a coded variable.

In addition, the observed difference between the DAS28 responders (patients with a dcrit of ≤ -1.8 at 5 of 7 visits) and the DAS28 nonresponders (dcrit > -1.8) is tested using the general linear model. Missing data are replaced using the Last observation carried forward (LOCF) method.

1.11 Time points of statistical analysis

Analysis time point of AGIL-CV as a supplement to AGIL:

Statistical analyses for the primary research questions are planned for Months 12, 24 and 60. For the secondary research questions, previous cardiovascular results are taken into account at these analysis time points.

1.12 References

The following references are to be added to the list:

- (1) Peters, M.J.L., Symmons, D.P.M, Mcarey, D., et al. (2010). EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. *Ann Rheum Dis*; 69(2), 325-331.
- (2) Del Rincon, I.D., Williams, K., Stern, M.P., et al. (2001). High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. *Arthritis Rheum*; 44(12), 2737-2745.
- (3) Han, C., Robinson, D.W.J., Hackett, M.V., et al. (2006). Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *J Rheumatol*; 63(11), 2167-2172.
- (4) Ross, R. (1999). Atherosclerosis-an inflammatory disease. *N Engl J Med*; 340(2), 115-126.
- (5) Maradit-Kremers, H., Nicola, P.J., Crowson, C.S., et al. (2005). Cardiovascular death in rheumatoid arthritis: a population-based study. *Arthritis Rheum*; 52(3), 722-732.
- (6) Dixon, W.G., Watson, K.D., Lunt, M., et al (2007). Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor-alpha therapy: results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum*; 56(9), 2905-2912.
- (7) Park, Y.B., Lee, S.K., Lee, W.K., (1999). Lipid profiles in untreated patients with rheumatoid arthritis. *J Rheumatol*; 26(8), 1701-1704.
- (8) Vis, M., Nurmohamed, M. T., Wolbink, G., et al (2005). Short term effects of infliximab on the lipid profile in patients with rheumatoid arthritis. *J Rheumatol*; 32(2), 252-255.
- (9) Van Halm, V.P., Peters M.J., Voskuyl, A.E., et al. (2009). Rheumatoid arthritis versus type 2 diabetes as a risk factor for cardiovascular disease: a cross-sectional study. *Ann Rheum Dis*; 68(9), 1395-1400.
- (10) Popa, C., Netea, M.G., Radstake, T. et al. (2005). Influence of anti-tumor necrosis factor therapy on cardiovascular risk factors in patients with active rheumatoid arthritis. *Ann Rheum Dis*; 64(2), 303-305.
- (11) Jacobsson, L.T., Turesson, C., Gulfe, A., et al. (2005). Treatment with tumor necrosis factor blockers is associated with a lower incidence of first cardiovascular events in patients with rheumatoid arthritis. *J Rheumatol*; 32(7), 1213- 1218.



- (12) Naranjo, A., Sokka, T., Descalzo, M.A., et al. (2008). Cardiovascular disease in patients with rheumatoid arthritis. Results from the QUEST-RA study. *Arth Res Ther*; 10(2), R30.
- (13) Conroy, R.M., Pyorala, K., Fitzgerald, A.P, et al. (2003). Estimation of ten-year risk of fatal cardiovascular disease in Europe. The SCORE project. *EIR Heart J*; 24(11), 987-2003.
- (14) Mok CC, Ko GT, Ho LY, et al. (2011). Prevalence of atherosclerotic risk factors and the metabolic syndrome in patients with chronic inflammatory arthritis. *Arthritis Care Res (Hoboken)*. Feb;63(2):195-202.

Appendix 3 Case Report Form (English Translation Excerpt)

Physician Documentation

Patient-No.:

At baseline - Month 0

Date:

Day		Month		Year	

- Patients with rheumatoid arthritis -

Doctor 's Seal

Inclusion Criteria

		yes	no												
1. Diagnosis	confirmed moderate to severe rheumatoid arthritis and/or severe, active and progressive rheumatoid arthritis	<input type="radio"/>	<input type="radio"/>												
2. Informed consent	Written informend consent signed on	<table border="1"> <tr> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> <td style="width: 20px; height: 20px;"></td> </tr> <tr> <td colspan="2">Day</td> <td colspan="2">Month</td> <td colspan="2">Year</td> </tr> </table>								Day		Month		Year	
Day		Month		Year											

All inclusion and all exclusion criteria, such as moderate to severe heart insufficiency (NYHA III/IV) and severe infections (e.g. Sepsis, opportunistic infections), listed in the Fachinformation for HUMIRA® met.

If the inclusion and exclusion criteria are not completely complied, the patient cannot participate on the study!

Demographic Data

Age Years Gender male female

Height cm Weight kg

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Tobacco consumption**Tobacco consumption**

no yes, please specify package years (1 package year ist defined as daily consumption of one packet of cigarettes including 20 cigarett more than 1 year)

Initial diagnosis

Date of initial diagnosis of rheumatoid arthritis

Day/ Month / Year**Diagnosis criteria****Radiological finding**

Date of current radiography (hands, forefeet)?

Month / YearErosive changes? no yes

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Previous therapy

from to continuing

Previous DMARD

- | | | | | | | | | | | | |
|-------------------------------------|--|--|--|--|--|--|--|--|--|--|-----------------------|
| <input type="radio"/> MTX | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | <input type="radio"/> |
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Previous glucocorticoids

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Previous biologic therapy

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| <input type="radio"/> Etanercept | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | |
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| <input type="radio"/> Rituximab | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | |
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| <input type="radio"/> Tocilizumab | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | <table border="1" style="width: 100%; height: 20px;"> <tr><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td><td style="width: 25%;"></td></tr> </table> <p style="text-align: center; font-size: small;">Month / Year</p> | | | | | |
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Last biologic therapy before HUMIRA® discontinued because of:

- Intolerance/ contraindication of therapy
- no primary response to treatment
- loss of efficacy despite initial effect
- Other reason: _____

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Concomitant diseases and their therapy

	Currently present	Medical treatment?	Compound	Dose
Arterial hypertension	<input type="radio"/>	<input type="radio"/>	_____	_____
Coronary heart disease	<input type="radio"/>	<input type="radio"/>	_____	_____
Stroke	<input type="radio"/>	<input type="radio"/>	_____	_____
Hyperlipoproteinemia	<input type="radio"/>	<input type="radio"/>	_____	_____
Diabetes Type I	<input type="radio"/>	<input type="radio"/>	_____	_____
Diabetes Type II	<input type="radio"/>	<input type="radio"/>	_____	_____
Chronic obstructive pulmonary disease	<input type="radio"/>	<input type="radio"/>	_____	_____
Osteoporosis	<input type="radio"/>	<input type="radio"/>	_____	_____
Degenerative arthropathy	<input type="radio"/>	<input type="radio"/>	_____	_____
Degenerative spine disease				
Mental disorders (z.B. depression)				
Other diseases, in particular autoimmune diseases and/or neurological diseases (please list)	<input type="radio"/>		_____	_____
_____	<input type="radio"/>		_____	_____
_____	<input type="radio"/>		_____	_____
_____	<input type="radio"/>		_____	_____
_____	<input type="radio"/>		_____	_____

Indication for current HUMIRA®-Therapie (multiple answers possible)

- high disease activity
- lack of efficacy in previous therapy
- Intolerance of previous therapy
- rapid radiological progression
- others: _____

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Current HUMIRA®-Therapie

Begin of therapy:

--	--	--	--	--	--

Day / Month / Year

Dose

 mg/Apl.

every other week other: _____

Current RA concomitant medication

Any DMARD additional to HUMIRA® ?

yes no

Dose (mg)

MTX

,

 /w

SASP

 /d

Leflunomid

 /d

others: _____

 /d

Any systemic glucocorticoid?

yes no

Equivalent to prednisolone
(estimated average of daily dose)

--	--	--	--

 mg/d

Any other therapies?

yes no

Compound

Dose

NSAIDs, COX inhibitors _____

Analgetics _____

others: _____ _____

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Disease activity

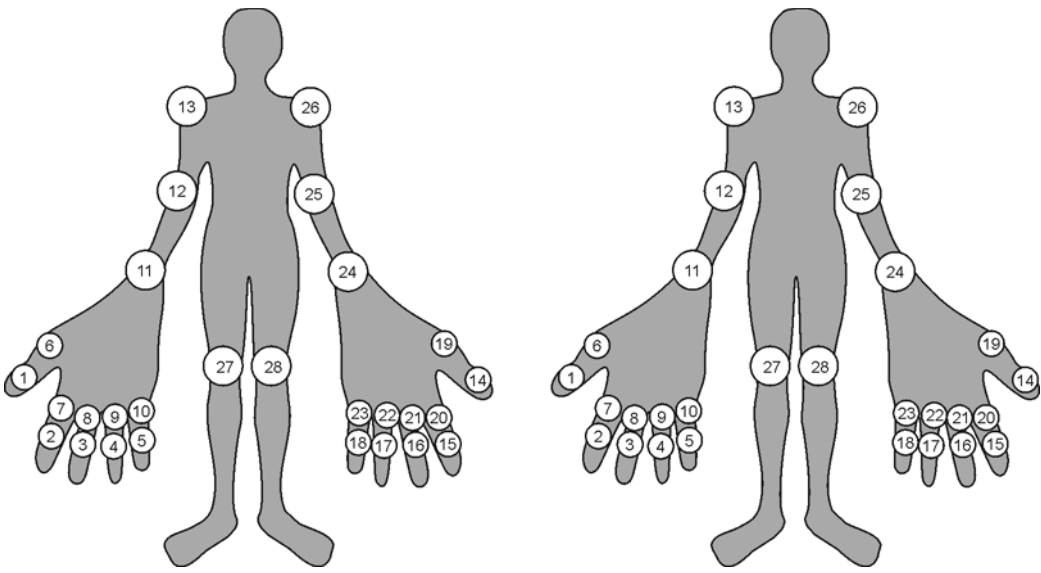
According to patient's self-assessment, how active is the disease currently?

inactive 0 1 2 3 4 5 6 7 8 9 10 highly active

Current Joint Status (Please tick tender and swollen joints)

tender

swollen



None of these 28 joints is tender

None of these 28 joints is swollen

Is morning stiffness present? no yes, please specify min.

Do rheumatoid nodules exist? no yes

Previous joint surgery? no yes, please specify joint(s) and type of surgery

1. _____
2. _____
3. _____

Physician Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Current baseline status - Laboratory*

Diagnostic paramters

RF negative positive
 CCP negative positive

Inflammation markers

CRP mg/l **Attention! Unit is mg/l, no comma!**
 ESR mm/h
 Hb g/dl

Infections

Hepatitis B negative positive
 Hepatitis C negative positive

Latent tuberculosis?

no yes

if yes, prophylaxis conducted?

no yes

Pregnangy test

(women with chidlbearing potential only)

negative positive

Begin of prophylaxis
 Day/ Month / Year

End of prophylaxis
 Day / Month / Year

Other labratory values, **only if outside normal range only!**

Parameter	Normal range	Result	Unit

* If performed

I hereby confirm the accuracy of the information on pages 1 - 7.

Date
 Day / Month / Year

Signature 195

Long term Documentation of the Safety and Efficacy as well as the Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis under HUMIRA® (Adalimumab) in Routine Clinical Practice (AGIL)

Information for Participating Patients

Dear patient,

For the treatment of your inflammatory rheumatic disease, a long term drug therapy will be used with the drug HUMIRA® of the company Abbott GmbH & Co. KG. All clinical trials have shown that this drug is effective, safe, and well-tolerated. To block your inflammatory rheumatic disease effectively in the long term, a continued therapy will be usually necessary. To document the occurrence of seldom adverse drug reactions, which can occur even in well-tolerated drugs, a long term observation of a large number of patients is necessary. This can only be achieved by the cooperation of many physicians and patients. Therefore, your attending physician participates in a documentation of the long term efficacy and tolerability of HUMIRA® initiated by the company Abbott GmbH & Co. KG.

From all patients for whom a therapy with HUMIRA® is newly initiated, anonymous data about disease progression and side effects will be collected and centrally analyzed. Therefore, your attending physician will document data on your course of disease, your treatment, and the disease activity of your inflammatory rheumatic disease.

Data/Privacy protection

The data will be documented anonymously. Circulation of the data is subject to patient/physician confidentiality as well as the rules and regulations of the Federal Data Protection Act and the State Data Protection Acts, respectively. On no account, any conclusion can be drawn from the data concerning your name and your personal circumstances.

As appropriate, the collected data may be forwarded to the Abbott GmbH & Co. KG or to a CRO which is charged with scientific evaluation by the Abbott GmbH & Co. KG without naming the patient. The anonymous data will be saved for 10 years.

A representative authorized by the Abbott GmbH & Co. KG, and the authorities in charge, respectively who is bound to professional secrecy can search the patient's file at the physician's site as appropriate.

Your physician will ask you today to complete a questionnaire on your health, the influence of your disease on your everyday life and your professional status at the beginning of the therapy and in regular intervals thereafter. The observation period is scheduled to last five years.

The long term documentation will not affect your treatment. You will neither be subjected to additional investigations nor will you receive a treatment different from what your physician has planned.

Of course, your participation is voluntary. If you choose not to participate or if you revoke your consent at a later date, you will suffer no disadvantages.

We ask you to carefully read the attached informed consent form and - upon agreement - to sign it. The informed consent form will remain with your attending physician and will not be forwarded. A copy will remain with you.

Thank you for your assistance!

Long term Documentation of the Safety and Efficacy as well as the Effects on Quality of Life and Work Productivity in Patients with Rheumatoid Arthritis under HUMIRA® (Adalimumab) in Routine Clinical Practice (AGIL)

Informed Consent

I have read the information page "long term documentation of rheumatoid arthritis" and I am willing to participate in the long term documentation under the following provisions:

The documentation of data will be anonymous.

The long term documentation will not influence the diagnostics and therapy of my disease.

I agree that data on my health collected within the limits of this long term documentation are documented anonymously on documentation forms and electronic data carriers, are processed and forwarded to Abbott GmbH & Co. KG or to a CRO which is charged with scientific evaluation by the Abbott GmbH & Co. KG. The anonymous data will be saved for ten years.

I agree that a representative authorized by the Abbott GmbH & Co. KG. and the authorities in charge, respectively who is bound to professional secrecy can search the patient's file at the physician's site as appropriate.

I have understood the contents of this informed consent and I agree with the described procedure.

A copy of the informed consent will remain with me.

(Please write in clearly legible block characters!)

Patient

Physician

Last name/surname

Last name/surname

Date

Date

Signature

Signature

Doctor's Seal

Personal Data

Age: YearsGender: m f

On the following pages, you will find a set of questions concerning your state of health and the impact of your disease on both your everyday life and your professional situation. Please answer these questions thoroughly. In case you have problems understanding or answering certain questions, please ask your physician or the office employees. All of the collected data will be anonymously analyzed with scientific methods and are designated to improve the health care situation of patients suffering from psoriasis. Thank you for your cooperation.

General Information

Which is your highest school-leaving qualification?

- no school-leaving qualification
- Hauptschulabschluss (qualifying lower secondary general education certificate)
- Realschulabschluss (mittlere Reife) (secondary school level I certificate)
- Fachhochschulreife / Allgemeine Hochschulreife (Abitur) (university-entrance diploma)

Which professional education have you acquired?

multiple answers possible

- none
- semi-skilled
- vocational training (school)
- dual vocational training (school and industrial)
- advanced vocational training
- University of applied sciences diploma
- University diploma

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

General Information (continued)**How is your current professional situation?**

- Employed full time (35 hours and more)
 Part time or per hour employed
 School / training / univeristy/ retraining
 Household / Upbringing
 Unemployed
 Retired

If you are retired: Are you early-retired due to your rheumatic disease?

- no yes

Which occupational status do you currently have?

- employed civil servant (tenure) executive position self-employed

Days of impairment

During the past **6 months**, have you been noticeably restrained in your non-occupational activities and duties due to your rheumatoid arthritis?

Household: no yes, altogether days

Upbringing: no yes, altogether days

Education: no yes, altogether days

Leisure time: no yes, altogether days

Missed working days

If you are working full time or part time, have you been on sick leave **due to your rheumatoid arthritis within the past six months?**

- no yes, altogether missed working days

How long due to **joint surgery?**

- none missed working days

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Consultation und Hospitalization

During the past **6 months**, have you been under medical treatment? no yes

If so, please provide the following information.

	Frequency during the past 6 Months	Total time
Visits to the rheumatologist	<input type="text"/>	---
Visits to the general practitioner	<input type="text"/>	---
Visits to the orthopedist	<input type="text"/>	---
Visits to other medical specialists	<input type="text"/>	---
Hospital treatment	<input type="text"/>	<input type="text"/> Days
Treatment at a health resort, inpatient rehabilitation	<input type="text"/>	<input type="text"/> Days
Physical therapy	<input type="text"/>	<input type="text"/> Days

Work Productivity and Activity Impairment General Health Questionnaire

The following questions ask about the effect of your health problems on your ability to work and perform regular activities. By health problems we mean any physical or emotional problems or symptom.
Please fill in the blanks or tick a number, as indicated.

1. Are you currently employed (working for pay)? no yes
If NO, check "no" and skip to question 6.

The next questions are about the **past seven days**, not including today.

2. During the past seven days, how many hours did you miss from work because of **your health problems**? Include hours missed on sick days, times you went in late, left early, etc., because of your health problems.

_____ Hours

3. During the past seven days, how many hours did you miss from work because of any other reasons, such as vacation or holidays?

_____ Hours

4. During the past seven days, how many hours did you actually work?

_____ Hours (If "0", skip to question 6.)

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Work Productivity and Activity Impairment General Health Questionnaire (continued)

5. During the past seven days, how much did your health problems affect your productivity **while you were working**?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If health problems affected your work only a little, choose a lower number. Choose a higher number if health problems affected your work a great deal.

Consider only how much **health problems** affected productivity **while you were working**.

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

6. During the past seven days, how much did your health problems affect your ability to do your regular activities, other than work at a job?

By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If health problems affected your work only a little, choose a lower number. Choose a higher number if health problems affected your work a great deal.

Consider only how much **health problems** affected productivity **while you were working**.

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Current physical condition

How much have you been suffered by abnormal exhaustion and fatigue **during the past 7 days**?

none

 strongly

How would you evaluate your pain during the past 7 days?

During the past 7 days, I had

no pain

 unbearable pain

Participation in the "Abbott Care" - service program

Do you participate in the "Abbott Care" service program?

No
 Yes

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Health Assessment Questionnaire (HAQ)

Please place an "x" in the box which best describes your abilities **over the past week:**

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
DRESSING AND GROOMING				
Are you able to:				
- Dress yourself, including shoelaces and buttons?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Shampoo your hair?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ARISING				
Are you able to:				
- Stand up from a straight chair?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Get in and out of bed?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
EATING				
Are you able to:				
- Cut your own meat?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Lift a full cup or glass to your mouth?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Open a new milk carton?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
WALKING				
Are you able to:				
- Walk outdoors on flat ground?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Climb up five steps?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Please check any AIDS OR DEVICES that you usually use for any of the above activities:				
<input type="radio"/> Cane	<input type="radio"/> Devices used for Dressing (button hook, zipper pull, etc.)			
<input type="radio"/> Walker	<input type="radio"/> Built up or special utensiles			
<input type="radio"/> Crutches	<input type="radio"/> Special built up chair			
<input type="radio"/> Wheelchair	<input type="radio"/> Others (which): _____)			
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:				
<input type="radio"/> dressing and grooming	<input type="radio"/> Eating			
<input type="radio"/> Arising	<input type="radio"/> Walking			

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Health Assessment Questionnaire (HAQ) (continued)

Please place an "x" in the box which best describes your abilities **over the past week**:

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
HYGIENE				
Are you able to:				
- Wash and dry your body?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Take a tub bath?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Get on and of the toilet?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from above your head?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Bend down to pick up clothing from the floor?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GRIP				
Are you able to:				
- Open car doors?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Open previously opened jars?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Turn faucets on and off?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ACTIVITIES				
Are you able to:				
- Run errands and shop?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Get in and out of a car?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Do chores such as vacuuming or yard work?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Please check any AIDS OR DEVICES that you usually use for any of the above activities:				
<input type="radio"/> Raised toilet seat	<input type="radio"/> Bathtub bar			
<input type="radio"/> Bathtub seat	<input type="radio"/> Long-handled appliances in bathroom			
<input type="radio"/> Jar opener (for jars previously opened)	<input type="radio"/> Long-handled appliances for reach			
	<input type="radio"/> Others (which): _____)			
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:				
<input type="radio"/> Hygiene	<input type="radio"/> Gripping and opening things			
<input type="radio"/> Reach	<input type="radio"/> Errands and chores			

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Health Status Questionnaire (EQ-5D)

By placing a tick in one box in each group below, please indicate which statement best describes your own health state today.

EQ 1. MobilityI have no problems in walking around I have some problems in walking around I am confined to bed **EQ 2. Self-Care**I have no problems in self-care I have some problems washing or dressing myself I am unable to wash or dress myself **EQ 3. Usual Activities (e.g. work, study, housework, family, or leisure activities)**I have no problems with performing my usual activities I have some problems with performing my usual activities I am unable to perform my usual activities **EQ 4. Pain / Discomfort**I have no pain or discomfort I have moderate pain or discomfort I have extreme pain or discomfort **EQ 5. Anxiety / Depression**I am not anxious or depressed I am moderately anxious or depressed I am extremely anxious or depressed

Patient Documentation

Patient-No.:

At baseline - Month 0

- Patients with rheumatoid arthritis -

Health Status Questionnaire (EQ-VAS)

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health state is today, in your opinion. Please do this by drawing a line from the box below to whichever point on this scale indicates how good or bad your health state is today.

Your own health state today

Best imaginable health state

100

90

80

70

60

50

40

30

20

10

Worst imaginable health state

0

205

Physician Documentation

Patient-No.:

Follow-Up Visit - Month 3

Date:

Day		Month		Year	

- Patients with rheumatoid arthritis -

Doctor 's Seal**Change History****Did any infections occurred since the last visit?**

no yes

If yes, which one? _____

Has the patient become pregnant?

no yes month of pregnancy

Outcome: abortion spontaneous miscarriage unknown
 normal delivery

Others: _____

Did any adverse events (AE)/serious adverse events (SAE) occur since the last visit?

no yes

If yes, please complete the additional form "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" (report about adverse events/ serious adverse events).

How do you rate the patient's compliance?

very good rather good rather poor very poor

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Physician Documentation

Patient-No.:

Follow-Up Visit - Month 3

- Patients with rheumatoid arthritis -

Changes in HUMIRA®-therapy

Has the HUMIRA®-therapy been changed?

- no
- yes If yes, please indicate the treatment changes below

Dose mg/ Date of change: Day / Month / Year

Has the HUMIRA®-therapy temporarily been discontinued?

- no
- yes If yes, please indicate below

Period of temporary discontinuation:

from (Day/Month/Year) to (if HUMIRA-therapy already continued) (Day/Month/Year)

Reason for temporary discontinuation:

- Pregnancy
- Infection
- Elective surgery
- Other reasons: _____

Discontinuation of RA-treatment

Has the RA treatment been discontinued?

- no
- yes If yes, please indicate the discontinued treatment below

Treatment	End of treatment (Day/Month/Year)	Reason for discontinuation			
		side-effects*	lack of efficacy	obsolete	other reasons
_____	<input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Please complete a form for adverse events.

Physician Documentation

Patient-No.:

Follow-Up Visit - Month 3

- Patients with rheumatoid arthritis -

Changes in Dos of RA-treatment

Has the dose of the RA-treatment been changed since the last visit?

no

yes If yes, please indicate the changes in treatment below

Treatment	Date of change <small>(Day/Month/Year)</small>	new dose (mg)	
MTX	_ _ _ _ _ _ _	_ _ _ , _	/w
SASP	_ _ _ _ _ _ _	_ _ _ _ _	/d
Leflunomid	_ _ _ _ _ _ _	_ _ _ _ _	/d
other: _____	_ _ _ _ _ _ _	_ _ _ _ _	/d
Glucocorticoids	_ _ _ _ _ _ _	_ _ _ , _	/d
Equivalent to prednisolone <small>(estimated average of daily dose)</small>			
		Compound	Dose
NSAIDs	_ _ _ _ _ _ _	_____	_____
COX inhibitors	_ _ _ _ _ _ _	_____	_____
Analgetics	_ _ _ _ _ _ _	_____	_____
Others	_ _ _ _ _ _ _	_____	_____

Concomitant disease

Did any concomitant diseases occur since the last visit?

no yes

If yes, which incidence? _____

Did the therapy of concomitant diseases change since the last visit?

no yes

If yes, which medication (dose) is new? _____

Which medication has been discontinued? _____

Physician Documentation

Patient-No.:

Follow-Up Visit - Month 3

- Patients with rheumatoid arthritis -

Disease activity

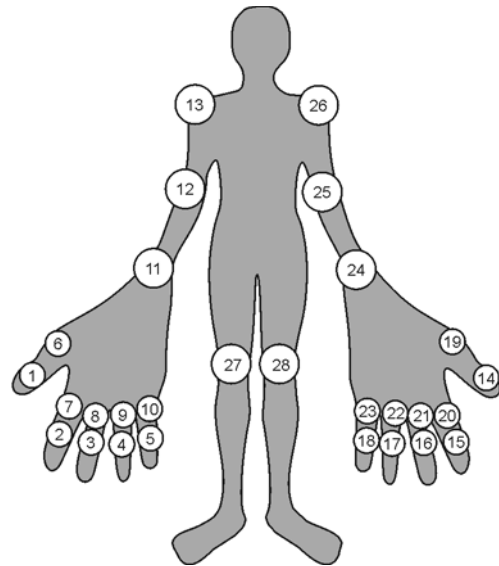
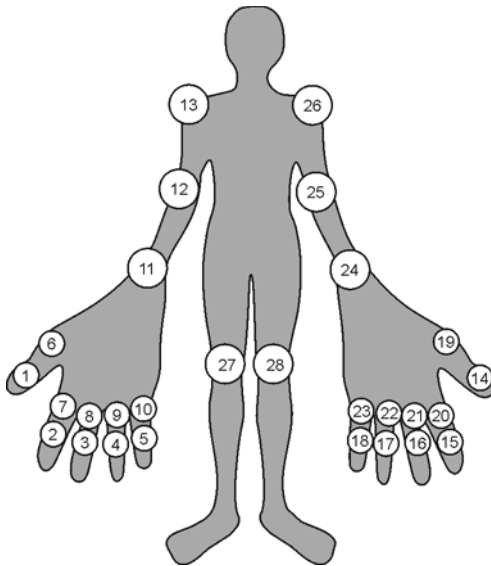
According to patient's self-assessment, how active is the disease currently?

inactive 0 1 2 3 4 5 6 7 8 9 10 highly active

Current Joint Status (Please tick the tender and swollen)

tender

swollen



None of these 28 joints is tender

None of these 28 joints is swollen

Is morning stiffness present?

no

yes, please specify

min.

Physician Documentation

Patient-No.:

Follow-Up Visit - Month 3

- Patients with rheumatoid arthritis -

Status at the Onset of Observation - Laboratory*

Inflammation parameters

CRP mg/l Please note: value in mg/l, no comma
 ESR mm/h
 Hb g/dl

Infections

Hepatitis B negative positive
 Hepatitis C negative positive

Left laboratory parameters, **if beyond normal range only!**

Parameter	Normal range	Result	Unit

* If performed

I herewith confirm the accuracy of the information on pages 1 - 5.

Date
Day / Month / Year

Signature 210

Doctor's Seal

Personal Data

Age: Years

Gender: m f

Work Productivity and Activity Impairment General Health Questionnaire

The following questions ask about the effect of your health problems on your ability to work and perform regular activities. By health problems we mean any physical or emotional problems or symptom.
Please fill in the blanks or tick a number, as indicated.

1. Are you currently employed (working for pay)? no yes
If NO, check "no" and skip to question 6.

The next questions are about the **past seven days**, not including today.

2. During the past seven days, how many hours did you miss from work because of **your health problems**?
Include hours missed on sick days, times you went in late, left early, etc., because of your health problems.

_____ Hours

3. During the past seven days, how many hours did you miss from work because of any other reasons,
such as vacation or holidays?

_____ Hours

4. During the past seven days, how many hours did you actually work?

_____ Hours (*If "0", skip to question 6.*)

5. During the past seven days, how much did your health problems affect your productivity **while you were working**?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If health problems affected your work only a little, choose a lower number. Choose a higher number if health problems affected your work a great deal.

Consider only how much **health problems** affected productivity **while you were working**.

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Patient Documentation

Patienten-No.:

Follow-Up - Month 3

- Patients with rheumatoid arthritis -

Work Productivity and Activity Impairment General Health Questionnaire (continued)

6. During the past seven days, how much did your health problems affect your ability to do your regular activities, other than work at a job?

By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If health problems affected your work only a little, choose a lower number. Choose a higher number if health problems affected your work a great deal.

Consider only how much **health problems** affected productivity **while you were working**.

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Current physical condition

How much have you been suffered by abnormal exhaustion and fatigue **during the past 7 days**?

none

 strongly

How would you evaluate your pain during the past 7 days?

During the past 7 days, I had

no pain

 unbearable pain

Therapy rating

Which of therapies for your rheumatoid arthritis you received so far do you consider to be the best one? _____

How would you rate the therapy with HUMIRA® in comparison with the other previous therapies?

- significantly better
 better
 comparable?
 worse
 significantly worse

Participation in the "Abbott Care" - service program

Do you participate in the "Abbott Care" service program? No Yes

Patient Documentation

Patienten-No.:

Follow-Up - Month 3

- Patients with rheumatoid arthritis -

Health Assessment Questionnaire (HAQ)

Please place an "x" in the box which best describes your abilities **over the past week**:

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
--	------------------------------	----------------------------	----------------------------	--------------------

DRESSING AND GROOMING

Are you able to:

- | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| - Dress yourself, including shoelaces and buttons? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Shampoo your hair? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

ARISING

Are you able to:

- | | | | | |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| - Stand up from a straight chair? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Get in and out of bed? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

EATING

Are you able to:

- | | | | | |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| - Cut your own meat? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Lift a full cup or glass to your mouth? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Open a new milk carton? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

WALKING

Are you able to:

- | | | | | |
|---------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| - Walk outdoors on flat ground? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Climb up five steps? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

- | | |
|----------------------------------|--|
| <input type="radio"/> Cane | <input type="radio"/> Devices used for Dressing (button hook, zipper pull, etc.) |
| <input type="radio"/> Walker | <input type="radio"/> Built up or special utensiles |
| <input type="radio"/> Crutches | <input type="radio"/> Special built up chair |
| <input type="radio"/> Wheelchair | <input type="radio"/> Others (which): _____ |

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

- | | |
|---|-------------------------------|
| <input type="radio"/> dressing and grooming | <input type="radio"/> Eating |
| <input type="radio"/> Arising | <input type="radio"/> Walking |

Patient Documentation

Patienten-No.:

Follow-Up - Month 3

- Patients with rheumatoid arthritis -

Health Assessment Questionnaire (HAQ) (continued)

Please place an "x" in the box which best describes your abilities **over the past week**:

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
HYGIENE				
Are you able to:				
- Wash and dry your body?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Take a tub bath?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Get on and of the toilet?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from above your head?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Bend down to pick up clothing from the floor?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GRIP				
Are you able to:				
- Open car doors?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Open previously opened jars?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Turn faucets on and off?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ACTIVITIES				
Are you able to:				
- Run errands and shop?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Get in and out of a car?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Do chores such as vacuuming or yard work?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Please check any AIDS OR DEVICES that you usually use for any of the above activities:				
<input type="radio"/> Raised toilet seat	<input type="radio"/> Bathtub bar			
<input type="radio"/> Bathtub seat	<input type="radio"/> Long-handled appliances in bathroom			
<input type="radio"/> Jar opener (for jars previously opened)	<input type="radio"/> Long-handled appliances for reach			
	<input type="radio"/> Others (which): _____)			
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:				
<input type="radio"/> Hygiene	<input type="radio"/> Gripping and opening things			
<input type="radio"/> Reach	<input type="radio"/> Errands and chores			

Health Status Questionnaire (EQ-5D)

By placing a tick in one box in each group below, please indicate which statement best describes your own health state today.

EQ 1. Mobility

I have no problems in walking around

I have some problems in walking around

I am confined to bed

EQ 2. Self-Care

I have no problems in self-care

I have some problems washing or dressing myself

I am unable to wash or dress myself

EQ 3. Usual Activities (e.g. work, study, housework, family, or leisure activities)

I have no problems with performing my usual activities

I have some problems with performing my usual activities

I am unable to perform my usual activities

EQ 4. Pain / Discomfort

I have no pain or discomfort

I have moderate pain or discomfort

I have extreme pain or discomfort

EQ 5. Anxiety / Depression

I am not anxious or depressed

I am moderately anxious or depressed

I am extremely anxious or depressed

Health Status Questionnaire (EQ-VAS)

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health state is today, in your opinion. Please do this by drawing a line from the box below to whichever point on this scale indicates how good or bad your health state is today.

Your own health state today

Best imaginable health state

100

90

80

70

60

50

40

30

20

10

Worst imaginable health state

0

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Appendix 4 Complete Case Report Form (AGIL and AGIL-CV, German)

Patienten-Logbuch zur nicht-interventionellen Studie AGIL

Name des Patienten	Alter	Geschlecht	Patienten-Nr.
		<input type="checkbox"/> m <input type="checkbox"/> w	

	zur Visite einbestellt zum: (bitte Datum eintragen)	Visite hat stattgefunden		ggfs. abweichendes Datum eintragen
		nein	ja	
Visite zu Beobachtungsbeginn		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 3 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 6 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 12 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 24 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 36 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 48 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 60 Monaten		<input type="radio"/>	<input type="radio"/>	

Wenn der Patient die Beobachtungsstudie vorzeitig beendet hat, geben Sie bitte **nur den Hauptgrund** und das Datum an:
(**bitte keine Mehrfachnennungen**)

Tag / Monat / Jahr					

- kein primäres Ansprechen
- Wirkverlust nach anfänglicher Wirkung
- Unverträglichkeit
- andere Gründe: _____

Bitte entfernen Sie vor Rückgabe der Dokumentationsunterlagen an den Sponsor das Original des Patientenlogbuches aus der Mappe. Das Original verbleibt beim Arzt. Der Durchschlag ist für den Sponsor bestimmt.

Patienten-Logbuch zur nicht-interventionellen Studie AGIL

Name des Patienten	Alter	Geschlecht	Patienten-Nr.
		<input type="checkbox"/> m <input type="checkbox"/> w	

	zur Visite einbestellt zum: (bitte Datum eintragen)	Visite hat stattgefunden		ggfs. abweichendes Datum eintragen
		nein	ja	
Visite zu Beobachtungsbeginn		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 3 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 6 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 12 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 24 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 36 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 48 Monaten		<input type="radio"/>	<input type="radio"/>	
Folgevisite nach 60 Monaten		<input type="radio"/>	<input type="radio"/>	

Wenn der Patient die Beobachtungsstudie vorzeitig beendet hat, geben Sie bitte **nur den Hauptgrund** und das Datum an:
(bitte **keine** Mehrfachnennungen)

Tag / Monat / Jahr					

- kein primäres Ansprechen
- Wirkverlust nach anfänglicher Wirkung
- Unverträglichkeit
- andere Gründe: _____

Bitte entfernen Sie vor Rückgabe der Dokumentationsunterlagen an den Sponsor das Original des Patientenlogbuches aus der Mappe. Das Original verbleibt beim Arzt. Der Durchschlag ist für den Sponsor bestimmt.

Ärztlicher Basisbogenzu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Datum:

Tag / Monat / Jahr				

Arztstempel

--

Aktuelle HUMIRA®-Therapie

Beginn der Therapie:

Tag / Monat / Jahr				

Dosis

 mg/Apl.
 14-täglich anderes Dosisregime: _____
Aufnahme in die NIS AGIL

Entscheidung zur Aufnahme in die NIS AGIL

Tag / Monat / Jahr				

Einverständniserklärung

Der Patient hat schriftlich sein Einverständnis erklärt am

Tag / Monat / Jahr				

Diagnosemäßige bis schwere aktive rheumatoide Arthritis
gemäß der Zulassung für HUMIRA®
 nein ja
Bitte beachten Sie die Ausschlusskriterien der aktuellen Fachinformation HUMIRA®!**Indikation für die aktuelle HUMIRA®-Therapie** (Mehrfachnennungen möglich)

- | | |
|--|---|
| <input type="radio"/> hohe Krankheitsaktivität | <input type="radio"/> Unverträglichkeit der vorherigen Therapie |
| <input type="radio"/> rasche radiologische Progression | <input type="radio"/> mangelnder Wirksamkeit der vorangegangenen Therapie |
| <input type="radio"/> Andere: _____ | |

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Ärztlicher Basisbogenzu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Demographische Daten

Alter Jahre Geschlecht männlich weiblich

Körpergröße cm Gewicht kg

Tabakkonsum**Raucher/-in**

nein ja, und zwar Packungsjahre (1 Packungsjahr ist definiert als Konsum einer Schachtel von 20 Zigaretten täglich über 1 Jahr)

Erstdiagnose

Datum der Erstdiagnose rheumatoide Arthritis Monat / Jahr

Radiologischer Befund

Liegt eine Röntgenaufnahme vor? ja nein

Datum aktuelle Röntgenaufnahme Monat / Jahr

Arthritistypische erosive Veränderungen ja nein

Falls ja, betroffene Gelenke Hände
 Vorfüße

Ärztlicher Basisbogen

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

RA-Begleitmedikation

	jemals gegeben	aktuell gegeben	aktuelle Dosis
MTX	<input type="radio"/>	<input type="radio"/>	<input type="text"/> , <input type="text"/> mg/w
SASP	<input type="radio"/>	<input type="radio"/>	
Leflunomid	<input type="radio"/>	<input type="radio"/>	
NSAID, Coxibe	<input type="radio"/>	<input type="radio"/>	
Analgetika	<input type="radio"/>	<input type="radio"/>	
Glukokortikoide	<input type="radio"/>	<input type="radio"/>	<input type="text"/> , <input type="text"/> mg/d Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)
Sonstige: _____	<input type="radio"/>	<input type="radio"/>	

Bisherige Biologikatherapien

keine bisherige Biologikatherapie

	von	bis
<input type="radio"/> Infliximab	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Etanercept	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Golimumab	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Certolizumab	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Abatacept	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Rituximab	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Tocilizumab	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr
<input type="radio"/> Sonstige: _____	<input type="text"/> Monat / Jahr	<input type="text"/> Monat / Jahr

Ärztlicher Basisbogen

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Bisherige Biologikatherapien (Fortsetzung)

Hauptgrund für das Absetzen der letzten Biologika-Therapie vor HUMIRA®:
(bitte keine Mehrfachnennungen)

- kein primäres Ansprechen
- Wirkverlust nach anfänglicher Wirkung
- Unverträglichkeit
- anderer Grund: _____

Begleiterkrankungen und deren Therapie

keine Begleiterkrankung

	Liegt aktuell vor	Wird medika- mentös behandelt	Präparat	Dosis
Diabetes Typ I	<input type="radio"/>	<input type="radio"/>	_____	_____
Chronisch-entzündliche Darmerkrankung	<input type="radio"/>	<input type="radio"/>	_____	_____
Chronische obstruktive Atemwegserkrankung	<input type="radio"/>	<input type="radio"/>	_____	_____
Osteoporose	<input type="radio"/>	<input type="radio"/>	_____	_____
Degenerative Gelenkerkrankung	<input type="radio"/>	<input type="radio"/>	_____	_____
Degenerative Wirbelsäulenerkrankung	<input type="radio"/>	<input type="radio"/>	_____	_____
Psychische Erkrankung (z.B. Depression)	<input type="radio"/>	<input type="radio"/>	_____	_____
Sonstige Erkrankungen, insbesondere andere Autoimmunerkrankungen, neurologische Erkrankungen etc. (bitte eintragen)		<input type="radio"/>	_____	_____
_____		<input type="radio"/>	_____	_____
_____		<input type="radio"/>	_____	_____
_____		<input type="radio"/>	_____	_____
_____		<input type="radio"/>	_____	_____

Ärztlicher Basisbogen

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

Liegt Morgensteifigkeit vor? nein ja, und zwar Min.

Sind Rheumaknoten vorhanden? nein ja

Frühere Gelenkoperationen? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____ Monat / Jahr

2. _____ Monat / Jahr

3. _____ Monat / Jahr

Ärztlicher Basisbogen

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

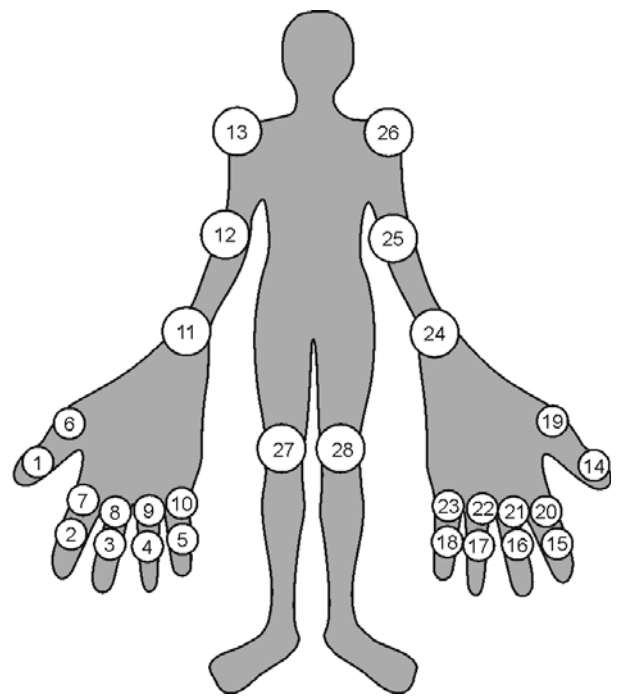
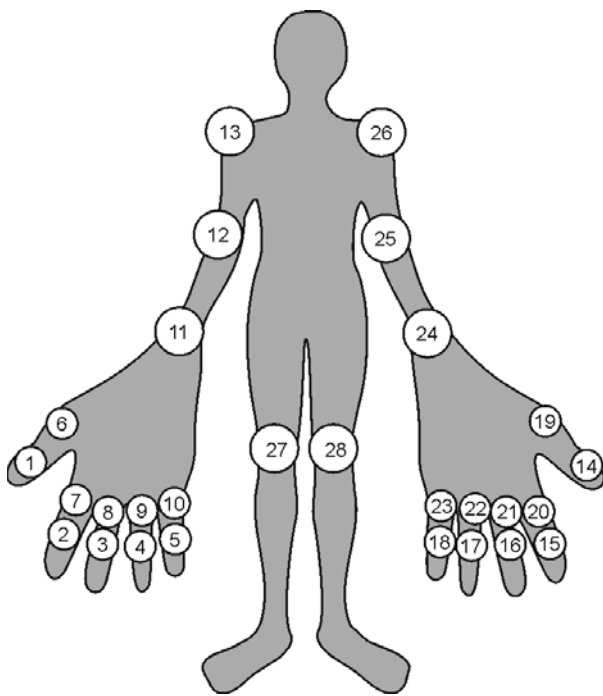
Patienten-Nr.:

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Laborstatus (Falls durchgeführt)

Diagnostische Parameter

RF negativ positiv
 CCP negativ positiv

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Hepatitis-Serologie (Hinweis auf **chronische** Form)

Hepatitis B nein ja
 Hepatitis C nein ja

Liegt eine latente Tuberkulose vor?

nein ja

Falls ja, Prophylaxe durchgeführt?

nein ja, beendet ja, läuft noch

Beginn der Prophylaxe Tag / Monat / Jahr

Ende der Prophylaxe Tag / Monat / Jahr

Schwangerschaftstest

(nur bei gebärfähigen Frauen)

negativ positiv

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 7.

Datum Tag / Monat / Jahr

Unterschrift

Ärztlicher Basisbogenzu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Datum:

--	--	--	--	--

Tag / Monat / Jahr

KörpermaßeTaillenumfang
*(5 cm oberhalb der Spina iliaca
anterior superior)*

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm**Vitalparameter (im Sitzen nach 3 Minuten Ruhe)**

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min**Alkoholkonsum****Trinkt die Patientin/der Patient Alkohol?** nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g
reiner Alkohol und entspricht 0,125 l
Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Familiäre Vorerkrankungen**Leidet ein Elternteil an Diabetes mellitus?** ja nein**Leidet ein Elternteil an Adipositas?** ja nein**Hat ein Elternteil vor dem 60. Lebensjahr einen Herzinfarkt erlitten?** ja nein**Kardiovaskuläre Ereignisse****Sind die folgenden kardiovaskulären Ereignisse bislang aufgetreten?** Herzinfarkt Schlaganfall Keine Ereignisse bislang aufgetreten

Ärztlicher Basisbogen

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Kardiovaskuläre und metabolische Begleiterkrankungen

Bitte geben Sie alle vorliegenden Erkrankungen an.

- Arterielle Hypertonie
- Koronare Herzerkrankung
- Hyperlipidämie
- Diabetes Typ II
- Sonstige kardiovaskuläre oder metabolische Erkrankung: _____
- Keine Begleiterkrankung

Kardiovaskuläre oder metabolische Begleitmedikation

Bitte geben Sie die derzeitige Medikation für kardiovaskuläre oder metabolische Erkrankungen an.

Präparat	Dosis
_____	_____
_____	_____
_____	_____
_____	_____

- Keine entsprechende Begleitmedikation

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/dL	CRP	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/L
Triglyceride	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift 228

Langzeitdokumentation zu Verträglichkeit und Wirksamkeit sowie Auswirkungen auf die Arbeitsproduktivität bei Patienten mit mäßigen bis schweren aktiven entzündlich - rheumatischen Gelenkerkrankungen unter HUMIRA® in der klinischen Routine (AGIL)

Information für teilnehmende Patienten

Sehr geehrte Patientin, sehr geehrter Patient,

zur Behandlung Ihrer entzündlich-rheumatischen Gelenkerkrankung unterziehen Sie sich einer Therapie mit dem Medikament HUMIRA® der Firma Abbott GmbH & Co. KG. Ihre behandelnde Ärztin/Ihr behandelnder Arzt beteiligt sich an einer Langzeitdokumentation zu Wirksamkeit und Verträglichkeit von HUMIRA®, die von der Firma Abbott GmbH & Co. KG ins Leben gerufen wurde. Diese Dokumentation dient dazu, zusätzliche Daten zur Sicherheit bei der langfristigen Anwendung von HUMIRA® bei rheumatoider Arthritis zu gewinnen und die Wirksamkeit unter den Bedingungen der klinischen Routine erneut zu prüfen. Darüber hinaus soll in dieser Langzeitdokumentation untersucht werden, inwieweit eine HUMIRA®-Therapie die Arbeitsfähigkeit von Patientinnen und Patienten mit entzündlich-rheumatischen Gelenkerkrankungen verbessert. Zusätzlich soll untersucht werden, ob eine HUMIRA®-Therapie das Risiko für Herz-Kreislauf-Erkrankungen positiv beeinflussen kann.

Ihre Ärztin/Ihr Arzt dokumentiert Ihre Krankengeschichte und Ihren Behandlungsverlauf sowie die Aktivität der entzündlich-rheumatischen Gelenkerkrankung. Zusätzlich werden Daten zu Herz-Kreislauf-Erkrankungen und Risikofaktoren für solche Erkrankungen dokumentiert.

Von allen Patienten, die eine Therapie mit HUMIRA® erhalten, sollen in verschlüsselter Form Daten über den Krankheitsverlauf und aufgetretene Unerwünschte Ereignisse gesammelt und zentral ausgewertet werden.

Datenschutz

Die Dokumentation der Daten erfolgt in verschlüsselter Form. Ausschließlich zur Weitergabe der studienrelevanten Daten wird die Ärztin/der Arzt von der ärztlichen Schweigepflicht entbunden. Die Weitergabe dieser Daten unterliegt den Vorschriften und den Richtlinien des Bundesdatenschutzgesetzes bzw. der anwendbaren Landesdatenschutzgesetze. Keinesfalls kann aus den Daten ein Rückschluss auf Ihren Namen und Ihre persönlichen Verhältnisse gezogen werden.

Soweit erforderlich, dürfen die erhobenen Daten verschlüsselt an Abbott GmbH & Co. KG oder eine von Abbott GmbH & Co. KG zum Zwecke der wissenschaftlichen Auswertung beauftragte Stelle weitergegeben werden. Die verschlüsselten Daten werden für die Zeit von 10 Jahren gespeichert.

Außerdem kann ein autorisierter und zur Verschwiegenheit verpflichteter Beauftragter der Abbott GmbH & Co. KG bzw. der zuständigen Behörden in die beim Prüfarzt vorhandenen personenbezogenen Daten Einsicht nehmen, soweit dies für die Überprüfung der Studie notwendig ist.

Ihre Ärztin/Ihr Arzt bittet Sie, zu Beginn der Behandlung und danach in regelmäßigen Abständen einen Fragebogen, der im Mittel 30 bis 40 Minuten zur Bearbeitung benötigt, zu Ihrem Befinden, zu dem Einfluss der Erkrankung auf Ihren Alltag und zu Ihrer beruflichen Situation auszufüllen. Die Beobachtungsdauer ist auf fünf Jahre festgelegt. Insgesamt sind acht Fragebögen auszufüllen.

Die Langzeitdokumentation nimmt keinen Einfluss auf die Art Ihrer Behandlung.

Sie werden also weder zusätzlichen Untersuchungen unterzogen noch erhalten Sie eine andere als die für Sie vom Arzt vorgesehene Behandlung.

Selbstverständlich ist die Teilnahme freiwillig. Wenn Sie sich gegen eine Teilnahme entscheiden oder wenn Sie später Ihre Einwilligung zurückziehen, entstehen Ihnen dadurch keinerlei Nachteile.

Wir bitten Sie, die beiliegende Einwilligungserklärung genau zu lesen und – Ihre Zustimmung vorausgesetzt – zu unterschreiben. Die Einwilligungserklärung sowie diese Patienteninformation wird bei Ihrem behandelnden Arzt verbleiben und wird nicht weitergeleitet. Die Durchschläge beider Dokumente werden Ihnen ausgehändigt.

Vielen Dank für Ihre Mithilfe!

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Langzeitdokumentation zu Verträglichkeit und Wirksamkeit sowie Auswirkungen auf die Arbeitsproduktivität bei Patienten mit mäßigen bis schweren aktiven entzündlich - rheumatischen Gelenkerkrankungen unter HUMIRA® in der klinischen Routine (AGIL)

Einwilligungserklärung

Ich habe das Informationsblatt zu der oben bezeichneten Langzeitdokumentation gelesen und willige unter folgenden Voraussetzungen ein, an der Langzeitdokumentation teilzunehmen:

Die Langzeitdokumentation nimmt keinen Einfluss auf Diagnostik und Therapie meiner Erkrankung.

Ich kann die Teilnahme an der Langzeitdokumentation jederzeit ohne Angabe von Gründen widerrufen; dadurch entstehen mir keinerlei Nachteile.

Ich erkläre mich damit einverstanden, dass im Rahmen dieser Langzeitdokumentation erhobene Daten/Angaben über meine Gesundheit verschlüsselt auf Fragebögen und elektronischen Datenträgern aufgezeichnet und verarbeitet werden und an Abbott GmbH & Co. KG oder eine von Abbott GmbH & Co. KG zum Zwecke der wissenschaftlichen Auswertung beauftragte Stelle weitergegeben werden. Die verschlüsselten Daten werden für die Zeit von 10 Jahren gespeichert.

Außerdem erkläre ich mich damit einverstanden, dass ein autorisierter und zur Verschwiegenheit verpflichteter Beauftragter der Abbott GmbH & Co. KG bzw. der zuständigen Behörden in meine beim Prüfarzt vorhandenen personenbezogenen Daten Einsicht nehmen kann, soweit dies für die Überprüfung der Studie notwendig ist.

Den Inhalt der vorliegenden Einwilligungserklärung habe ich verstanden und bin mit der geschilderten Vorgehensweise einverstanden.

Ich erhalte eine Kopie dieser Einwilligungserklärung und der Information für teilnehmende Patienten.

(Bitte gut lesbar in Druckbuchstaben schreiben!)

Patient/in

Arzt/Ärztin

Vorname/Name

Vorname/Name

Datum/Ort

Datum/Ort

Unterschrift

Unterschrift

Arztstempel**Angaben zur Person**Alter: JahreGeschlecht: m w

Auf den nachfolgenden Seiten finden Sie eine Reihe von Fragen zu Ihrem Befinden, zu dem Einfluss Ihrer Erkrankung auf Ihren Alltag und zu den Auswirkungen auf Ihre berufliche Situation. Wir bitten Sie, die Fragen gewissenhaft zu beantworten. Falls Sie bestimmte Fragen nicht verstehen oder nicht beantworten können, wenden Sie sich bitte an Ihren Arzt oder das Praxispersonal. Alle hier erhobenen Daten werden in anonymisierter Form wissenschaftlich ausgewertet und sollen uns helfen, die Versorgungssituation von Patienten mit rheumatoider Arthritis zu verbessern. Vielen Dank für Ihre Mithilfe.

Schule/ Ausbildung**Welches ist Ihr höchster Schulabschluss?**

- ohne Schulabschluss
- Hauptschulabschluss
- Realschulabschluss (mittlere Reife)
- Fachhochschulreife / Allgemeine Hochschulreife (Abitur)

Welche Berufsausbildung haben Sie absolviert?

Mehrfachantworten möglich

- keine
- angelernt
- schulische Berufsausbildung
- duale Berufsausbildung (in Betrieb und Schule)
- Fachschulabschluss / Meisterausbildung
- Fachhochschulabschluss
- Universitätsabschluss

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie sich im Ruhestand befinden: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 6 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 6 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

- Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben
- Infekten AU-Tage aus diesem Grund nicht krank geschrieben
- Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben
- Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 6 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 6 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 7 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten**

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

- 3.** Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

- 4.** Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Arbeitsfähigkeit: Ende

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?

Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil?

 Ja

 Nein

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| - Sich ganz waschen und abtrocknen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Ein Vollbad nehmen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Sich auf die Toilette setzen und wieder aufstehen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

NACH ETWAS GREIFEN

Konnten Sie:

- | | | | | |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| - Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

GREIFEN UND ÖFFNEN

Konnten Sie:

- | | | | | |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| - Autotüren öffnen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Konservengläser öffnen, die schon einmal offen waren? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Wasserhähne auf- und zudrehen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

ANDERE TÄTIGKEITEN

Konnten Sie:

- | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| - Besorgungen machen und einkaufen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - In ein Auto ein- und aussteigen? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| - Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

- Patienten mit rheumatoider Arthritis -

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / MobilitätIch habe keine Probleme herumzugehen Ich habe einige Probleme herumzugehen Ich bin ans Bett gebunden **EQ 2. Für sich selbst sorgen**Ich habe keine Probleme, für mich selbst zu sorgen Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen **EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)**Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen **EQ 4. Schmerzen / Körperliche Beschwerden**Ich habe keine Schmerzen oder Beschwerden Ich habe mäßige Schmerzen oder Beschwerden Ich habe extreme Schmerzen oder Beschwerden **EQ 5. Angst / Niedergeschlagenheit**Ich bin nicht ängstlich oder deprimiert Ich bin mäßig ängstlich oder deprimiert Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

zu **Beobachtungsbeginn - Monat 0**

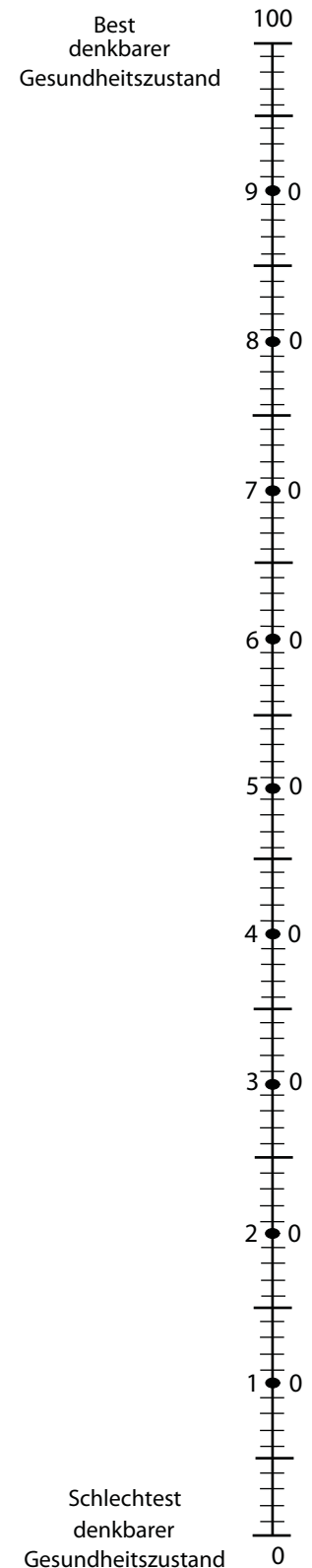
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

Datum:

Tag		Monat		Jahr

- Patienten mit rheumatoider Arthritis -

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein ja →Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?** nein ja →Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Ist eine Schwangerschaft eingetreten?** nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/ Frequenz Datum der Änderung: / / Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

/ / Tag / Monat / Jahr

/ / Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

keine Dosisänderung vorgenommen

Datum der Therapieänderung

neue Dosis

MTX

Tag	Monat	Jahr		

	,				
mg		w			

Glukokortikoide

Tag	Monat	Jahr		

	,				
mg/d					
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)					

Neueinleitung von RA-Begleitmedikation

keine Neueinleitung vorgenommen

Datum des Therapiebeginns

Dosis

MTX

Tag	Monat	Jahr		

	,				
mg		w			

SASP

Tag	Monat	Jahr		

Leflunomid

Tag	Monat	Jahr		

NSAID, Coxibe

Tag	Monat	Jahr		

Analgetika

Tag	Monat	Jahr		

Glukokortikoide

Tag	Monat	Jahr		

	,				
mg/d					
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)					

Sonstige: _____

Tag	Monat	Jahr		

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen**Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?** nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden? nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität**Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?**inaktiv

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 hoch aktiv**Gelenkstatus**

Liegt Morgensteifigkeit vor?

 nein ja, und zwar

--	--	--	--

 Min.

Ärztlicher Basisbogen

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

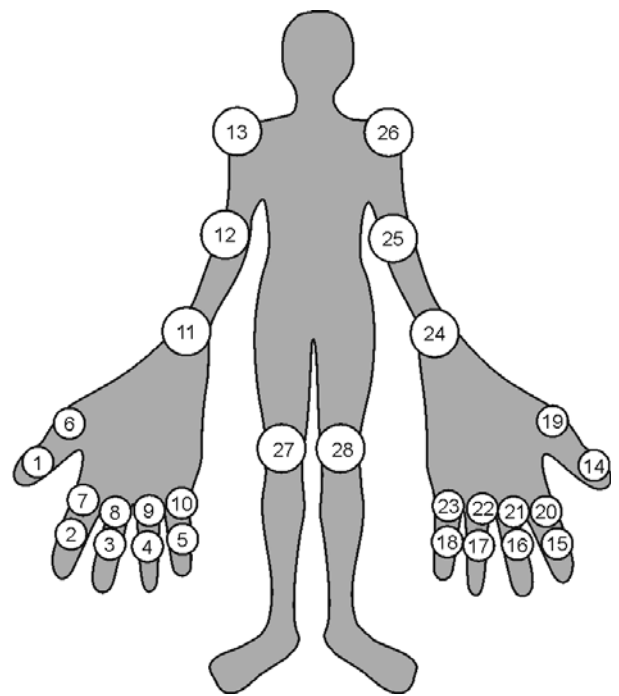
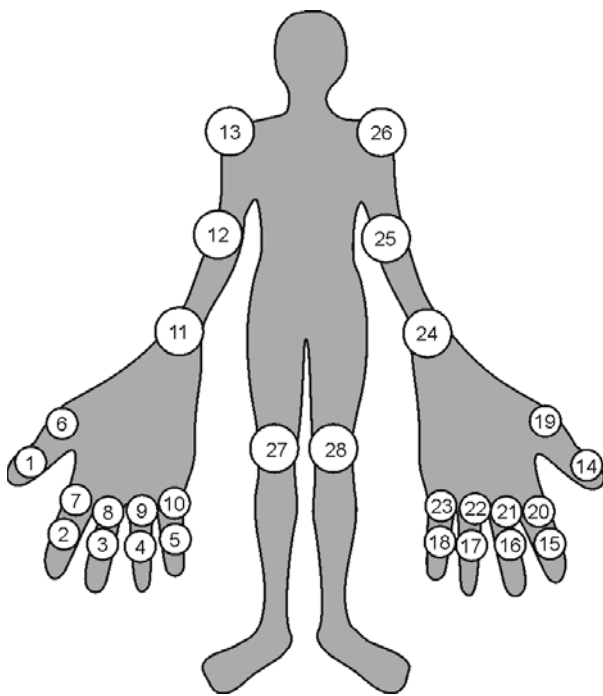
Patienten-Nr.:

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**

BSG mm/h

Hb g/dl

Bei latenter TB: Prophylaxe

- abgeschlossen am
Tag / Monat / Jahr
- läuft noch

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
Tag / Monat / Jahr

Unterschrift

Körpermaße

 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg

Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min

Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

 nein ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

 nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

 Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Verabreichung

- Ich verabreiche mir HUMIRA® selbst
- Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
- besser
- vergleichbar
- schlechter
- deutlich schlechter

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 4 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

1. Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

2. Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 3

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Arbeitsfähigkeit: Ende**Tägliche Aktivitäten in den vergangenen sieben Tagen**

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil?

Ja

Nein

253

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopfföfner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- Sich ganz waschen und abtrocknen?
- Ein Vollbad nehmen?
- Sich auf die Toilette setzen und wieder aufstehen?

NACH ETWAS GREIFEN

Konnten Sie:

- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?

GREIFEN UND ÖFFNEN

Konnten Sie:

- Autotüren öffnen?
- Konservengläser öffnen, die schon einmal offen waren?
- Wasserhähne auf- und zudrehen?

ANDERE TÄTIGKEITEN

Konnten Sie:

- Besorgungen machen und einkaufen?
- In ein Auto ein- und aussteigen?
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 3

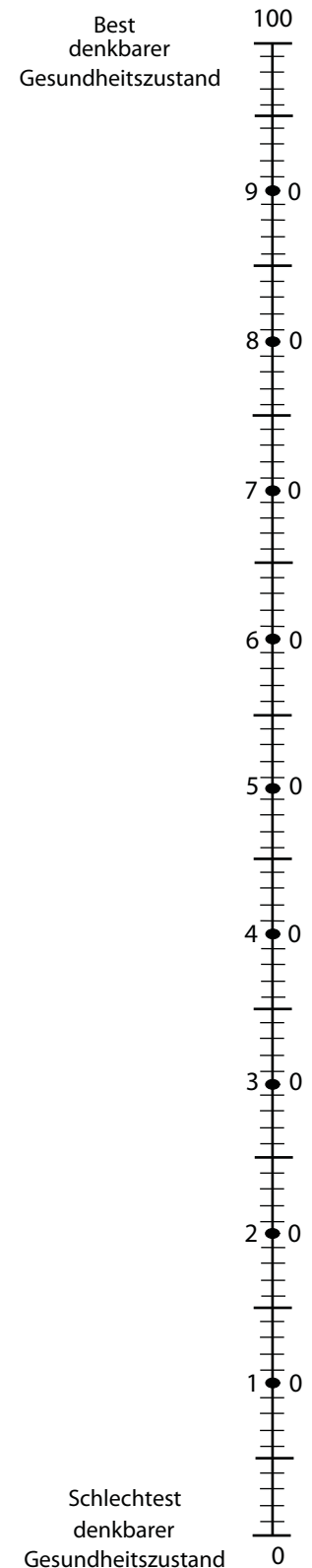
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Tag		Monat		Jahr

Arztstempel

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja \longrightarrow Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja \longrightarrow Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im Monat
- trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
- komplikationsfreie Geburt
- Anderes, nämlich: _____

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/ Frequenz Datum der Änderung: Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag / Monat / Jahr

mg /w

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag / Monat / Jahr

mg/w

- SASP

Tag / Monat / Jahr

- Leflunomid

Tag / Monat / Jahr

- NSAID, Coxibe

Tag / Monat / Jahr

- Analgetika

Tag / Monat / Jahr

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag / Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

inaktiv 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 hoch aktiv

Gelenkstatus

Liegt Morgensteifigkeit vor? nein ja, und zwar Min.

Gelenkoperationen in den letzten 6 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____ /
 Monat / Jahr

2. _____ /
 Monat / Jahr

3. _____ /
 Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

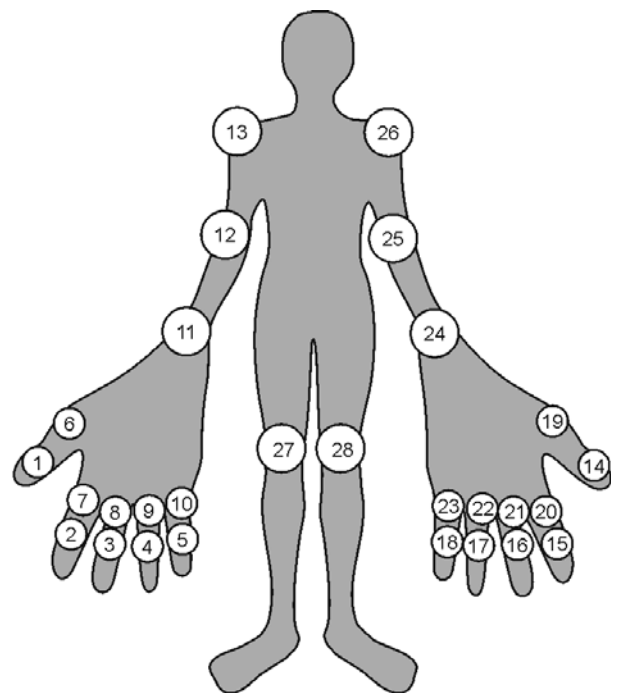
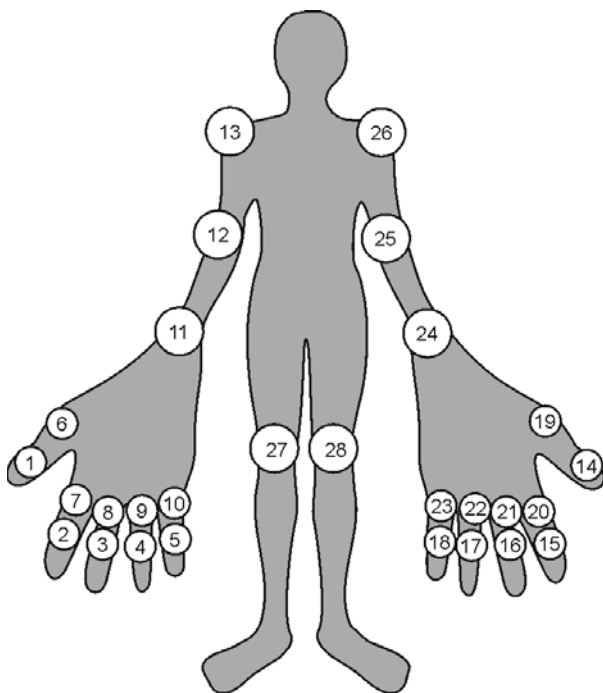
- Patienten mit rheumatoider Arthritis -

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Bei latenter TB: Prophylaxe

- abgeschlossen am
 Tag / Monat / Jahr
- läuft noch

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Körpermaße

 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg

Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min

Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

 nein ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

 nein ja, und zwar

--	--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

 Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Verabreichung

- Ich verabreiche mir HUMIRA® selbst Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil? Ja Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 6 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 6 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 6 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

- Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben
- Infekten AU-Tage aus diesem Grund nicht krank geschrieben
- Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben
- Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 6 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 6 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

270

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 6

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- Sich ganz waschen und abtrocknen?
- Ein Vollbad nehmen?
- Sich auf die Toilette setzen und wieder aufstehen?

NACH ETWAS GREIFEN

Konnten Sie:

- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?

GREIFEN UND ÖFFNEN

Konnten Sie:

- Autotüren öffnen?
- Konservengläser öffnen, die schon einmal offen waren?
- Wasserhähne auf- und zudrehen?

ANDERE TÄTIGKEITEN

Konnten Sie:

- Besorgungen machen und einkaufen?
- In ein Auto ein- und aussteigen?
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 6

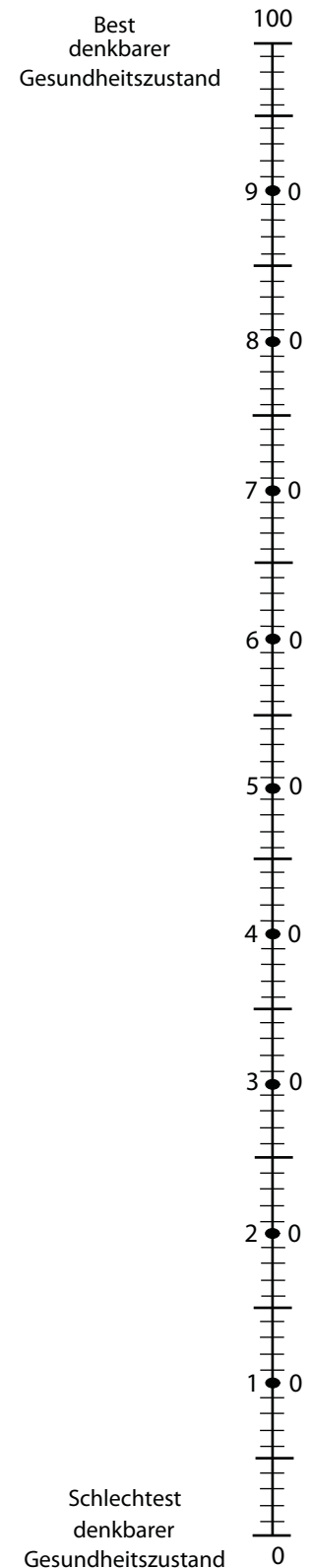
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 12

Datum:

- Patienten mit rheumatoider Arthritis -

Tag		Monat		Jahr

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein ja →

Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten? nein ja →

Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten? nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____**Radiologischer Befund****Liegt eine aktuelle Röntgenaufnahme vor?** ja nein

Datum der Röntgenaufnahme

Monat		Jahr	

Arthritistypische erosive Veränderungen ja neinFalls ja, betroffene Gelenke Hände Vorfüße

276

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
 Frequenz

Datum der Änderung:
 Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

keine Dosisänderung vorgenommen

Datum der Therapieänderung

neue Dosis

MTX

Tag	Monat	Jahr		

	,			
mg		w		

Glukokortikoide

Tag	Monat	Jahr		

	,			
mg/d				

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

keine Neueinleitung vorgenommen

Datum des Therapiebeginns

Dosis

MTX

Tag	Monat	Jahr		

	,			
mg		w		

SASP

Tag	Monat	Jahr		

Leflunomid

Tag	Monat	Jahr		

NSAID, Coxibe

Tag	Monat	Jahr		

Analgetika

Tag	Monat	Jahr		

Glukokortikoide

Tag	Monat	Jahr		

	,			
mg/d				

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Sonstige: _____

Tag	Monat	Jahr		

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen**Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?** nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden? nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität**Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?**inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv**Gelenkstatus**Liegt Morgensteifigkeit vor? nein ja, und zwar Min.Gelenkoperationen in den letzten 6 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____

Monat / Jahr

2. _____

Monat / Jahr

3. _____

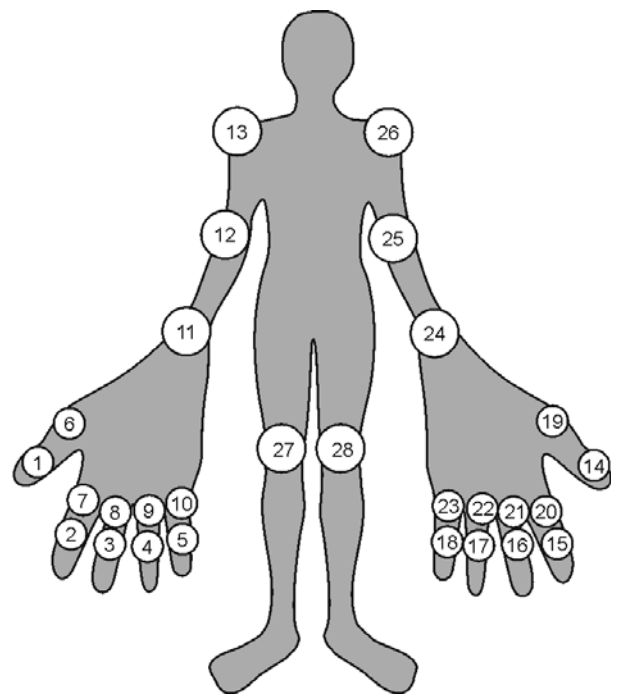
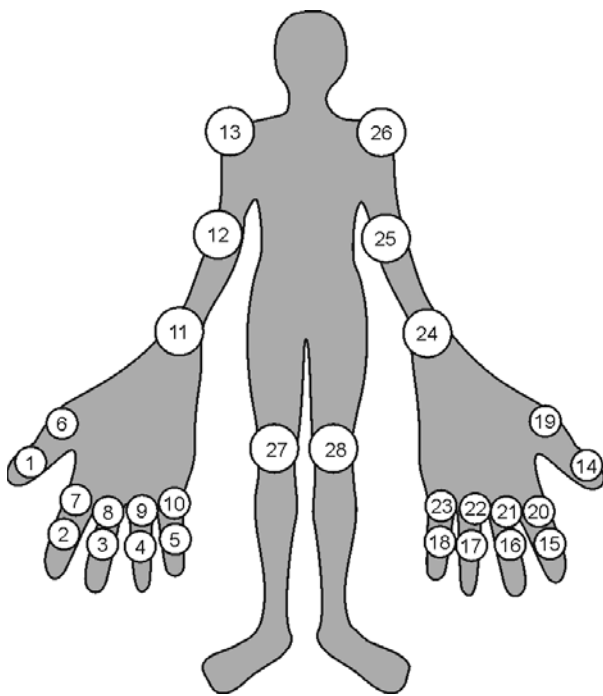
Monat / Jahr

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

**Ärztlicher Basisbogen
 Folgevisite - Monat 12**

Patienten-Nr.:

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Bei latenter TB: Prophylaxe

- abgeschlossen am
 Tag / Monat / Jahr
- läuft noch

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Körpermaße

Taillenumfang
(5 cm oberhalb der Spina iliaca
anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg
Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min
Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

nein

ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

nein

ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g
reiner Alkohol und entspricht 0,125 l
Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

Herzinfarkt

Schlaganfall

Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen unerträgliche Schmerzen

Verabreichung

Ich verabreiche mir HUMIRA® selbst

Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil? Ja Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 6 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 6 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 12

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 6 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

- Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben
- Infekten AU-Tage aus diesem Grund nicht krank geschrieben
- Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben
- Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 6 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 6 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

ANZIEHEN & KÖRPERPFLEGE

Konnten Sie:

- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?
- Sich die Haare waschen?

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

AUFSTEHEN

Konnten Sie:

- Von einem Stuhl ohne Armlehne aufstehen?
- Sich ins Bett legen und aufstehen?

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

ESSEN

Konnten Sie:

- Fleisch schneiden?
- Eine volle Tasse oder ein volles Glas zum Mund führen?
- Einen neuen Milchkarton (TetraPak) öffnen?

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

GEHEN

Konnten Sie:

- Draußen auf ebenem Untergrund gehen?
- Fünf Treppenstufen hochgehen?

<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|---|--|
| <input type="radio"/> Gehstock | <input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.) |
| <input type="radio"/> Gehhilfe (Rollator) | <input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen) |
| <input type="radio"/> Krücken | <input type="radio"/> Speziell angepasster Stuhl |
| <input type="radio"/> Rollstuhl | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|---|-----------------------------|
| <input type="radio"/> Anziehen und Körperpflege | <input type="radio"/> Essen |
| <input type="radio"/> Aufstehen | <input type="radio"/> Gehen |

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- Sich ganz waschen und abtrocknen?
- Ein Vollbad nehmen?
- Sich auf die Toilette setzen und wieder aufstehen?

NACH ETWAS GREIFEN

Konnten Sie:

- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?

GREIFEN UND ÖFFNEN

Konnten Sie:

- Autotüren öffnen?
- Konservengläser öffnen, die schon einmal offen waren?
- Wasserhähne auf- und zudrehen?

ANDERE TÄTIGKEITEN

Konnten Sie:

- Besorgungen machen und einkaufen?
- In ein Auto ein- und aussteigen?
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

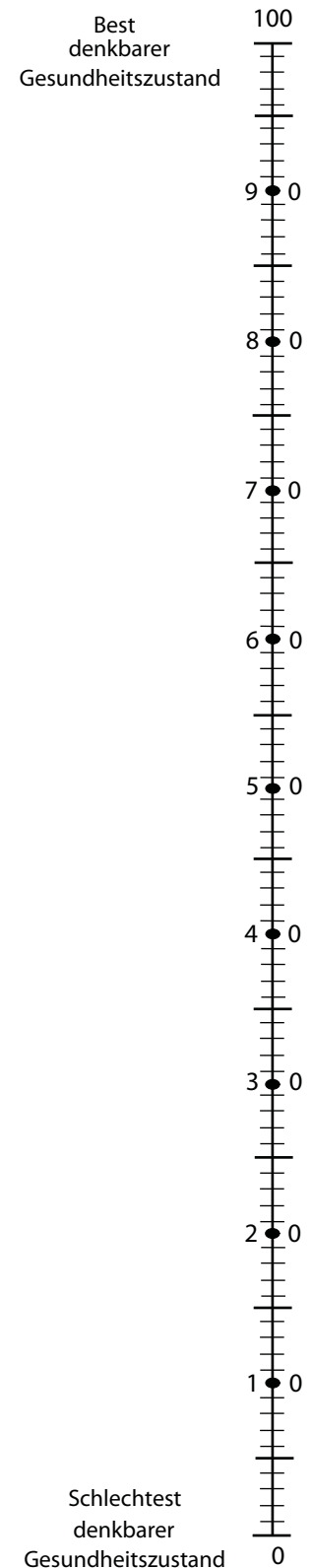
Ich bin extrem ängstlich oder deprimiert

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

Datum:

Tag		Monat		Jahr

- Patienten mit rheumatoider Arthritis -

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein jaBitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?** nein jaBitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Ist eine Schwangerschaft eingetreten?** nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____**Radiologischer Befund****Liegt eine aktuelle Röntgenaufnahme vor?** ja nein

Datum der Röntgenaufnahme

Monat		Jahr	

Arthritistypische erosive Veränderungen

 ja nein

Falls ja, betroffene Gelenke

 Hände Vorfüße

294

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
 Frequenz

Datum der Änderung:
 Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

keine Dosisänderung vorgenommen

Datum der Therapieänderung

neue Dosis

MTX

Tag / Monat / Jahr

mg /w

Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

keine Neueinleitung vorgenommen

Datum des Therapiebeginns

Dosis

MTX

Tag / Monat / Jahr

mg/w

SASP

Tag / Monat / Jahr

Leflunomid

Tag / Monat / Jahr

NSAID, Coxibe

Tag / Monat / Jahr

Analgetika

Tag / Monat / Jahr

Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Sonstige: _____

Tag / Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

Liegt Morgensteifigkeit vor? nein ja, und zwar Min.

Gelenkoperationen in den letzten 12 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____ / / /
Monat / Jahr

2. _____ / / /
Monat / Jahr

3. _____ / / /
Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

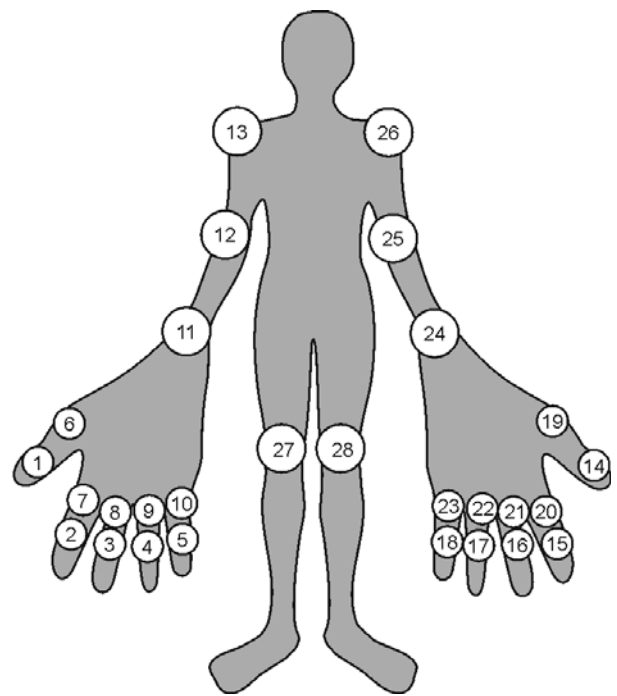
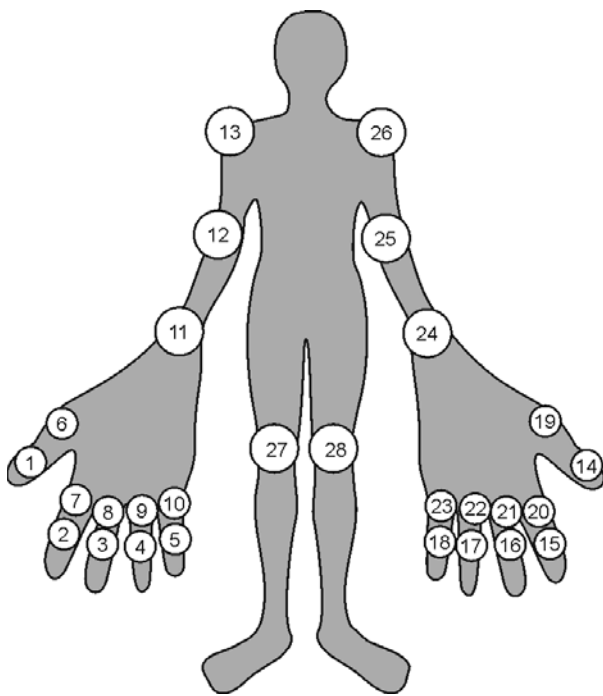
- Patienten mit rheumatoider Arthritis -

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Körpermaße

 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg

Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min

Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

 nein ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

 nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

 Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter:

 Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen

0	1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	---	----

 unerträgliche Schmerzen

Verabreichung

- Ich verabreiche mir HUMIRA® selbst Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil? Ja Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 12 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 12 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 24

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 12 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben

Infekten AU-Tage aus diesem Grund nicht krank geschrieben

Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben

Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 12 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 12 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- Sich ganz waschen und abtrocknen?
- Ein Vollbad nehmen?
- Sich auf die Toilette setzen und wieder aufstehen?

NACH ETWAS GREIFEN

Konnten Sie:

- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?

GREIFEN UND ÖFFNEN

Konnten Sie:

- Autotüren öffnen?
- Konservengläser öffnen, die schon einmal offen waren?
- Wasserhähne auf- und zudrehen?

ANDERE TÄTIGKEITEN

Konnten Sie:

- Besorgungen machen und einkaufen?
- In ein Auto ein- und aussteigen?
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 24

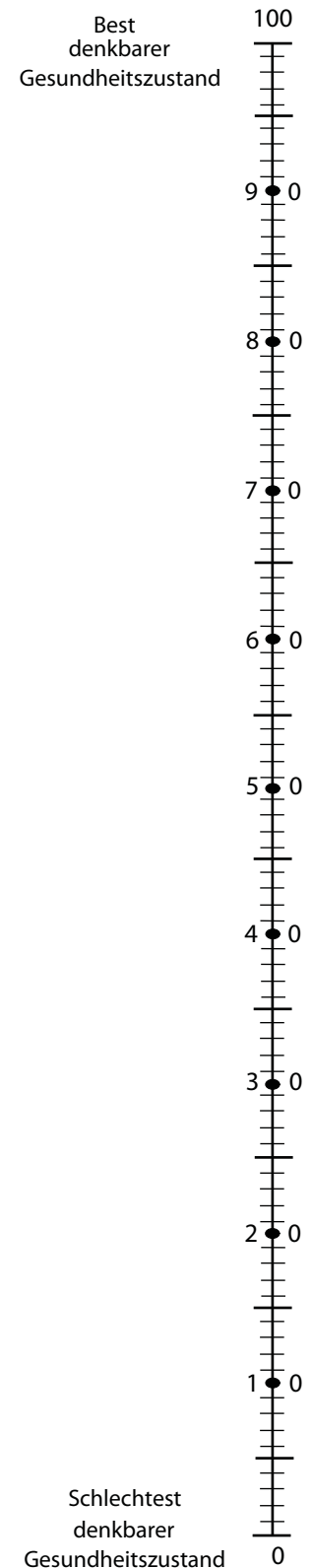
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

Datum:

- Patienten mit rheumatoider Arthritis -

Tag		Monat		Jahr

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein ja →

Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten? nein ja →

Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten? nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____**Radiologischer Befund****Liegt eine aktuelle Röntgenaufnahme vor?** ja nein

Datum der Röntgenaufnahme

Monat		Jahr	

Arthritistypische erosive Veränderungen ja nein

Falls ja, betroffene Gelenke

 Hände Vorfüße

312

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie**Wurde die HUMIRA®-Therapie verändert?**

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
FrequenzDatum der Änderung:
Tag / Monat / Jahr**Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?**

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:**von**
Tag / Monat / Jahr**bis (falls HUMIRA® bereits wieder aufgenommen)**
Tag / Monat / Jahr**Grund des Aussetzens:**

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation**Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?**

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum**Grund des Abbruchs (bitte keine Mehrfachnennungen)**

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

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Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

keine Dosisänderung vorgenommen

Datum der Therapieänderung

neue Dosis

MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)			

Neueinleitung von RA-Begleitmedikation

keine Neueinleitung vorgenommen

Datum des Therapiebeginns

Dosis

MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

SASP

Tag	Monat	Jahr		

Leflunomid

Tag	Monat	Jahr		

NSAID, Coxibe

Tag	Monat	Jahr		

Analgetika

Tag	Monat	Jahr		

Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)			

Sonstige: _____

Tag	Monat	Jahr		

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen**Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?** nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden? nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität**Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?**inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv**Gelenkstatus**Liegt Morgensteifigkeit vor? nein ja, und zwar Min.Gelenkoperationen in den letzten 12 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____

Monat / Jahr

2. _____

Monat / Jahr

3. _____

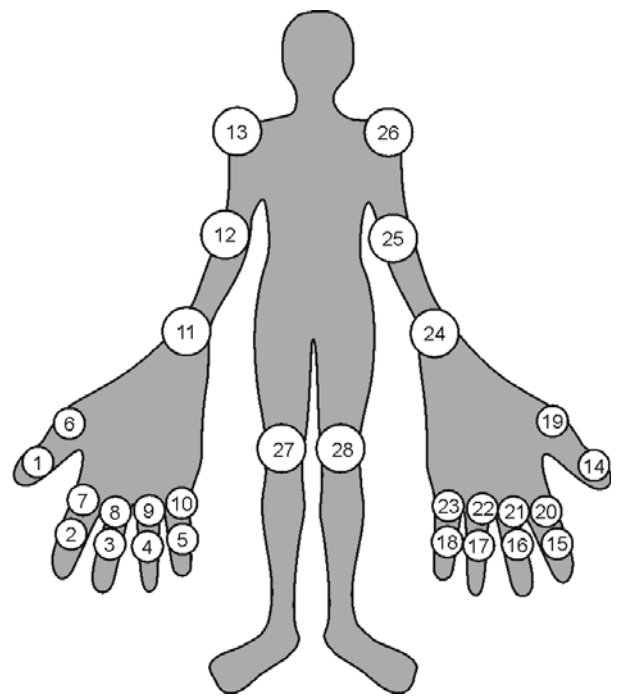
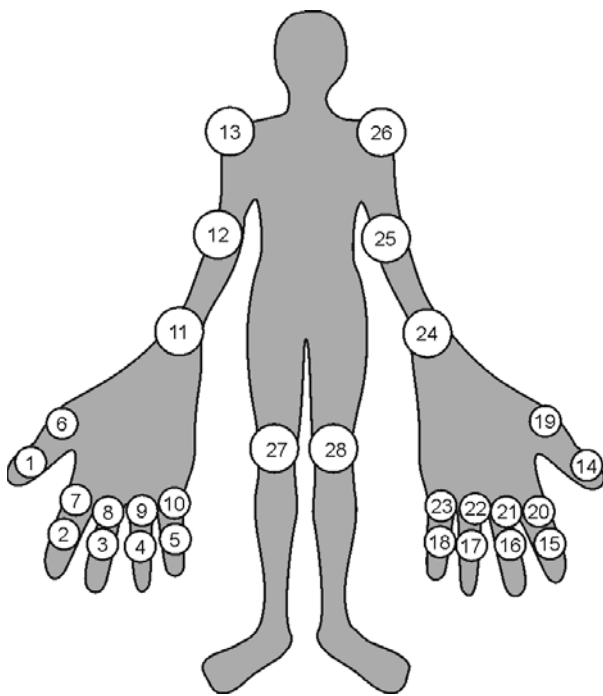
Monat / Jahr

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Körpermaße
 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg
Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min
Tabakkonsum**Ist die Patientin/der Patient Raucher/-in?** nein ja**Alkoholkonsum****Trinkt die Patientin/der Patient Alkohol?** nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse**Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?** Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen unerträgliche Schmerzen

Verabreichung

Ich verabreiche mir HUMIRA® selbst

Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil? Ja Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 12 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 12 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 12 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

- Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben
- Infekten AU-Tage aus diesem Grund nicht krank geschrieben
- Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben
- Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 12 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 12 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

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Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 36

- Patienten mit rheumatoider Arthritis -

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
- Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
- Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
- Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 36

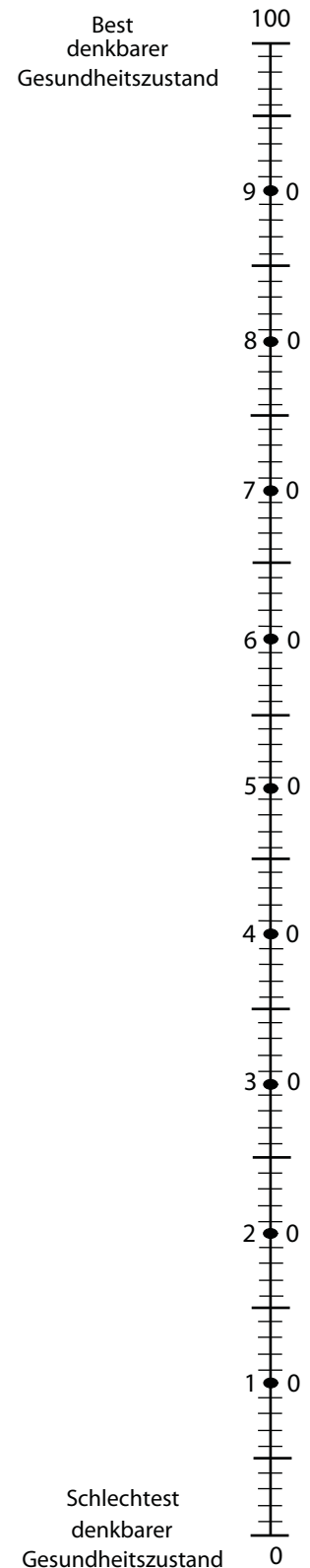
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 48

Datum:

- Patienten mit rheumatoider Arthritis -

Tag		Monat		Jahr

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein jaBitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?** nein jaBitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Ist eine Schwangerschaft eingetreten?** nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____**Radiologischer Befund****Liegt eine aktuelle Röntgenaufnahme vor?** ja nein

Datum der Röntgenaufnahme

Monat		Jahr	

Arthritistypische erosive Veränderungen

 ja nein

Falls ja, betroffene Gelenke

 Hände Vorfüße

330

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
Frequenz

Datum der Änderung:
Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen**Folgevisite - Monat 48**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Dosisänderung von RA-Begleitmedikation

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag / Monat / Jahr

mg /w

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag / Monat / Jahr

mg/w

- SASP

Tag / Monat / Jahr

- Leflunomid

Tag / Monat / Jahr

- NSAID, Coxibe

Tag / Monat / Jahr

- Analgetika

Tag / Monat / Jahr

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag / Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

Liegt Morgensteifigkeit vor? nein ja, und zwar Min.

Gelenkoperationen in den letzten 12 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____ Monat / Jahr

2. _____ Monat / Jahr

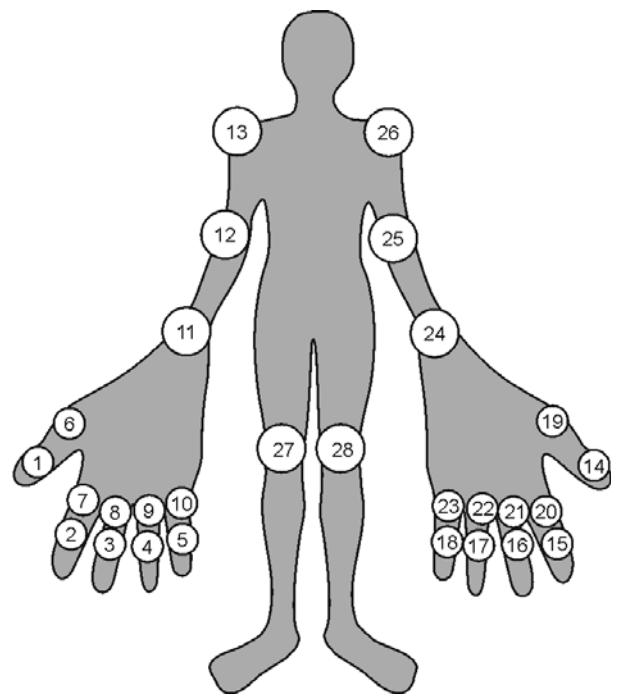
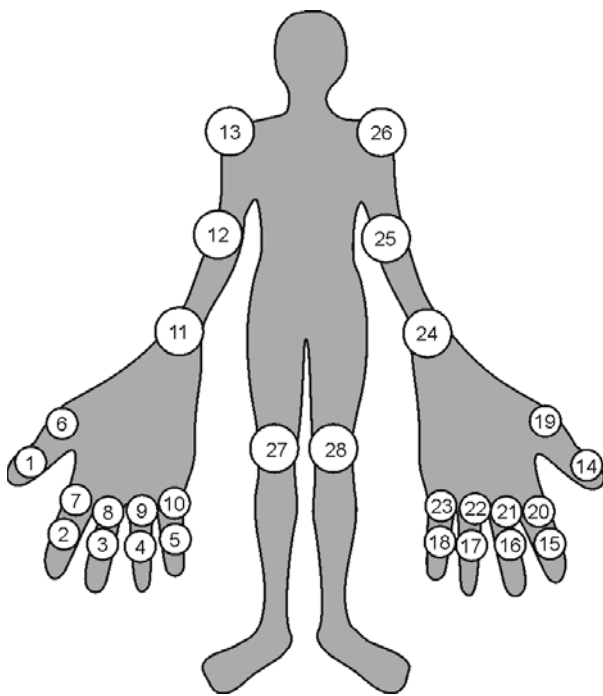
3. _____ Monat / Jahr

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Körpermaße

 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg

Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min

Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

 nein ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

 nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

 Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen unerträgliche Schmerzen

Verabreichung

Ich verabreiche mir HUMIRA® selbst

Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil? Ja Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 12 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 12 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 12 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

- Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben
- Infekten AU-Tage aus diesem Grund nicht krank geschrieben
- Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben
- Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 12 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 12 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
 vorwiegend physisch (körperlich) belastend
 psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
 Ich kann meine Arbeit ausführen, habe aber Beschwerden
 Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
 Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
 Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
 Meiner Meinung nach bin ich völlig arbeitsunfähig

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 48

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

342

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0 1 2 3 4 5 6 7 8 9 10

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

ANZIEHEN & KÖRPERPFLEGE

Konnten Sie:

- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?

- Sich die Haare waschen?

AUFSTEHEN

Konnten Sie:

- Von einem Stuhl ohne Armlehne aufstehen?

- Sich ins Bett legen und aufstehen?

ESSEN

Konnten Sie:

- Fleisch schneiden?

- Eine volle Tasse oder ein volles Glas zum Mund führen?

- Einen neuen Milchkarton (TetraPak) öffnen?

GEHEN

Konnten Sie:

- Draußen auf ebenem Untergrund gehen?

- Fünf Treppenstufen hochgehen?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

Gehstock

Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)

Gehhilfe (Rollator)

Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)

Krücken

Speziell angepasster Stuhl

Rollstuhl

Andere (welche: _____)

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:

Anziehen und Körperpflege

Essen

Aufstehen

Gehen

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
- Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
- Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
- Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 48

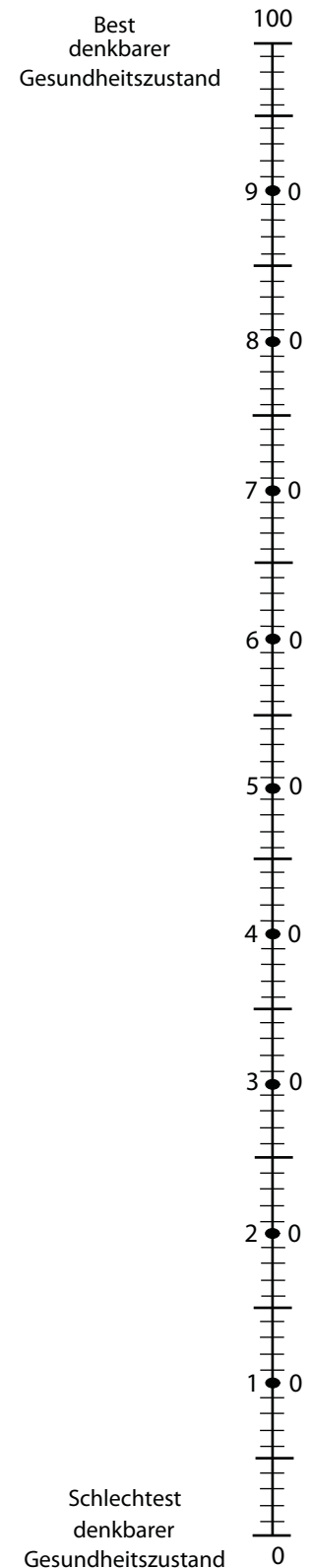
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

Datum:

- Patienten mit rheumatoider Arthritis -

Tag		Monat		Jahr

Arztstempel**Zwischenanamnese****Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?** nein ja →Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?** nein ja →Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/
schwerwiegende unerwünschte Ereignisse" ausfüllen.**Ist eine Schwangerschaft eingetreten?** nein jaSchwangerschaft im Monat trifft nicht zuAusgang: Abbruch Spontanabort unbekannt komplikationsfreie Geburt Anderes, nämlich: _____**Radiologischer Befund****Liegt eine aktuelle Röntgenaufnahme vor?** ja nein

Datum der Röntgenaufnahme

Monat		Jahr	

Arthritistypische erosive Veränderungen ja nein

Falls ja, betroffene Gelenke

 Hände Vorfüße

348

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/ Frequenz Datum der Änderung: Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Dosisänderung von RA-Begleitmedikation

keine Dosisänderung vorgenommen

Datum der Therapieänderung

neue Dosis

MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)			

Neueinleitung von RA-Begleitmedikation

keine Neueinleitung vorgenommen

Datum des Therapiebeginns

Dosis

MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

SASP

Tag	Monat	Jahr		

Leflunomid

Tag	Monat	Jahr		

NSAID, Coxibe

Tag	Monat	Jahr		

Analgetika

Tag	Monat	Jahr		

Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
Prednisolon-Äquivalenzdosis (geschätzte mittlere Tagesdosis)			

Sonstige: _____

Tag	Monat	Jahr		

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

Liegt Morgensteifigkeit vor? nein ja, und zwar Min.

Gelenkoperationen in den letzten 12 Monaten? nein ja, bitte Gelenk(e), Art und Datum des Eingriffs angeben

1. _____ / / /
Monat / Jahr

2. _____ / / /
Monat / Jahr

3. _____ / / /
Monat / Jahr

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

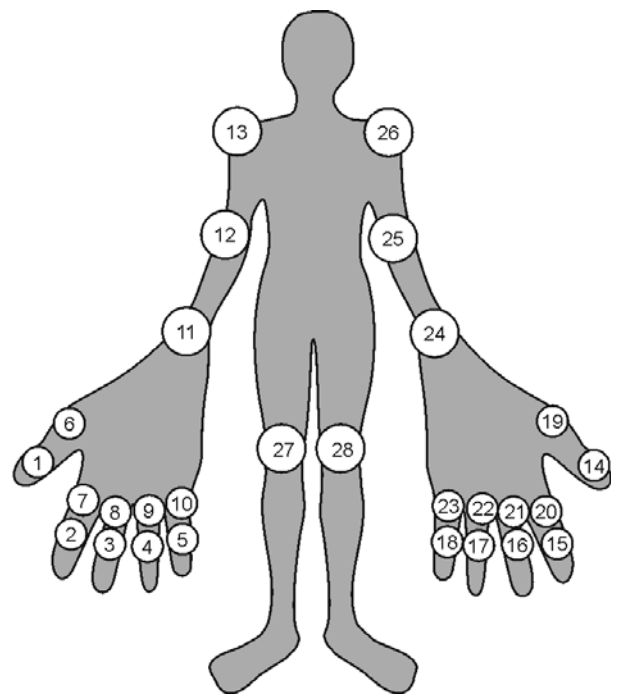
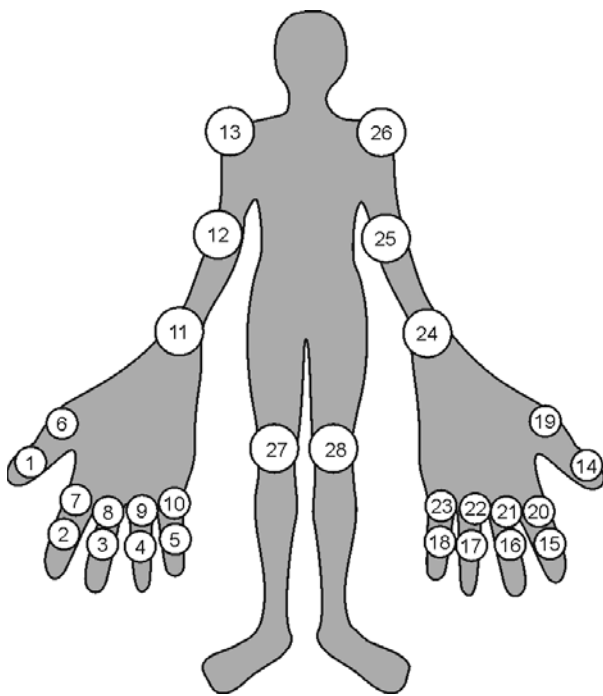
- Patienten mit rheumatoider Arthritis -

Gelenkstatus (Fortsetzung)

Aktueller Gelenkstatus (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

geschwollen



Keines dieser 28 Gelenke ist druckschmerzempfindlich

Keines dieser 28 Gelenke ist geschwollen

**Ärztlicher Basisbogen
 Folgevisite - Monat 60**

Patienten-Nr.:

- Patienten mit rheumatoider Arthritis -

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l
 und ohne Komma!**

BSG mm/h

Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ärztlicher Basisbogen**Folgevisite - Monat 60 oder letzte Visite**

- Patienten mit rheumatoider Arthritis -

Patienten-Nr.:

Datum:

Tag / Monat / Jahr				

Ende der Beobachtung

Datum der letzten Visite:

Tag / Monat / Jahr				

Hat der Patient die Beobachtungsstudie vollständig absolviert?

- Patient hat die Beobachtungsstudie vollständig absolviert

 Patient hat die Beobachtungsstudie vorzeitig beendet

Wenn der Patient die Beobachtungsstudie vorzeitig beendet hat, geben Sie bitte den Monat der letzten Visite an (z.B. Monat 06).

Monat:

--	--

Wenn der Patient die Beobachtungsstudie vorzeitig beendet hat, geben Sie bitte **nur den Hauptgrund** und das Datum an: (bitte keine Mehrfachnennungen)

Tag / Monat / Jahr				

- kein primäres Ansprechen
 Wirkverlust nach anfänglicher Wirkung
 Unverträglichkeit
 andere Gründe

(bitte die entsprechenden UEs / SUEs angeben)

Abschlussbeurteilung

Beurteilung der Wirksamkeit von HUMIRA® :

- sehr gut gut mäßig unzureichend

Beurteilung der Verträglichkeit von HUMIRA® :

- sehr gut gut mäßig unzureichend

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1-7.

Datum

Tag / Monat / Jahr				

Unterschrift

354

Körpermaße

 Taillenumfang
 (5 cm oberhalb der Spina iliaca
 anterior superior)

--	--	--	--

 cm

Hüftumfang

--	--	--	--

 cm

Gewicht

--	--	--	--

 kg

Vitalparameter (im Sitzen nach 3 Minuten Ruhe)

Blutdruck (systolisch)

--	--	--	--

 mmHg

Blutdruck (diastolisch)

--	--	--	--

 mmHg

Puls

--	--	--	--

 Schläge/min

Tabakkonsum

Ist die Patientin/der Patient Raucher/-in?

 nein ja

Alkoholkonsum

Trinkt die Patientin/der Patient Alkohol?

 nein ja, und zwar

--	--

 Einheiten pro Woche

(1 Alkoholeinheit ist definiert als 10 g reiner Alkohol und entspricht 0,125 l Wein, 0,25 l Bier oder 2,5 cl Spirituosen)

Neu aufgetretene kardiovaskuläre Ereignisse

Sind seit der letzten Visite die folgenden kardiovaskulären Ereignisse neu aufgetreten?

 Herzinfarkt Schlaganfall Keine Ereignisse neu aufgetreten

Ärztlicher Basisbogen

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Änderungen in der kardiovaskuläre oder metabolische Begleitmedikation

Wurden seit der letzten Visite Änderungen in der Begleitmedikation (Abbruch, Dosisänderung, Neueinleitung) vorgenommen?

nein ja Wenn ja, bitte nachfolgend die Änderungen angeben

Therapeutikum	Welche Änderung wurde vorgenommen?			Dosis (bei Neueinleitung oder Dosisänderung)
	Abbruch	Neueinleitung	Dosisänderung	
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

Laborparameter

Bitte geben Sie die nachfolgenden Laborwerte - soweit Sie diese haben bestimmen lassen - in den aufgeführten Einheiten an.

Lipidwerte und Glukose sollten im nüchternen Zustand bestimmt worden sein.

Glukose	<input type="text"/>	mg/dL	CRP	<input type="text"/>	mg/L
Triglyceride	<input type="text"/>	mg/dL	HDL-Cholesterin	<input type="text"/>	mg/dL
LDL-Cholesterin	<input type="text"/>	mg/dL	Gesamtcholesterin	<input type="text"/>	mg/dL

Ich bestätige hiermit die Richtigkeit der Angaben auf Seite 1 bis 2.

Datum
Tag / Monat / Jahr

Unterschrift

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre **Krankheitsaktivität in den letzten 7 Tagen?**

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **letzten 7 Tagen unter ungewöhnlicher Erschöpfung und Müdigkeit** gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die **Stärke Ihrer Schmerzen in den letzten 7 Tagen** einschätzen?

Ich hatte in den **letzten 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Verabreichung

Ich verabreiche mir HUMIRA® selbst

Ich bekomme HUMIRA® von einer anderen Person verabreicht (z.B. von Verwandten oder ambulanten Pflegekräften)

Teilnahme am "Abbott Care" - Serviceprogramm

Nehmen Sie am "Abbott Care" - Serviceprogramm teil?

Ja

Nein

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Therapiebeurteilung

Welche Rheumatherapie war für Sie bislang die Beste? _____

Wie beurteilen Sie die Therapie mit HUMIRA® im Vergleich zu den anderen vorangegangenen Rheumatherapien?

- deutlich besser
 besser
 vergleichbar
 schlechter
 deutlich schlechter

Berufliche Situation**Wie ist Ihre derzeitige Erwerbssituation?**

- Vollzeit erwerbstätig (35 Stunden und mehr)
 Teilzeit oder stundenweise erwerbstätig
 Schule / Ausbildung / Studium / Umschulung
 häusliche Tätigkeit / Erziehung
 arbeitslos
 Ruhestand

Wenn Sie in den letzten 12 Monaten in den Ruhestand gegangen sind: Sind Sie **aufgrund** Ihrer Rheumaerkrankung **vorzeitig** in den Ruhestand gegangen?

- nein ja

Wenn Sie berufstätig sind: In welcher beruflichen Stellung sind Sie derzeit beschäftigt?

- angestellt verbeamtet leitende Funktion selbständig

Tage mit Einschränkungen

Waren Sie in den **letzten 12 Monaten** in den unten aufgeführten außerberuflichen Aktivitäten und Verpflichtungen deutlich spürbar eingeschränkt?

Haushalt: nein ja, insgesamt Tage trifft nicht zu

Erziehung: nein ja, insgesamt Tage trifft nicht zu

Ausbildung: nein ja, insgesamt Tage trifft nicht zu

Freizeit: nein ja, insgesamt Tage trifft nicht zu

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Arbeitsunfähigkeit (AU)

Wenn Sie Teil- oder Vollzeit erwerbstätig sind: Waren Sie in den **letzten 12 Monaten** vom Arzt arbeitsunfähig (krank) geschrieben?

nein ja, insgesamt AU-Tage

Und wie lange davon aufgrund von...

Gelenkbeschwerden AU-Tage aus diesem Grund nicht krank geschrieben

Infekten AU-Tage aus diesem Grund nicht krank geschrieben

Gelenkoperationen AU-Tage aus diesem Grund nicht krank geschrieben

Sonstigem AU-Tage keine anderen Gründe

Arztbesuche und Krankenhausaufenthalte

Waren Sie in den **letzten 12 Monaten** in medizinischer Behandlung? nein ja

Wenn ja, machen Sie bitte die folgenden Angaben:

	Häufigkeit innerhalb der letzten 12 Monate	Gesamtdauer
Besuche beim Rheumatologen	<input type="text"/>	---
Besuche beim Hausarzt	<input type="text"/>	---
Besuche beim Orthopäden	<input type="text"/>	---
Besuche bei anderen Fachärzten	<input type="text"/>	---
Stationäre Krankenhausaufenthalte	<input type="text"/>	<input type="text"/> Tage
Kur, stationäre REHA	<input type="text"/>	<input type="text"/> Tage
Physikalische Therapie (z.B. Krankengymnastik)	<input type="text"/>	---

Arbeitsfähigkeit: Beginn (modifizierter WAI)

Die nachfolgenden Fragen beziehen sich auf Ihre Arbeit und Ihre Arbeitsfähigkeit und die Auswirkungen Ihrer Gesundheitsprobleme darauf. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Bitte beantworten Sie diese Fragen nur, **wenn Sie Teil- oder Vollzeit erwerbstätig sind**. Wenn Sie nicht erwerbstätig sind, fahren Sie bitte mit der Beantwortung des Abschnitts "Tägliche Aktivitäten in den vergangenen sieben Tagen" auf Seite 6 fort.

Wie ist Ihre Arbeit:

- vorwiegend psychisch (geistig) belastend
- vorwiegend physisch (körperlich) belastend
- psychisch (geistig) und physisch (körperlich) belastend

1. Derzeitige Arbeitsfähigkeit im Vergleich zu der besten, je erreichten Arbeitsfähigkeit

Wenn Sie Ihre beste, je erreichte Arbeitsfähigkeit mit 10 Punkten bewerten: Wieviele Punkte würden Sie dann für Ihre derzeitige Arbeitsfähigkeit geben?

0 bedeutet, dass Sie derzeit arbeitsunfähig sind. **10** steht für "derzeit die beste Arbeitsfähigkeit".

- 0 1 2 3 4 5 6 7 8 9 10

2. Arbeitsunfähigkeit in Relation zur Arbeitsanforderung

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **körperlichen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

Wie schätzen Sie Ihre derzeitige Arbeitsfähigkeit in Relation zu den **psychischen** Arbeitsanforderungen ein?

- sehr gut eher gut mittelmäßig eher schlecht sehr schlecht

3. Geschätzte Beeinträchtigung der Arbeitsleistung durch Krankheiten

Behindern Ihre **Gesundheitsprobleme** Sie derzeit bei der Arbeit?
Falls nötig, kreuzen Sie bitte mehr als eine Antwortmöglichkeit an.

- Keine Beeinträchtigung / Ich habe keine Erkrankung
- Ich kann meine Arbeit ausführen, habe aber Beschwerden
- Ich bin **manchmal** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Ich bin **oft** gezwungen, langsamer zu arbeiten oder meine Arbeitsmethoden zu ändern
- Wegen meiner Krankheit bin ich nur in der Lage, Teilzeitarbeit zu verrichten
- Meiner Meinung nach bin ich völlig arbeitsunfähig

360

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit (modifizierter WAI) Fortsetzung**4. Einschätzung der eigenen Arbeitsfähigkeit in zwei Jahren**

Glauben Sie, dass Sie, ausgehend von Ihrem jetzigen Gesundheitszustand, Ihre derzeitige Arbeit auch in den nächsten zwei Jahren ausüben können?

- unwahrscheinlich nicht sicher ziemlich sicher

5. Psychische Leistungsreserven

Haben Sie in der letzten Zeit Ihre täglichen Aufgaben mit Freude erledigt?

- häufig eher häufig manchmal eher selten niemals

Waren Sie in letzter Zeit aktiv und rege?

- immer eher häufig manchmal eher selten niemals

Waren Sie in der letzten Zeit zuversichtlich, was die Zukunft betrifft?

- ständig eher häufig manchmal eher selten niemals

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI)

Die folgenden Fragen beziehen sich auf die Auswirkungen Ihrer Gesundheitsprobleme auf Ihre Fähigkeit zu arbeiten und normalen Aktivitäten nachzugehen. Unter Gesundheitsproblemen verstehen wir alle körperlichen oder seelischen Probleme oder Symptome. Die Fragen beziehen sich auf die **vergangenen sieben Tage** (den heutigen Tag nicht eingeschlossen). Antworten bitte in die freien Stellen eintragen oder eine Zahl ankreuzen, je nachdem.

- 1.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen wegen **Ihrer Gesundheitsprobleme** bei der Arbeit?

Alle Stunden einbeziehen, die aufgrund Ihrer Gesundheitsprobleme an Krankenstandstagen, Tagen an denen Sie später kamen oder früher gingen etc., fehlten. Rechnen Sie die Zeit, die Sie wegen der Teilnahme an der Studie fehlten, bitte nicht ein.

_____ Stunden

- 2.** Wie viele Stunden fehlten Sie in den vergangenen sieben Tagen aus anderen Gründen bei der Arbeit - z.B. Urlaub, Feiertagen, freigenommene Zeit für die Teilnahme an der Studie?

_____ Stunden

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Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 60

- Patienten mit rheumatoider Arthritis -

Arbeitsfähigkeit in den vergangenen sieben Tagen (modifizierter WPAI) Fortsetzung

3. Wie viele Stunden haben Sie in den vergangenen sieben Tagen tatsächlich gearbeitet?

_____ Stunden (Falls "0" - Frage 4 nicht beachten)

4. Wie sehr wirkten sich Gesundheitsprobleme in den vergangenen Tagen auf Ihre Produktivität während der Arbeit aus?

Denken Sie hierbei an Tage, an denen das Arbeitspensum oder die Art der Arbeit, die Sie ausführen konnten, eingeschränkt war, Tage, an denen Sie weniger leisten konnten als Sie wollten, oder Tage, an denen Sie Ihre Arbeit nicht so sorgfältig wie sonst erledigen konnten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Arbeit auswirken, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Arbeit auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **Arbeit** ausgewirkt?

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Arbeitsfähigkeit: Ende

Tägliche Aktivitäten in den vergangenen sieben Tagen

Wie sehr wirkten sich Ihre Gesundheitsprobleme in den **vergangenen sieben Tagen** auf Ihre normalen täglichen Aktivitäten aus (Berufstätigkeit ausgenommen)?

Mit normalen Aktivitäten meinen wir die üblichen Aktivitäten wie Hausarbeit, Einkaufen, Kinderversorgung, Sport, Lernen etc. Denken Sie hierbei an Zeiten, an denen das Pensum oder die Art der Aktivität, die Sie ausführen konnten, eingeschränkt war, und die Zeiten, in denen Sie weniger tun konnten als Sie wollten. Falls sich Ihre Gesundheitsprobleme nur wenig auf Ihre Aktivitäten auswirkten, wählen Sie eine niedrige Zahl. Wählen Sie eine hohe Zahl, falls sich Ihre Gesundheitsprobleme stark auf Ihre Aktivitäten auswirken.

Wie stark haben sich Ihre **Gesundheitsprobleme** auf Ihre **normalen täglichen Aktivitäten** ausgewirkt?

0
 1
 2
 3
 4
 5
 6
 7
 8
 9
 10

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
- Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
- Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
- Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
- Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
- Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock	<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)			
<input type="radio"/> Gehhilfe (Rollator)	<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)			
<input type="radio"/> Krücken	<input type="radio"/> Speziell angepasster Stuhl			
<input type="radio"/> Rollstuhl	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege	<input type="radio"/> Essen			
<input type="radio"/> Aufstehen	<input type="radio"/> Gehen			

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
--	----------------------	------------------------------	----------------------------	------------------

HYGIENE

Konnten Sie:

- Sich ganz waschen und abtrocknen?
- Ein Vollbad nehmen?
- Sich auf die Toilette setzen und wieder aufstehen?

NACH ETWAS GREIFEN

Konnten Sie:

- Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?
- Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?

GREIFEN UND ÖFFNEN

Konnten Sie:

- Autotüren öffnen?
- Konservengläser öffnen, die schon einmal offen waren?
- Wasserhähne auf- und zudrehen?

ANDERE TÄTIGKEITEN

Konnten Sie:

- Besorgungen machen und einkaufen?
- In ein Auto ein- und aussteigen?
- Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?

Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:

- | | |
|--|--|
| <input type="radio"/> Erhöhter Toilettensitz | <input type="radio"/> Badewannenhandgriff |
| <input type="radio"/> Badewannensitz | <input type="radio"/> Greifhilfe mit langem Handgriff |
| <input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren) | <input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste) |
| | <input type="radio"/> Andere (welche: _____) |

Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigt haben:

- | | |
|--|---|
| <input type="radio"/> Hygiene | <input type="radio"/> Greifen und Öffnen von Gegenständen |
| <input type="radio"/> Nach etwas greifen | <input type="radio"/> Besorgungen und Hausarbeit |

Gesundheitsfragebogen (EQ - 5D)

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in einen Kreis jeder Gruppe machen.

EQ 1. Beweglichkeit / Mobilität

Ich habe keine Probleme herumzugehen

Ich habe einige Probleme herumzugehen

Ich bin ans Bett gebunden

EQ 2. Für sich selbst sorgen

Ich habe keine Probleme, für mich selbst zu sorgen

Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen

Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen

EQ 3. Allgemeine Tätigkeiten (z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen

Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen

EQ 4. Schmerzen / Körperliche Beschwerden

Ich habe keine Schmerzen oder Beschwerden

Ich habe mäßige Schmerzen oder Beschwerden

Ich habe extreme Schmerzen oder Beschwerden

EQ 5. Angst / Niedergeschlagenheit

Ich bin nicht ängstlich oder deprimiert

Ich bin mäßig ängstlich oder deprimiert

Ich bin extrem ängstlich oder deprimiert

Patientenbefragung

Patienten-Nr.:

Folgevisite - Monat 60

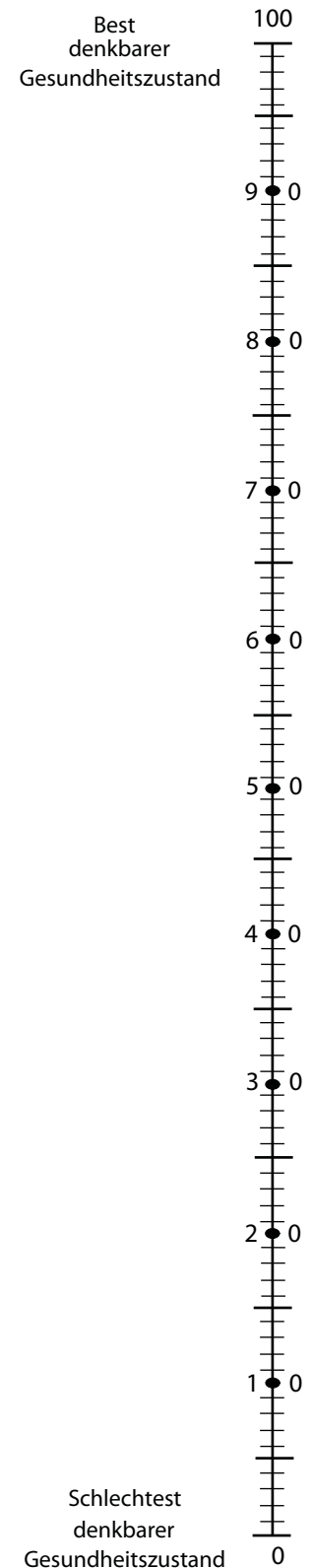
- Patienten mit rheumatoider Arthritis -

Skala zum Gesundheitszustand (EQ VAS)

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer **100** gekennzeichnet, der schlechteste mit **0**.

Wir möchten Sie nun bitten, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte verbinden Sie dazu den untenstehenden Kasten mit dem Punkt auf der Skala, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

**Ihr heutiger
Gesundheitszustand**



Zwischenvisite 1: Arztbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Dieser Bogen dient der Dokumentation von außerplanmäßigen Visiten zwischen den festgelegten Visitenzeitpunkten. Es sind daher nur Angaben erforderlich, die für diese Zwischenvisite relevant sind (d.h. nicht alle Bögen müssen vollständig ausgefüllt sein).

Anlass für die Zwischenvisite

- mangelnde Verträglichkeit
 mangelnde Wirksamkeit
 neu aufgetretene Erkrankungen
 Sonstiges: _____

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im Monat
 trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
 komplikationsfreie Geburt
 Anderes, nämlich: _____ 367

Zwischenvisite 1: Arztbogen

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
Frequenz

Datum der Änderung:
Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Zwischenvisite 1: Arztbogen**Dosisänderung von RA-Begleitmedikation**

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag / Monat / Jahr

mg /w

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag / Monat / Jahr

mg/w

- SASP

Tag / Monat / Jahr

- Leflunomid

Tag / Monat / Jahr

- NSAID, Coxibe

Tag / Monat / Jahr

- Analgetika

Tag / Monat / Jahr

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag / Monat / Jahr

Zwischenvisite 1: Arztbogen

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

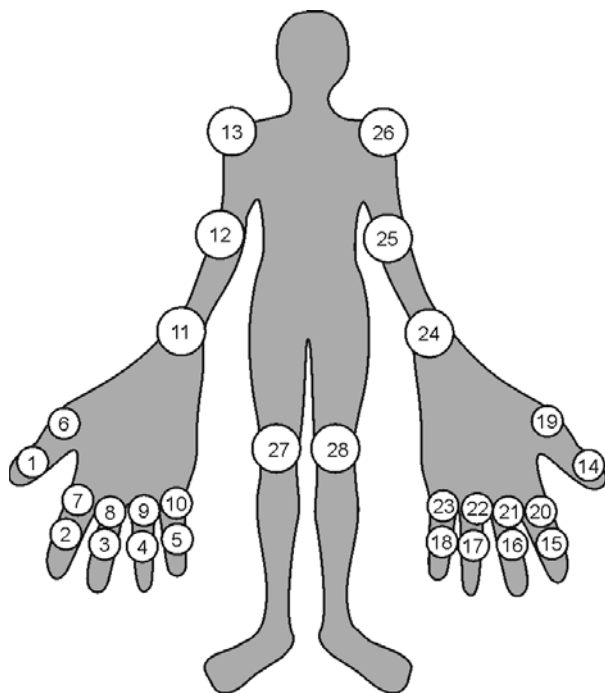
inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

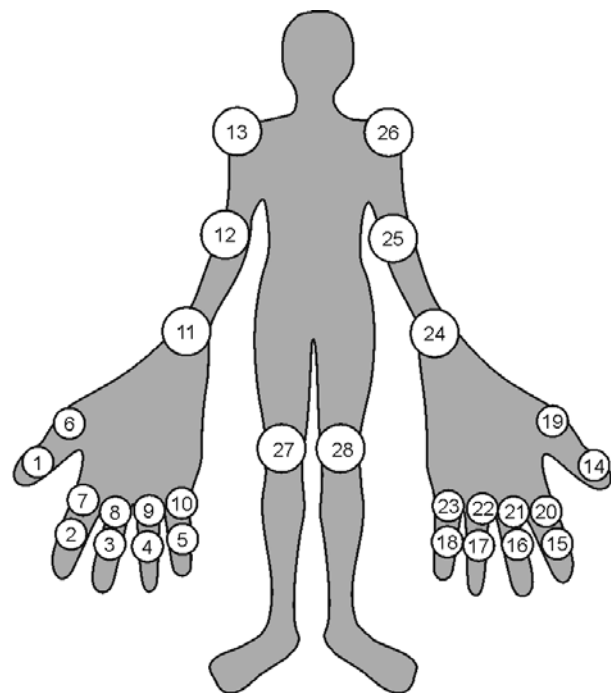
Liegt Morgensteifigkeit vor? nein ja, und zwar | | | Min.

Zwischenvisite 1: Arztbogen**Gelenkstatus (Fortsetzung)****Aktueller Gelenkstatus** (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich



geschwollen

 **Keines dieser 28 Gelenke
ist druckschmerzempfindlich** **Keines dieser 28 Gelenke
ist geschwollen**

Zwischenvisite 1: Arztbogen

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Zwischenvisite 1: Patientenbogen

Datum:

Tag	/	Monat	/	Jahr

Arztstempel**Angaben zur Person**Alter: JahreGeschlecht: m w**Aktuelle Krankheitsaktivität**

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller GesundheitszustandWie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?

Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Zwischenvisite 1: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
– Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
– Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
– Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
– Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock		<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)		
<input type="radio"/> Gehhilfe (Rollator)		<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)		
<input type="radio"/> Krücken		<input type="radio"/> Speziell angepasster Stuhl		
<input type="radio"/> Rollstuhl		<input type="radio"/> Andere (welche: _____)		
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege		<input type="radio"/> Essen		
<input type="radio"/> Aufstehen		<input type="radio"/> Gehen		

Zwischenvisite 1: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
– Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
– Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
– Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
– Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Zwischenvisite 2: Arztbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Dieser Bogen dient der Dokumentation von außerplanmäßigen Visiten zwischen den festgelegten Visitenzeitpunkten. Es sind daher nur Angaben erforderlich, die für diese Zwischenvisite relevant sind (d.h. nicht alle Bögen müssen vollständig ausgefüllt sein).

Anlass für die Zwischenvisite

- mangelnde Verträglichkeit
 mangelnde Wirksamkeit
 neu aufgetretene Erkrankungen
 Sonstiges: _____

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im Monat
 trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
 komplikationsfreie Geburt
 Anderes, nämlich: _____

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Zwischenvisite 2: Arztbogen

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
Frequenz

Datum der Änderung:
Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

Tag / Monat / Jahr

bis (falls HUMIRA® bereits wieder
aufgenommen)

Tag / Monat / Jahr

Grund des Aussetzens:

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

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Zwischenvisite 2: Arztbogen**Dosisänderung von RA-Begleitmedikation**

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

- Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
--	---	--	------

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

- SASP

Tag	Monat	Jahr		

- Leflunomid

Tag	Monat	Jahr		

- NSAID, Coxibe

Tag	Monat	Jahr		

- Analgetika

Tag	Monat	Jahr		

- Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
--	---	--	------

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag	Monat	Jahr		

Zwischenvisite 2: Arztbogen

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

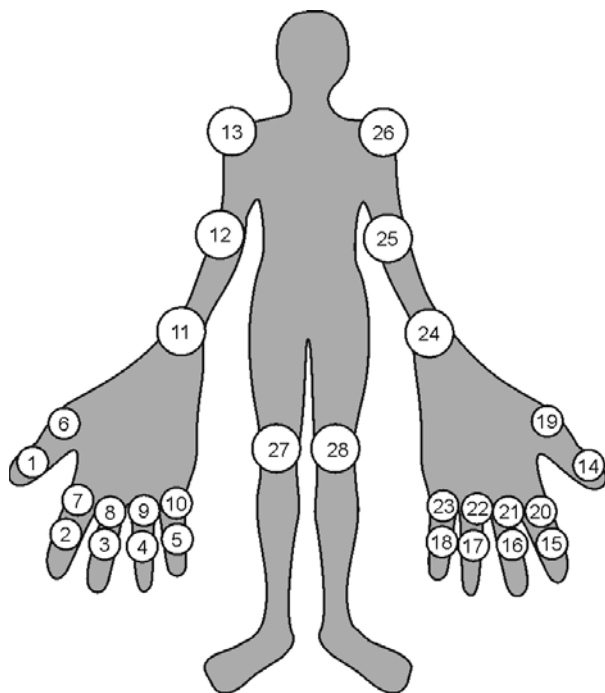
inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

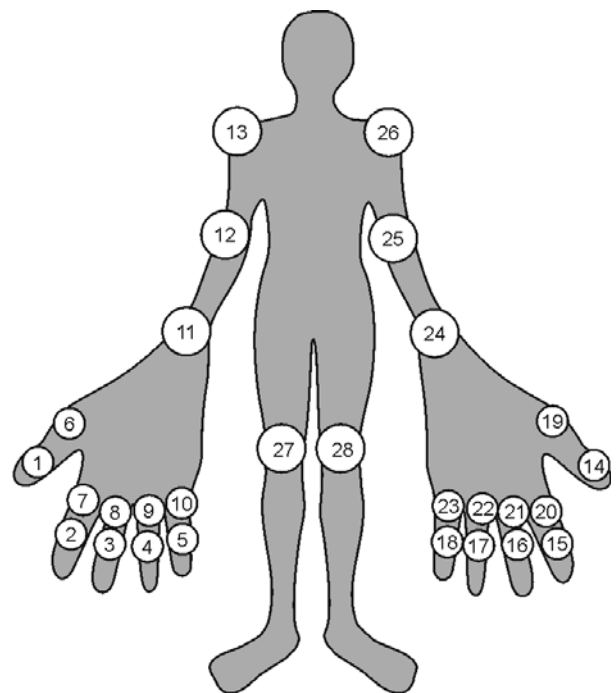
Liegt Morgensteifigkeit vor? nein ja, und zwar | | | Min.

Zwischenvisite 2: Arzbogen**Gelenkstatus (Fortsetzung)****Aktueller Gelenkstatus** (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

 **Keines dieser 28 Gelenke ist druckschmerzempfindlich**

geschwollen

 **Keines dieser 28 Gelenke ist geschwollen**

Zwischenvisite 2: Arztbogen

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Zwischenvisite 2: Patientenbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?
Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Zwischenvisite 2: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
– Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
– Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
– Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
– Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock		<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)		
<input type="radio"/> Gehhilfe (Rollator)		<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)		
<input type="radio"/> Krücken		<input type="radio"/> Speziell angepasster Stuhl		
<input type="radio"/> Rollstuhl		<input type="radio"/> Andere (welche: _____)		
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege		<input type="radio"/> Essen		
<input type="radio"/> Aufstehen		<input type="radio"/> Gehen		

Zwischenvisite 2: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
– Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
– Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
– Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
– Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Zwischenvisite 3: Arztbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Dieser Bogen dient der Dokumentation von außerplanmäßigen Visiten zwischen den festgelegten Visitenzeitpunkten. Es sind daher nur Angaben erforderlich, die für diese Zwischenvisite relevant sind (d.h. nicht alle Bögen müssen vollständig ausgefüllt sein).

Anlass für die Zwischenvisite

- mangelnde Verträglichkeit
 mangelnde Wirksamkeit
 neu aufgetretene Erkrankungen
 Sonstiges: _____

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im Monat
 trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
 komplikationsfreie Geburt
 Anderes, nämlich: _____

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Zwischenvisite 3: Arztbogen

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
Frequenz

Datum der Änderung:
Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

Tag / Monat / Jahr

Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Zwischenvisite 3: Arztbogen**Dosisänderung von RA-Begleitmedikation**

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag	Monat	Jahr		

	,			
mg		w		

- Glukokortikoide

Tag	Monat	Jahr		

	,			
mg		d		

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag	Monat	Jahr		

	,			
mg		w		

- SASP

Tag	Monat	Jahr		

- Leflunomid

Tag	Monat	Jahr		

- NSAID, Coxibe

Tag	Monat	Jahr		

- Analgetika

Tag	Monat	Jahr		

- Glukokortikoide

Tag	Monat	Jahr		

	,			
mg		d		

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag	Monat	Jahr		

Zwischenvisite 3: Arztbogen

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

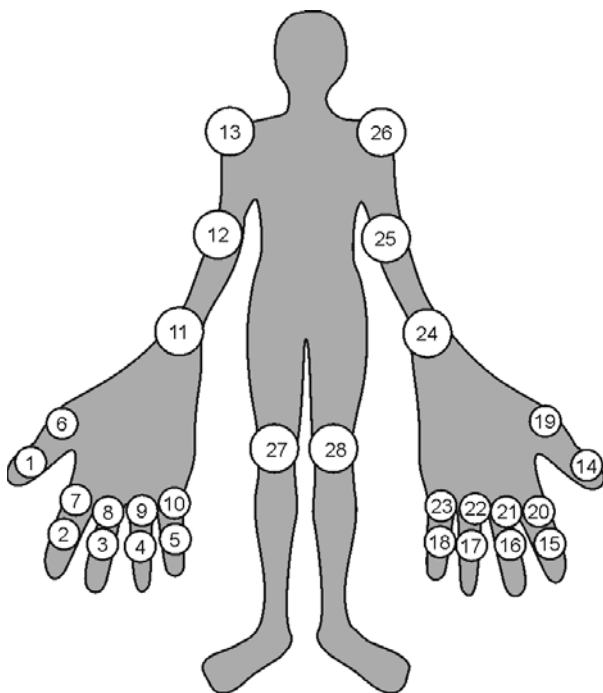
inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

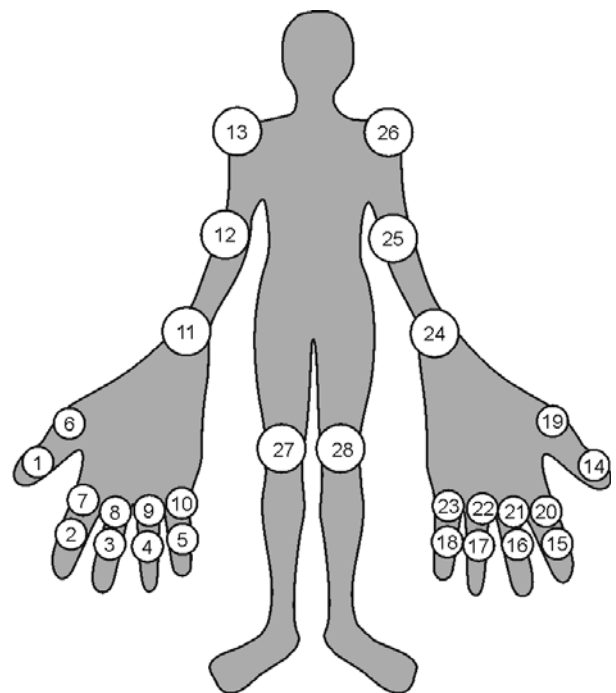
Liegt Morgensteifigkeit vor? nein ja, und zwar | | | Min.

Zwischenvisite 3: Arztbogen**Gelenkstatus (Fortsetzung)****Aktueller Gelenkstatus** (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich



geschwollen

 **Keines dieser 28 Gelenke
ist druckschmerzempfindlich** **Keines dieser 28 Gelenke
ist geschwollen**

Zwischenvisite 3: Arztbogen

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Zwischenvisite 3: Patientenbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?

Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Zwischenvisite 3: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
– Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
– Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
– Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
– Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock				<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)
<input type="radio"/> Gehhilfe (Rollator)				<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)
<input type="radio"/> Krücken				<input type="radio"/> Speziell angepasster Stuhl
<input type="radio"/> Rollstuhl				<input type="radio"/> Andere (welche: _____)
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege				<input type="radio"/> Essen
<input type="radio"/> Aufstehen				<input type="radio"/> Gehen

Zwischenvisite 3: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
– Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
– Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
– Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
– Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Zwischenvisite 4: Arztbogen

Patienten-Nr.:

Datum:

Tag		Monat		Jahr

Arztstempel

Dieser Bogen dient der Dokumentation von außerplanmäßigen Visiten zwischen den festgelegten Visitenzeitpunkten. Es sind daher nur Angaben erforderlich, die für diese Zwischenvisite relevant sind (d.h. nicht alle Bögen müssen vollständig ausgefüllt sein).

Anlass für die Zwischenvisite

- mangelnde Verträglichkeit
 mangelnde Wirksamkeit
 neu aufgetretene Erkrankungen
 Sonstiges: _____

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im _____ Monat
 trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
 komplikationsfreie Geburt
 Anderes, nämlich: _____

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Zwischenvisite 4: Arztbogen

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
Frequenz

Datum der Änderung:
Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

Tag / Monat / Jahr

bis (falls HUMIRA® bereits wieder aufgenommen)

Tag / Monat / Jahr

Grund des Aussetzens:

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Zwischenvisite 4: Arztbogen**Dosisänderung von RA-Begleitmedikation**

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag / Monat / Jahr

mg/w

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag / Monat / Jahr

mg/w

- SASP

Tag / Monat / Jahr

- Leflunomid

Tag / Monat / Jahr

- NSAID, Coxibe

Tag / Monat / Jahr

- Analgetika

Tag / Monat / Jahr

- Glukokortikoide

Tag / Monat / Jahr

mg/d
Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag / Monat / Jahr

Zwischenvisite 4: Arztbogen

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

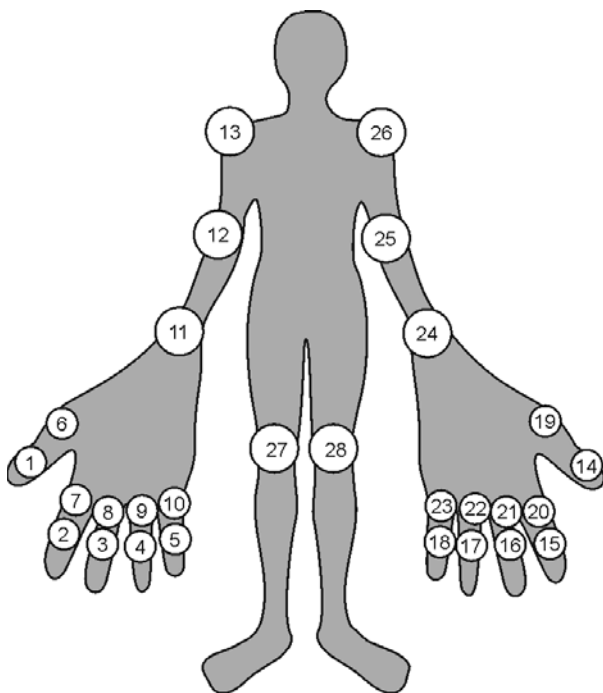
inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

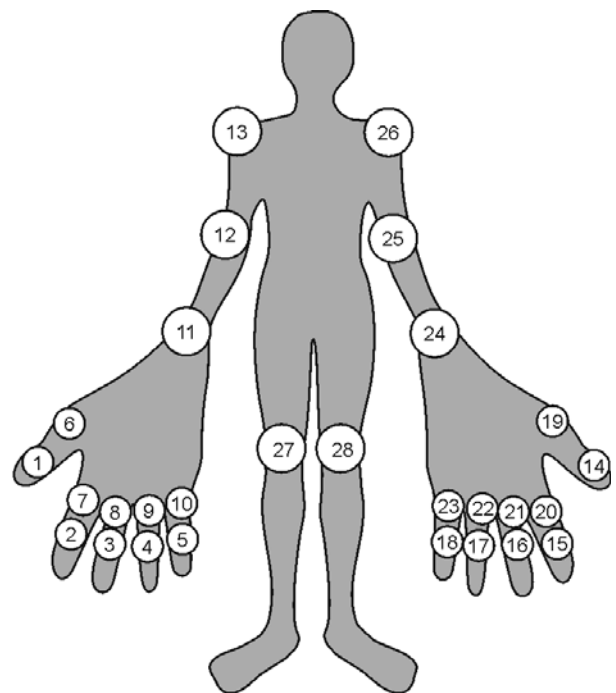
Liegt Morgensteifigkeit vor? nein ja, und zwar | | | Min.

Zwischenvisite 4: Arzbogen**Gelenkstatus (Fortsetzung)****Aktueller Gelenkstatus** (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich

 **Keines dieser 28 Gelenke ist druckschmerzempfindlich**

geschwollen

 **Keines dieser 28 Gelenke ist geschwollen**

Zwischenvisite 4: Arztbogen

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Zwischenvisite 4: Patientenbogen

Datum:

Tag	/	Monat	/
Jahr			

Arztstempel**Angaben zur Person**Alter: JahreGeschlecht: m w**Aktuelle Krankheitsaktivität**

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller GesundheitszustandWie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?

Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Zwischenvisite 4: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
– Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
– Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
– Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
– Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock		<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)		
<input type="radio"/> Gehhilfe (Rollator)		<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)		
<input type="radio"/> Krücken		<input type="radio"/> Speziell angepasster Stuhl		
<input type="radio"/> Rollstuhl		<input type="radio"/> Andere (welche: _____)		
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege		<input type="radio"/> Essen		
<input type="radio"/> Aufstehen		<input type="radio"/> Gehen		

Zwischenvisite 4: Patientenbogen**Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung**

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
– Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
– Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
– Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
– Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Zwischenvisite 5: Arztbogen

Patienten-Nr.:

Datum:

Tag		Monat		Jahr

Arztstempel

Dieser Bogen dient der Dokumentation von außerplanmäßigen Visiten zwischen den festgelegten Visitenzeitpunkten. Es sind daher nur Angaben erforderlich, die für diese Zwischenvisite relevant sind (d.h. nicht alle Bögen müssen vollständig ausgefüllt sein).

Anlass für die Zwischenvisite

- mangelnde Verträglichkeit
 mangelnde Wirksamkeit
 neu aufgetretene Erkrankungen
 Sonstiges: _____

Zwischenanamnese

Sind seit der letzten Vorstellung des Patienten Infektionen aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Sind seit der letzten Untersuchung unerwünschte Ereignisse (UE)/ schwerwiegende unerwünschte Ereignisse (SUE) aufgetreten?

- nein ja → Bitte Zusatzbogen "Bericht über unerwünschte Ereignisse/ schwerwiegende unerwünschte Ereignisse" ausfüllen.

Ist eine Schwangerschaft eingetreten?

- nein ja Schwangerschaft im Monat
 trifft nicht zu Ausgang: Abbruch Spontanabort unbekannt
 komplikationsfreie Geburt
 Anderes, nämlich: _____

403

Zwischenvisite 5: Arztbogen

Änderungen in der HUMIRA®-Therapie

Wurde die HUMIRA®-Therapie verändert?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieänderung eintragen

Dosis mg/
 Frequenz

Datum der Änderung: / /
 Tag / Monat / Jahr

Haben Sie die HUMIRA®-Therapie temporär ausgesetzt?

- nein
- ja Wenn ja, bitte nachfolgend die Änderungen eintragen

Zeitraum des Aussetzens:

von

bis (falls HUMIRA® bereits wieder aufgenommen)

Grund des Aussetzens:

/ /
 Tag / Monat / Jahr

/ /
 Tag / Monat / Jahr

- Schwangerschaft
- Infektion
- elektive OP
- andere Gründe: _____

Abbruch der RA-Begleitmedikation

Wurde eine RA - Begleittherapie seit der letzten Visite abgebrochen?

- nein
- ja Wenn ja, bitte nachfolgend die Therapieabbrüche eintragen

Therapeutikum

Grund des Abbruchs (bitte keine Mehrfachnennungen)

	Nebenwirkungen*	Wirkversagen	Remission	andere Gründe
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____
_____	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	_____

* Falls schwerwiegend, bitte einen Berichtsbogen über schwerwiegende unerwünschte Ereignisse ausfüllen.

Zwischenvisite 5: Arztbogen**Dosisänderung von RA-Begleitmedikation**

- keine Dosisänderung vorgenommen

Datum der Therapieänderung**neue Dosis**

- MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

- Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
--	---	--	------

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

Neueinleitung von RA-Begleitmedikation

- keine Neueinleitung vorgenommen

Datum des Therapiebeginns**Dosis**

- MTX

Tag	Monat	Jahr		

	,		mg/w
--	---	--	------

- SASP

Tag	Monat	Jahr		

- Leflunomid

Tag	Monat	Jahr		

- NSAID, Coxibe

Tag	Monat	Jahr		

- Analgetika

Tag	Monat	Jahr		

- Glukokortikoide

Tag	Monat	Jahr		

	,		mg/d
--	---	--	------

Prednisolon-Äquivalenzdosis
(geschätzte mittlere Tagesdosis)

- Sonstige: _____

Tag	Monat	Jahr		

Zwischenvisite 5: Arztbogen

Begleiterkrankungen

Sind seit der letzten Visite neue Begleiterkrankungen aufgetreten?

nein ja

Wenn ja, welche Neuerkrankungen? _____

Ist die Therapie der Begleiterkrankungen seit der letzten Visite geändert worden?

nein ja

Wenn ja, welche Medikation (Dosis) ist neu? _____

Welche Medikation ist abgesetzt? _____

Krankheitsaktivität

Wie schätzen Sie die Krankheitsaktivität im Augenblick ein?

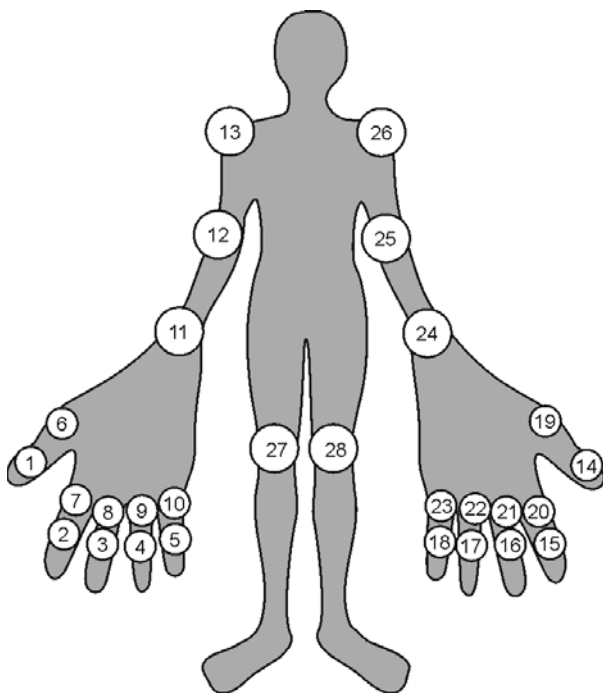
inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Gelenkstatus

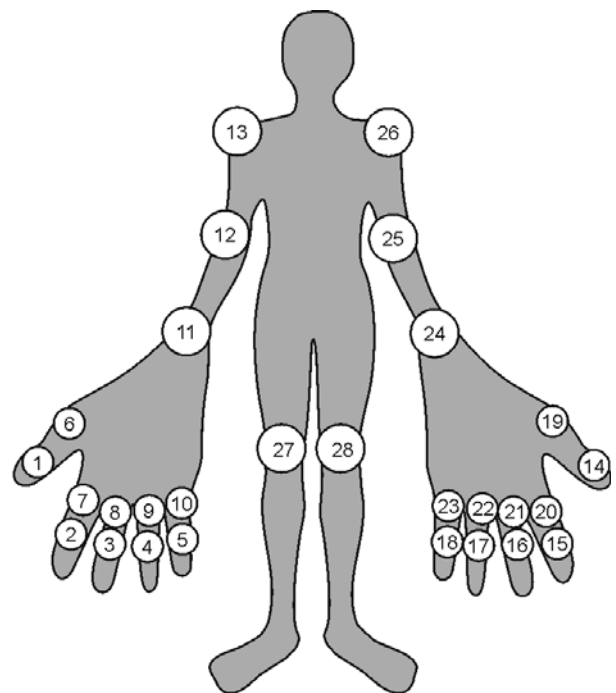
Liegt Morgensteifigkeit vor? nein ja, und zwar | | | Min.

Zwischenvisite 5: Arzbogen**Gelenkstatus (Fortsetzung)****Aktueller Gelenkstatus** (Bitte kreuzen Sie druckschmerzempfindliche und geschwollene Gelenke an)

druckschmerzempfindlich



geschwollen

 **Keines dieser 28 Gelenke
ist druckschmerzempfindlich** **Keines dieser 28 Gelenke
ist geschwollen**

Zwischenvisite 5: Arztbogen

Laborstatus (Falls durchgeführt)

Entzündungsparameter

CRP mg/l **Bitte beachten: Angabe in mg/l und ohne Komma!**
 BSG mm/h
 Hb g/dl

Übrige Laborwerte (Nur wenn außerhalb der Norm!)

Parameter	Normbereich	beobachteter Wert	Einheit

Ich bestätige hiermit die Richtigkeit der Angaben auf den Seiten 1 - 6.

Datum
 Tag / Monat / Jahr

Unterschrift

Zwischenvisite 5: Patientenbogen

Patienten-Nr.:

Datum:

Tag	/	Monat	/	Jahr

Arztstempel

Angaben zur Person

Alter: Jahre

Geschlecht: m w

Aktuelle Krankheitsaktivität

Wie beurteilen Sie Ihre Krankheitsaktivität in den letzten 7 Tagen?

inaktiv 0 1 2 3 4 5 6 7 8 9 10 hoch aktiv

Aktueller Gesundheitszustand

Wie sehr haben Sie in den **vergangenen 7 Tagen** unter ungewöhnlicher Erschöpfung und Müdigkeit gelitten?

gar nicht 0 1 2 3 4 5 6 7 8 9 10 sehr stark

Wie würden Sie die Stärke Ihrer Schmerzen in den vergangenen 7 Tagen einschätzen?
Ich hatte in den **vergangenen 7 Tagen**

keine Schmerzen 0 1 2 3 4 5 6 7 8 9 10 unerträgliche Schmerzen

Zwischenvisite 5: Patientenbogen

Fragebogen zum Gesundheitszustand (HAQ)

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
ANZIEHEN & KÖRPERPFLEGE				
Konnten Sie:				
– Sich selbst anziehen, einschließlich Schuhe binden und Knöpfe schließen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich die Haare waschen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
AUFSTEHEN				
Konnten Sie:				
– Von einem Stuhl ohne Armlehne aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich ins Bett legen und aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ESSEN				
Konnten Sie:				
– Fleisch schneiden?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Eine volle Tasse oder ein volles Glas zum Mund führen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Einen neuen Milchkarton (TetraPak) öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GEHEN				
Konnten Sie:				
– Draußen auf ebenem Untergrund gehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Fünf Treppenstufen hochgehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Gehstock				<input type="radio"/> Hilfsmittel zum Anziehen (Knopföffner, Schlitten für Reißverschlüsse, langer Schuhlöffel usw.)
<input type="radio"/> Gehhilfe (Rollator)				<input type="radio"/> Speziell angepasste Hilfsmittel (z.B. zum Essen und Kochen)
<input type="radio"/> Krücken				<input type="radio"/> Speziell angepasster Stuhl
<input type="radio"/> Rollstuhl				<input type="radio"/> Andere (welche: _____)
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Anziehen und Körperpflege				<input type="radio"/> Essen
<input type="radio"/> Aufstehen				<input type="radio"/> Gehen

Zwischenvisite 5: Patientenbogen**Fragebogen zum Gesundheitszustand (HAQ) Fortsetzung**

Kreuzen Sie bitte die Antwort an, die am besten beschreibt, was Sie **in der letzten Woche** tun konnten.

	Ohne Schwierigkeiten	Mit leichten Schwierigkeiten	Mit großen Schwierigkeiten	Konnte ich nicht
HYGIENE				
Konnten Sie:				
– Sich ganz waschen und abtrocknen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Ein Vollbad nehmen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich auf die Toilette setzen und wieder aufstehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
NACH ETWAS GREIFEN				
Konnten Sie:				
– Einen etwa 2 kg schweren Gegenstand von einer Stelle über Kopfhöhe herunterheben (z.B. eine große Tüte Zucker)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Sich bücken, um ein Kleidungsstück vom Fußboden aufzuheben?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
GREIFEN UND ÖFFNEN				
Konnten Sie:				
– Autotüren öffnen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Konservengläser öffnen, die schon einmal offen waren?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Wasserhähne auf- und zudrehen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ANDERE TÄTIGKEITEN				
Konnten Sie:				
– Besorgungen machen und einkaufen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– In ein Auto ein- und aussteigen?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
– Hausarbeiten und Gartenarbeit erledigen (z.B. Staubsaugen oder Unkraut jäten)?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bitte kreuzen Sie alle HILFSMITTEL an, die Sie für gewöhnlich für die oben genannten Tätigkeiten benutzt haben:				
<input type="radio"/> Erhöhter Toilettensitz	<input type="radio"/> Badewannenhandgriff			
<input type="radio"/> Badewannensitz	<input type="radio"/> Greifhilfe mit langem Handgriff			
<input type="radio"/> Öffner für Schraubverschlüsse (für Gläser, die schon einmal offen waren)	<input type="radio"/> Hilfsmittel mit langem Handgriff für Badezimmer (z.B. eine Bürste)			
	<input type="radio"/> Andere (welche: _____)			
Bitte kreuzen Sie alle Tätigkeiten an, bei denen Sie für gewöhnlich die HILFE einer anderen Person benötigen haben:				
<input type="radio"/> Hygiene	<input type="radio"/> Greifen und Öffnen von Gegenständen			
<input type="radio"/> Nach etwas greifen	<input type="radio"/> Besorgungen und Hausarbeit			

Berichtsbogen Unerwünschte Ereignisse

AGIL-Studie (Ger-08-05)

Patienten-Nr.

Ein unerwünschtes Ereignis ist jedes ungünstige Ereignis (einschließlich z.B. abnormaler Laborwerte), jedes Symptom oder jede Erkrankung, die im zeitlichen Zusammenhang mit dem Gebrauch eines Arzneimittels auftritt, unabhängig davon, ob ein Zusammenhang mit dem Arzneimittel angenommen wird oder nicht.

Alter zum
Zeitpunkt des UEs:

Datum Therapiebeginn
mit Adalimumab:
Tag / Monat / Jahr

Ereignis _____

Tag / Monat / Jahr

Minuten Stunden Tage

Tag / Monat / Jahr

Beginn

Dauer

Ende

besteht noch

Überprüfen Sie bitte, ob das Ereignis als schwerwiegend einzustufen ist!

Wenn ein unerwünschtes Ereignis folgende Bedingungen erfüllt, ist es als schwerwiegend einzustufen:

- | | | | |
|---|---|---|--|
| <input type="checkbox"/> Tod | <input type="checkbox"/> lebensbedrohlich | <input type="checkbox"/> dauerhafte oder erhebliche Behinderung | <input type="checkbox"/> Hospitalisierung/ Verlängerung der Hospitalisierung |
| <input type="checkbox"/> kongenitale Anomalie | <input type="checkbox"/> Spontanabort | <input type="checkbox"/> elektiver Schwangerschaftsabbruch | <input type="checkbox"/> anderes, nach medizinischer Einschätzung klinisch relevantes Ereignis |
| <input type="checkbox"/> nicht schwerwiegend | | | |

Kausalzusammenhang

Halten Sie einen Zusammenhang mit HUMIRA® für

wahrscheinlich

möglich

unwahrscheinlich

nicht gegeben

Welche andere Ursache oder Ursachen liegen Ihrer Meinung nach dem Ereignis zugrunde?

Welche? _____

Bitte beachten:

Wenn das Ereignis **schwerwiegend** ist, füllen Sie bitte auch den **Zusatzbogen über SCHWERWIEGENDE unerwünschte Ereignisse** aus und faxen Sie beide Bögen noch **am gleichen Tag** an Abbott GmbH & Co. KG, Abteilung Medizin, Fax-Nr. 06122 / 58 - 3199

(Praxis/Klinik-Stempel)

Datum
Tag / Monat / Jahr

Unterschrift 412

Zusatzbogen über schwerwiegende unerwünschte Ereignisse

AGIL-Studie

(Ger-08-05)

Patienten-Nr.

Firmen-Code Nr.	Patienten-Initialen V-name <input type="text"/> N-name <input type="text"/>	Geburtsdatum <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Geschlecht <input type="checkbox"/> m <input type="checkbox"/> w	Größe cm <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Gewicht kg <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Schwanger - schaftswoche:
Beobachtete unerwünschte Wirkungen aufgetreten am _____ Dauer _____						
Arzneimittel / Darreichungsform	Tagesdosis	Applikation	gegeben von / bis		wegen (Indikation)	
1. Charge-Nr.						
2. Charge-Nr.						
3. Charge-Nr.						
4. Charge-Nr.						
vermuteter Zusammenhang mit Arzneimittel Nr. <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4	diese früher gegeben <input type="checkbox"/> ja <input type="checkbox"/> nein	vertragen <input type="checkbox"/> ja <input type="checkbox"/> nein	ggf. Reexposition <input type="checkbox"/> negativ <input type="checkbox"/> positiv			
Grunderkrankung:			Begleiterkrankungen:			
Anamnestiche Besonderheiten:	<input type="checkbox"/> Stoffwechseldefekte ^{*)}	<input type="checkbox"/> Arzneimittelabusus ^{*)}	*) weitere Erläuterungen:			
	<input type="checkbox"/> Nikotin ^{*)}	<input type="checkbox"/> Alkohol ^{*)}				
	<input type="checkbox"/> Allergien ^{*)}	<input type="checkbox"/> Sonstige ^{*)}				
Veränderungen von Laborparametern in Zusammenhang mit der unerwünschten Arzneimittelwirkung: (ggf. Befund beifügen)						
Verlauf der unerwünschten Arzneimittelwirkung:	<input type="checkbox"/> nicht schwerwiegend <input type="checkbox"/> schwerwiegend, z. B.: lebensbedrohend, Hospitalisierung, bleibende Schädigung					
Ausgang der unerwünschten Arzneimittelwirkung:	<input type="checkbox"/> wiederhergestellt <input type="checkbox"/> bleibender Schaden <input type="checkbox"/> noch nicht wiederhergestellt <input type="checkbox"/> unbekannt <input type="checkbox"/> Exitus ↳ Todesursache: _____ Sektion: <input type="checkbox"/> nein <input type="checkbox"/> ja <input type="checkbox"/> unbekannt					
weitere Informationen:						
Beurteilung des Kausalzusammenhangs:	<input type="checkbox"/> wahrscheinlich <input type="checkbox"/> möglich <input type="checkbox"/> unwahrscheinlich <input type="checkbox"/> kein Zusammenhang					
Weitere Bemerkungen: (ggf. Anlage verwenden)						
Wer wurde informiert: <input type="checkbox"/> BfArM / PEI <input type="checkbox"/> Hersteller <input type="checkbox"/> Arzneim.-Komm.-Ärzte Sonstige: _____						
Adresse:					Datum:	
Name des Arztes: _____			Straße _____		413	
_____			PLZ Ort _____			
Klinik: <input type="checkbox"/> ja <input type="checkbox"/> nein			Telefon _____		Unterschrift:	

Appendix 5 Ethics Approval Letter (German)



Universitätsklinikum · Theodor-Stern-Kai 7 · 60590 Frankfurt

Ethik-Kommission
Der Vorsitzende



Mittwoch, 26. Mai 2010

Geschäfts-Nr.: 122/09 (Bitte stets angeben!)

Titel: Langzeitdokumentation zu Verträglichkeit und Wirksamkeit sowie Auswirkungen auf die Lebensqualität und Arbeitsproduktivität bei Patienten mit rheumatoider Arthritis unter HUMIRA® (Adalimumab) in der klinischen Routine (AGIL)

Geschäftsführung der
Ethik-Kommission

Sekretariat der
Ethik-Kommission

VOTUM

<http://ethik-kommission.klinik.uni-frankfurt.de>



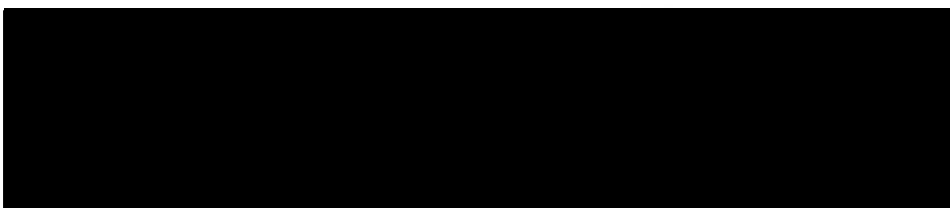
die Ethik-Kommission des Fachbereichs Medizin der J. W. Goethe-Universität Frankfurt am Main hat sich am 18.05.2009 mit Ihrem vorgenannten Antrag befasst und um einige Änderungen und Ergänzungen im Protokoll, in der Information und Einverständniserklärung gebeten.

Nachdem mit Schreiben vom 17.05.2010 die entsprechend geänderten Fassungen der Studienunterlagen vorgelegt wurden, kann ich Ihnen mitteilen, dass nunmehr keine berufsrechtlichen und berufsethischen Bedenken gegen die Durchführung der oben genannten Studie bestehen.

Wir bewerten die Studie zustimmend.

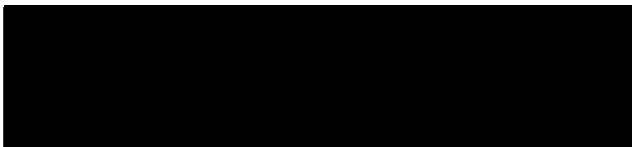
Eine Information über den Abschluss der Studie wird erbeten.

Nachfolgend sind die Mitglieder der Ethik-Kommission aufgeführt, die in der Sitzung am 18.05.2009 die o. g. Studie beurteilt haben:

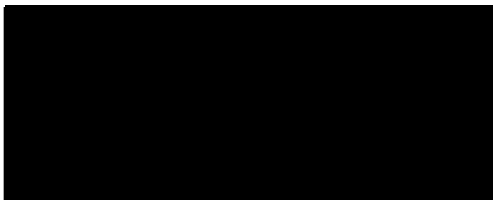


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Mit freundlichen Grüßen



Die Stellungnahme der Ethik-Kommission erfolgte aufgrund folgender eingereichter Unterlagen:

Dokument:	Version/ Nr.:	datiert vom:
Protokoll		17.05.2010
Information für teilnehmende Patienten		17.05.2010
Einwilligungserklärung		17.05.2010
Vertrag		März 2009
Fachinformation Humira 40 mg Injektionslösung im vorgefüllten Pen		August 2008
Fragebogen		01.03.2009

Appendix 6 Statistical Tables for Employed Patients

**Long-term Documentation of the
Safety, Effectiveness, and Effects on
Quality of Life and Work Productivity in
Patients with Rheumatoid Arthritis
during HUMIRA® (Adalimumab)
Therapy in Routine Clinical Practice
(AGIL) and Supplementary
Documentation to Record
Cardiovascular and Metabolic Risk
Factors (AGIL-CV)**

**Final analysis
Appendix: Statistical Tables for
Employed Patients**

March, 05 2018

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Employed patient data set

1. General parameters

1.1 Exclusion criteria for employed patient evaluation

	n	%
Exclusion criterion		
Patient base	7229	100.0
Patients not working (full time or part time) at baseline	3944	54.6

Employed patient data set
 1. General parameters
 1.2 Gender

	Gender				Total	
	Male		Female			
	n	%	n	%	n	%
Total	991	30.2	2291	69.8	3282	100.0

Employed patient data set

1. General parameters

1.3 Age (years)

1.3.1 Age - total

	Total
N	3285
Missing	0
Mean	48.3
SD	9.4
Min	18
Median	50.0
Max	83

Employed patient data set

1. General parameters

1.3 Age (years)

1.3.2 Age by gender

	Missing	Male	Female
N	3	991	2291
Missing	0	0	0
Mean	39.3	49.1	48.0
SD	10.8	9.0	9.6
Min	27	20	18
Median	44.0	50.0	49.0
Max	47	78	83

Employed patient data set

1. General parameters

1.4 Height (cm)

1.4.1 Height - total

	Total
N	3241
Missing	44
Mean	170.3
SD	8.9
Min	145
Median	170.0
Max	214

Employed patient data set

1. General parameters

1.4 Height (cm)

1.4.2 Height by gender

	Missing	Male	Female
N	3	978	2260
Missing	0	13	31
Mean	174.0	179.3	166.5
SD	9.6	7.2	6.5
Min	163	150	145
Median	178.0	179.0	166.0
Max	181	214	190

Employed patient data set

1. General parameters

1.5 Weight (kg)

1.5.1 Weight - total

	Total
N	3240
Missing	45
Mean	76.8
SD	17.1
Min	42
Median	75.0
Max	176

Employed patient data set

1. General parameters

1.5 Weight (kg)

1.5.2 Weight by gender

	Missing	Male	Female
N	3	977	2260
Missing	0	14	31
Mean	77.0	86.9	72.5
SD	13.9	15.1	16.0
Min	61	55	42
Median	85.0	85.0	70.0
Max	85	170	176

Employed patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.1 BMI - total

	Total
N	3239
Missing	46
Mean	26.4
SD	5.2
Min	17
Median	25.5
Max	65

Employed patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.2 BMI by gender

	Missing	Male	Female
N	3	976	2260
Missing	0	15	31
Mean	25.2	27.0	26.2
SD	2.0	4.3	5.6
Min	23	17	17
Median	25.9	26.2	25.0
Max	27	51	65

Employed patient data set

1. General parameters

1.7 Smoking habits

	Smoking habits				Total	
	Yes		No			
	n	%	n	%	n	%
Total	808	25.0	2420	75.0	3228	100.0

Employed patient data set
 1. General parameters
 1.8 Duration of disease (years)
 1.8.1 Duration - total

	Total
N	3227
Missing	58
Mean	7.9
SD	7.2
Min	0
Median	5.7
Max	54

	Duration of disease (grouped)																		Total	
	< 2 years		2 - 4 years		4 - 6 years		6 - 8 years		8 - 10 years		10 - 15 years		15 - 20 years		20 - 30 years		> 30 years			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	680	21.1	567	17.6	429	13.3	309	9.6	294	9.1	491	15.2	226	7.0	181	5.6	50	1.5	3227	100.0

Employed patient data set

1. General parameters

1.9 Erosive changes

	Erosive changes				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1500	58.8	1050	41.2	2550	100.0

Employed patient data set

1. General parameters

1.10 Indications for receiving adalimumab therapy

	n	%
Indications for current adalimumab therapy		
Patient base	3285	100.0
High disease activity	2614	79.6
Lack of effectiveness of previous therapy	2232	67.9
Intolerance of previous therapy	890	27.1
Rapid radiologic progression	523	15.9
Other	100	3.0

Employed patient data set
 1. General parameters
 1.11 Humira therapy
 1.11.1 Dose (mg) at baseline

	Dose				Total	
	40mg each 14 days		Other			
	n	%	n	%	n	%
Total	3218	98.1	62	1.9	3280	100.0

Employed patient data set

1. General parameters

1.11 Humira therapy

1.11.2 Exposure (years) of study drug

	Total
N	3275
Missing	10
Mean	2.05
SD	1.73
Min	0.0
Median	1.51
Max	6.4

Employed patient data set

1. General parameters

1.12 Physician global assessment of disease activity

	Total
N	3263
Missing	22
Mean	5.5
SD	2.3
Min	0
Median	6.0
Max	10

Employed patient data set

1. General parameters

1.13 Morning stiffness

1.13.1 Patients with morning stiffness(%)

	Morning stiffness				Total	
	Yes		No			
	n	%	n	%	n	%
Total	2387	73.9	843	26.1	3230	100.0

Employed patient data set

1. General parameters

1.13 Morning stiffness

1.13.2 Morning stiffness (minutes)

	Total
N	3201
Missing	84
Mean	54.0
SD	70.7
Min	0
Median	30.0
Max	800

Employed patient data set
 1. General parameters
 1.14 Rheumatic nodules

	Rheumatic nodules				Total	
	Yes		No			
	n	%	n	%	n	%
Total	364	11.2	2879	88.8	3243	100.0

Employed patient data set

1. General parameters

1.15 Prior joint surgery

	Prior joint surgery				Total	
	Yes		No			
	n	%	n	%	n	%
Total	539	16.6	2709	83.4	3248	100.0

Employed patient data set
 1. General parameters
 1.16 Joint involvement

		TJC (M0)	SJC (M0)
Total	N	3263	3263
	Missing	22	22
	Mean	6.9	4.7
	SD	6.5	5.0
	Min	0	0
	Median	5.0	3.0
	Max	28	28

Employed patient data set
 1. General parameters
 1.17 Laboratory
 1.17.1 Rheumatic factor

	Rheumatic Factor				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	1937	63.6	1107	36.4	3044	100.0

Employed patient data set
 1. General parameters
 1.17 Laboratory
 1.17.2 Anti-CCP

	Anti-ccp				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	1822	64.3	1012	35.7	2834	100.0

Employed patient data set

1. General parameters

1.17 Laboratory

1.17.3 CRP (mg/l)

	Total
N	3099
Missing	186
Mean	15.8
SD	45.8
Min	0
Median	5.0
Max	978

Employed patient data set

1. General parameters

1.17 Laboratory

1.17.4 ESR (mm/h)

1.17.4.1 ESR - total

	Total
N	2917
Missing	368
Mean	23.1
SD	19.6
Min	1
Median	18.0
Max	138

Employed patient data set

1. General parameters

1.17 Laboratory

1.17.4 ESR (mm/h)

1.17.4.2 ESR by gender

	Missing	Male	Female
N	1	869	2047
Missing	2	122	244
Mean	4.0	23.5	23.0
SD	.	21.9	18.6
Min	4	1	1
Median	4.0	17.0	18.0
Max	4	138	120

Employed patient data set

1. General parameters

1.17 Laboratory

1.17.5 Hemoglobin (g/dl)

	Total
N	3028
Missing	257
Mean	18.8
SD	26.6
Min	0
Median	13.0
Max	483

Employed patient data set
 1. General parameters
 1.17 Laboratory
 1.17.6 Hepatitis B

	Hepatitis B				Total	
	Yes		No			
	n	%	n	%	n	%
Total	11	0.4	2644	99.6	2655	100.0

Employed patient data set
 1. General parameters
 1.17 Laboratory
 1.17.7 Hepatitis C

	Hepatitis C				Total	
	Yes		No			
	n	%	n	%	n	%
Total	5	0.2	2634	99.8	2639	100.0

Employed patient data set
 1. General parameters
 1.17 Laboratory
 1.17.8 Latent tuberculosis

	Latent tuberculosis				Total	
	Yes		No			
	n	%	n	%	n	%
Total	104	3.3	3074	96.7	3178	100.0

Employed patient data set
 1. General parameters
 1.18 School leaving certificate

	School leaving certificate								Total	
	Without graduation		Secondary school certificate (Hauptschule)		Secondary school level I certificate (Realschulabschluss - mittlere Reife)		Diploma from German secondary school qualifying for university admission or matriculation (Abitur)			
	n	%	n	%	n	%	n	%	n	%
Total	36	1.1	867	26.6	1460	44.8	894	27.4	3257	100.0

Employed patient data set
 1. General parameters
 1.19 Professional education

	n	%
Professional education		
Patient base	3285	100.0
Alternance training (School and on-the-job training)	1569	47.8
Off-the-job training	595	18.1
Technical college / Master craftsman training	514	15.6
University	311	9.5
University of applied science	272	8.3
Semiskilled	150	4.6
None	129	3.9

Employed patient data set

1. General parameters

1.20 Employment

	Employment				Total	
	Full time job (35h and more)		Part-time work			
	n	%	n	%	n	%
Total	2156	65.6	1129	34.4	3285	100.0

Employed patient data set

1. General parameters

1.21 Early retirement due to rheumatic disease (only patients in retirement)

Not available for this patient set

Employed patient data set

1. General parameters

1.22 Occupational status (only patients with occupation)

	Occupational status								Total	
	Salaried		Civil servant		Leading function		Freelancer			
	n	%	n	%	n	%	n	%	n	%
Total	2633	82.0	131	4.1	158	4.9	290	9.0	3212	100.0

Employed patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.1 Household

	Household								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	2134	65.0	879	26.8	152	4.6	120	3.7	3285	100.0

	Household				Total	
	Yes		No			
	n	%	n	%	n	%
Total	2134	70.8	879	29.2	3013	100.0

Without not applicable and missings

	Total
N	2660
Missing	625
Mean	42.6
SD	58.2
Min	0
Median	15.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Employed patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.2 Parenting

	Parenting								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	286	8.7	1080	32.9	1252	38.1	667	20.3	3285	100.0

	Parenting				Total	
	Yes		No			
	n	%	n	%	n	%
Total	286	20.9	1080	79.1	1366	100.0

Without not applicable and missings

	Total
N	1313
Missing	1972
Mean	12.0
SD	37.4
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Employed patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.3 Education

	Education								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	115	3.5	950	28.9	1447	44.0	773	23.5	3285	100.0

	Education				Total	
	Yes		No			
	n	%	n	%	n	%
Total	115	10.8	950	89.2	1065	100.0

Without not applicable and missings

	Total
N	1042
Missing	2243
Mean	5.9
SD	27.8
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Employed patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.4 Recreational (free-time)

	Recreational(free-time)								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	2114	64.4	823	25.1	132	4.0	216	6.6	3285	100.0

	Recreational(free-time)				Total	
	Yes		No			
	n	%	n	%	n	%
Total	2114	72.0	823	28.0	2937	100.0

Without not applicable and missings

	Total
N	2577
Missing	708
Mean	45.3
SD	60.0
Min	0
Median	20.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Employed patient data set

1. General parameters

1.24 Missed work days in the last 6 month

	M00				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1725	53.9	1475	46.1	3200	100.0

Missed work days in the last 6 month (% of patients)

	Total
N	3156
Missing	129
Mean	19.2
SD	38.4
Min	0
Median	3.0
Max	183

Number of missed work days in the last 6 month

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.1 Number of visits at the rheumatologist

	Total
N	3251
Missing	34
Mean	3.1
SD	2.9
Min	0
Median	2.0
Max	70

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.2 Number of visits at the general practitioner

	Total
N	3250
Missing	35
Mean	3.5
SD	4.5
Min	0
Median	2.0
Max	52

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.3 Number of visits at the orthopaedic specialist

	Total
N	3250
Missing	35
Mean	0.7
SD	2.0
Min	0
Median	0.0
Max	40

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.4 Number of visits at other medical specialists

	Total
N	3250
Missing	35
Mean	1.1
SD	2.5
Min	0
Median	0.0
Max	60

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.5 Number of hospitalizations

	Total
N	3250
Missing	35
Mean	0.3
SD	1.4
Min	0
Median	0.0
Max	28

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.6 Total duration of hospitalizations (days)

	Total
N	3250
Missing	35
Mean	1.5
SD	5.3
Min	0
Median	0.0
Max	120

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.7 Number of convalescent cares, stationary rehabilitations

	Total
N	3250
Missing	35
Mean	0.2
SD	1.8
Min	0
Median	0.0
Max	42

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.8 Total duration of convalescent cares, stationary rehabilitations (days)

	Total
N	3250
Missing	35
Mean	1.7
SD	6.8
Min	0
Median	0.0
Max	128

Employed patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.9 Number of physical therapies, for example physiotherapy

	Total
N	3250
Missing	35
Mean	3.5
SD	9.2
Min	0
Median	0.0
Max	80

Employed patient data set
1. General parameters
1.26 Modified WAI

	Total
N	2110
Missing	1175
Mean	32.2
SD	7.7
Min	7
Median	32.5
Max	49

Employed patient data set
1. General parameters
1.27 WPAI
1.27.1 Presenteeism (%)

	Total
N	2758
Missing	527
Mean	46.7
SD	26.9
Min	0
Median	50.0
Max	100

Employed patient data set
1. General parameters
1.27 WPAI
1.27.2 Absenteeism (%)

	Total
N	2253
Missing	1032
Mean	21.0
SD	36.6
Min	0
Median	0.0
Max	100

Employed patient data set

1. General parameters

1.27 WPAI

1.27.3 Total work productivity impairment (%)

	Total
N	2026
Missing	1259
Mean	50.9
SD	28.9
Min	0
Median	50.0
Max	100

Employed patient data set

1. General parameters

1.27 WPAI

1.27.4 Total activity impairment (%)

	Total
N	3248
Missing	37
Mean	51.7
SD	25.9
Min	0
Median	50.0
Max	100

Employed patient data set

1. General parameters

1.28 Patient global assessment of disease activity

	Total
N	3248
Missing	37
Mean	5.4
SD	2.5
Min	0
Median	6.0
Max	10

Employed patient data set

1. General parameters

1.29 Fatigue

	Total
N	3259
Missing	26
Mean	5.4
SD	2.9
Min	0
Median	6.0
Max	10

Employed patient data set
1. General parameters
1.30 Pain

	Total
N	3259
Missing	26
Mean	5.3
SD	2.6
Min	0
Median	6.0
Max	10

Employed patient data set
1. General parameters
1.31 HAQ-DI

	Total
N	3265
Missing	20
Mean	0.95
SD	0.68
Min	0.0
Median	0.88
Max	3.0

Employed patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.1 Mobility

	Mobility						Total	
	No problems		Some problems		Confined to bed			
	n	%	n	%	n	%	n	%
Total	1719	53.0	1522	46.9	4	0.1	3245	100.0

Employed patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.2 Self-care

	Self-care						Total	
	No problems		Some problems		Unable to wash or dress myself			
	n	%	n	%	n	%	n	%
Total	2462	75.9	752	23.2	28	0.9	3242	100.0

Employed patient data set

1. General parameters

1.32 EQ-5D

1.32.3 Usual activities (e.g., work, study, housework, family or leisure activities)

	Usual activities						Total	
	No problems		Some problems		Unable to perform			
	n	%	n	%	n	%	n	%
Total	1105	34.1	2062	63.6	77	2.4	3244	100.0

Employed patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.4 Pain/discomfort

	Pain/discomfort						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	277	8.5	2294	70.7	674	20.8	3245	100.0

Employed patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.5 Anxiety/depression

	Anxiety/depression						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	1749	53.9	1339	41.3	156	4.8	3244	100.0

Employed patient data set
1. General parameters
1.32 EQ-5D
1.32.6 Mean EQ VAS

	Total
N	3241
Missing	44
Mean	54.7
SD	21.9
Min	0
Median	51.0
Max	100

Employed patient data set
1. General parameters
1.33 DAS28

	Total
N	2874
Missing	411
Mean	4.43
SD	1.49
Min	0.0
Median	4.51
Max	8.5

Employed patient data set
 1. General parameters
 1.34 Participation in Abbott Care

	Participation in Abbott Care service program				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1043	35.7	1879	64.3	2922	100.0

Employed patient data set
2. Concomitant diseases

	n	%
Previous concomitant diseases		
Patient base	3285	100.0
Total	1811	55.1
Other disease	938	28.6
Arterial hypertension	746	22.7
Degenerative joint disease	357	10.9
Degenerative spinal disease	283	8.6
Osteoporosis	226	6.9
Hyperlipidemia	156	4.7
Mental illness (e.g. depression)	149	4.5
Diabetes Type II	143	4.4
Chronic obstructive pulmonary disease	101	3.1
Chronic inflammatory disease	60	1.8
Coronary heart disease	54	1.6
Diabetes Type I	40	1.2

Employed patient data set
 3.Previous and concomitant medication
 3.1 Previous documented DMARDs

	n	%
Previous documented DMARDs		
Patient base	3285	100.0
MTX	1984	60.4
Leflunomide	1734	52.8
Glucocorticoides	1439	43.8
NSAID, Coxibe	1132	34.5
SASP	1002	30.5
Analgesics	635	19.3
Other	459	14.0

Employed patient data set
 3.Previous and concomitant medication
 3.2 Documented DMARDs at baseline

	n	%
Documented DMARDs at baseline		
Patient base	3285	100.0
Glucocorticoides	2063	62.8
MTX	1813	55.2
NSAID, Coxibe	683	20.8
Leflunomide	380	11.6
Analgesics	296	9.0
Other	127	3.9
SASP	118	3.6

Employed patient data set

3.Previous and concomitant medication

3.3 Documented DMARDs during study, baseline included

	n	%
Concomitant DMARDs		
Total	2983	90.8
Glucocorticoids	2223	67.7
MTX	1981	60.3
NSAIDs, Coxibe	756	23.0
Leflunomide	416	12.7
Analgesics	332	10.1
Other	304	9.3
SASP	134	4.1

Employed patient data set

3.Previous and concomitant medication

3.4 Glucocorticoid dosage at baseline and maximum dosage during study

		Glucocorticode dosage at baseline mg/d	Maximum Glucocorticode dosage during study mg/d
Total	N	2029	2198
	Missing	1256	1087
	Mean	7.6	9.1
	SD	6.2	8.5
	Min	1	1
	Median	5.0	5.0
	Max	103	103

Employed patient data set

3.Previous and concomitant medication

3.5 MTX dosage at baseline and maximum dosage during study

		MTX dosage at baseline mg/w	Maximum MTX dosage during study mg/w
Total	N	1778	1953
	Missing	1507	1332
	Mean	14.7	14.6
	SD	5.0	5.0
	Min	1	1
	Median	15.0	15.0
	Max	50	50

Employed patient data set
 3.Previous and concomitant medication
 3.6 Previous biologic therapies
 3.6.1 Percentage previous biologics

	n	%
Documented previous biologics at baseline		
Patient base	3285	100.0
Etanercept	443	13.5
Other	161	4.9
Infliximab	83	2.5
Tocilizumab	80	2.4
Certolizumab	68	2.1
Golimumab	57	1.7
Abatacept	35	1.1
Rituximab	29	0.9

Employed patient data set

3.Previous and concomitant medication

3.6 Previous biologic therapies

3.6.2 Mean duration of previous biologics (month)

		Infliximab	Etanercept	Golimumab	Certolizumab	Abatacept	Rituximab	Tocilizumab
Total	N	82	440	57	68	34	27	80
	Missing	3203	2845	3228	3217	3251	3258	3205
	Mean	37.0	24.1	15.5	9.4	10.2	12.9	11.7
	SD	41.2	28.7	25.2	11.1	10.2	14.7	14.4
	Min	1	1	1	1	1	1	1
	Median	19.5	13.0	7.0	6.0	6.0	8.0	7.0
	Max	177	188	169	62	50	51	96

Employed patient data set
 3.Previous and concomitant medication
 3.7 Number of previous biologics

	Number of previous biologics						Total	
	0		1		>=2			
	n	%	n	%	n	%	n	%
Total	2484	75.6	682	20.8	119	3.6	3285	100.0

Employed patient data set

3.Previous and concomitant medication

3.8 Main reasons for discontinuing the previous biologic therapy

	Reason for discontinuing the previous biologic therapy						Total	
	Lack of effectiveness		Lack of tolerance		Other reason			
	n	%	n	%	n	%	n	%
Total	509	63.0	160	19.8	139	17.2	808	100.0

Employed patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.1 Withdrawal reasons by visit

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Employed patients at M0	Adverse drug reaction	53	1.7	30	1.2	21	1.0	13	0.8	2	0.2	4	0.5	1	0.2
	Lack of effectiveness	173	5.7	153	5.9	156	7.1	131	8.3	55	5.1	18	2.4	15	2.6
	Other reason	93	3.1	53	2.0	85	3.9	84	5.3	62	5.7	38	5.0	39	6.7
	Unknown Reason	4	0.1	5	0.2	5	0.2	8	0.5	8	0.7	3	0.4	0	0.0
	Ongoing patients at the end of visit	2713	89.4	2348	90.7	1915	87.8	1349	85.1	961	88.3	701	91.8	527	90.5
	Total	3036	100.0	2589	100.0	2182	100.0	1585	100.0	1088	100.0	764	100.0	582	100.0

Employed patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.2 Disposition of patients (cumulated withdrawal rates)

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Employed patients at M0	Adverse drug reaction	53	1.6	83	2.5	104	3.2	117	3.6	119	3.6	123	3.7	124	3.8
	Lack of effectiveness	173	5.3	326	9.9	482	14.7	613	18.7	668	20.3	686	20.9	701	21.3
	Other reason	93	2.8	146	4.4	231	7.0	315	9.6	377	11.5	415	12.6	454	13.8
	Unknown Reason	4	0.1	9	0.3	14	0.4	22	0.7	30	0.9	33	1.0	33	1.0
	Lost to follow up (cummulated)	130	4.0	271	8.2	475	14.5	806	24.5	1076	32.8	1274	38.8	1446	44.0
	Ongoing patients at the end of visit	2713	82.6	2348	71.5	1915	58.3	1349	41.1	961	29.3	701	21.3	527	16.0
	Single visit missing (a later visit is following)	119	3.6	102	3.1	64	1.9	63	1.9	54	1.6	53	1.6	0	0.0
	Total	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0

Employed patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.3 Disposition of patients (shortened)

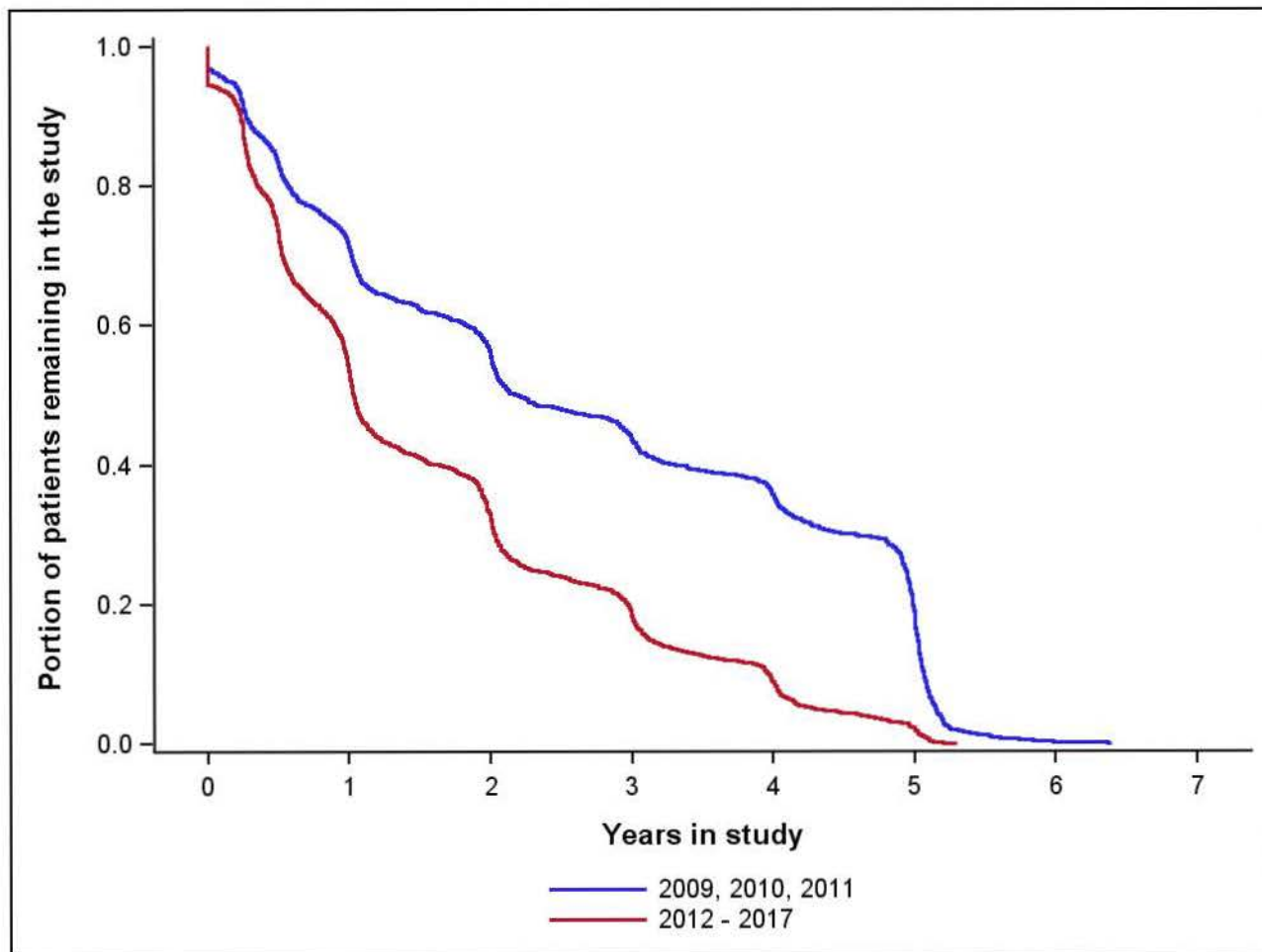
		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Employed patients at M0	Cummulative documented withdrawals	323	9.8	564	17.2	831	25.3	1067	32.5	1194	36.3	1257	38.3	1312	39.9
	Ongoing patients at the end of visit	2713	82.6	2348	71.5	1915	58.3	1349	41.1	961	29.3	701	21.3	527	16.0
	Single visit missing (a later visit is following)	119	3.6	102	3.1	64	1.9	63	1.9	54	1.6	53	1.6	0	0.0
	Lost to follow up (cummulated)	130	4.0	271	8.2	475	14.5	806	24.5	1076	32.8	1274	38.8	1446	44.0
	Total	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0	3285	100.0

This table is based on the attended visits and the withdrawal reasons documented on final visit
 Withdrawal reasons are cumulated, ongoing patients and single visit missing are not cumulated

Employed patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.4 Total duration of study (Kaplan-Meier, computed by visit dates) by year of baseline



Employed patient data set
 5. Work disability
 5.1 Employment status over time

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Employment status														
Total	Full time job (35h and more)	2156	65.6	1560	63.5	1290	62.3	903	61.2	625	61.0	412	57.5	285	53.7
	Part-time work	1129	34.4	767	31.2	622	30.0	413	28.0	268	26.2	186	25.9	129	24.3
	School, education, studying	0	0.0	12	0.5	8	0.4	5	0.3	4	0.4	3	0.4	1	0.2
	Home making, child-rearing	0	0.0	23	0.9	22	1.1	23	1.6	14	1.4	14	2.0	11	2.1
	Unemployed	0	0.0	49	2.0	51	2.5	52	3.5	26	2.5	17	2.4	21	4.0
	Retirement	0	0.0	47	1.9	79	3.8	80	5.4	87	8.5	85	11.9	84	15.8
	Total	3285	100.0	2458	100.0	2072	100.0	1476	100.0	1024	100.0	717	100.0	531	100.0

Employed patient data set

5. Work disability

5.2 Mean missed work days

		M00	M06	M12	M24	M36	M48	M60
Total	N	3156	2326	1906	1321	890	613	426
	Missing	129	959	1379	1964	2395	2672	2859
	Mean	19.2	12.4	11.4	7.4	6.8	5.1	7.9
	SD	38.4	33.9	31.8	19.7	18.7	13.0	21.8
	Min	0	0	0	0	0	0	0
	Median	3.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	183	183	183	183	183

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

		M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	2267	1855	1290	868	596	415
	Missing	1018	1430	1995	2417	2689	2870
	Mean	-4.3	-3.4	-5.6	-6.7	-6.4	-4.1
	SD	32.7	37.3	30.3	32.2	27.7	32.0
	Min	-183	-183	-183	-180	-183	-183
	Median	0.0	0.0	0.0	0.0	0.0	0.0
	Max	180	180	163	183	143	179

Differences

Employed patient data set

5. Work disability

5.3 Mean missing work days due to rheumatic disease

		M00	M06	M12	M24	M36	M48	M60
Total	N	3175	2335	1916	1334	893	617	426
	Missing	110	950	1369	1951	2392	2668	2859
	Mean	12.6	7.3	5.1	3.0	1.9	1.3	1.6
	SD	33.4	28.4	23.7	15.4	9.5	4.7	7.6
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	183	183	183	60	105

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

5. Work disability

5.4 Mean missing work days due to infection

		M00	M06	M12	M24	M36	M48	M60
Total	N	3175	2335	1916	1334	893	617	426
	Missing	110	950	1369	1951	2392	2668	2859
	Mean	1.4	1.3	1.5	1.1	1.3	1.4	0.9
	SD	5.6	4.8	6.9	3.2	3.7	6.1	2.5
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	120	180	50	45	132	23

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

5. Work disability

5.5 Mean missing work days due to joint operations

		M00	M06	M12	M24	M36	M48	M60
Total	N	3175	2335	1916	1334	893	617	426
	Missing	110	950	1369	1951	2392	2668	2859
	Mean	1.8	1.2	2.0	1.6	1.1	0.6	1.5
	SD	12.9	11.1	15.2	11.3	9.0	4.6	11.3
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	180	183	183	135	60	183

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 - 60 in the last 12 month here divided by 2.

Employed patient data set

5. Work disability

5.6 Mean missing work days due to other reasons

		M00	M06	M12	M24	M36	M48	M60
Total	N	3175	2335	1916	1334	893	617	426
	Missing	110	950	1369	1951	2392	2668	2859
	Mean	2.8	2.2	3.6	1.8	2.4	1.7	3.3
	SD	15.2	12.6	18.8	7.4	12.0	7.3	15.5
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	183	100	183	90	183

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 - 60 in the last 12 month here divided by 2.

Employed patient data set

5. Work disability

5.7 Missed work days (%)

5.7.1 Any missed work days

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Any missed work days														
Total	Yes	1725	53.9	939	39.8	728	37.9	636	47.7	416	46.0	285	46.0	213	49.5
	No	1475	46.1	1418	60.2	1194	62.1	696	52.3	489	54.0	335	54.0	217	50.5
	Total	3200	100.0	2357	100.0	1922	100.0	1332	100.0	905	100.0	620	100.0	430	100.0

Employed patient data set

5. Work disability

5.7 Missed work days (%)

5.7.2 Missed work days <= 5

5.7.2.1 Missed work days <= 5 all time points

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Percentage of patients with <= 5 missing work days														
Total	Yes	1744	55.3	1639	70.5	1363	71.5	953	72.1	657	73.8	465	75.9	315	73.9
	No	1412	44.7	687	29.5	543	28.5	368	27.9	233	26.2	148	24.1	111	26.1
	Total	3156	100.0	2326	100.0	1906	100.0	1321	100.0	890	100.0	613	100.0	426	100.0

Employed patient data set

5. Work disability

5.7 Missed work days (%)

5.7.2 Missed work days <= 5

5.7.2.2 Missed work days <= 5 - test for month 24

		Visit			
		M0		M24	
		n	%	n	%
	Percentage of patients with <= 5 missing work days				
Total	Yes	788	61.1	932	72.2
	No	502	38.9	358	27.8
	Total	1290	100.0	1290	100.0

Only patients with available values for M00 and M24, McNemar Test is based on this data

Employed patient data set

5. Work disability

5.7 Missed work days (%)

5.7.2 Missed work days <= 5

5.7.2.3 Missed work days <= 5 - test for month 60

		Visit			
		M0		M60	
		n	%	n	%
	Percentage of patients with <= 5 missing work days				
Total	Yes	265	63.9	306	73.7
	No	150	36.1	109	26.3
	Total	415	100.0	415	100.0

Only patients with available values for M00 and M60, McNemar Test is based on this data

Employed patient data set

5. Work disability

5.8 Modified WAI

5.8.1 Modified WAI - absolute values

		M00	M06	M12	M24	M36	M48	M60
Total	N	2110	2036	1573	1178	797	540	377
	Missing	1175	1249	1712	2107	2488	2745	2908
	Mean	32.2	34.9	36.1	36.7	37.2	38.0	37.7
	SD	7.7	7.6	7.5	7.3	7.2	6.8	7.2
	Min	7	7	10	7	9	11	12
	Median	32.5	36.0	37.0	37.5	38.0	39.0	39.0
	Max	49	49	49	49	49	49	49

Employed patient data set

5. Work disability

5.8 Modified WAI

5.8.2 Modified WAI - differences

		M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	1908	1442	986	666	452	318
	Missing	1377	1843	2299	2619	2833	2967
	Mean	2.5	3.0	3.2	3.6	3.3	3.0
	SD	5.9	6.7	6.8	7.0	6.6	7.0
	Min	-18	-20	-20	-20	-17	-21
	Median	2.0	2.5	3.0	3.0	3.0	2.5
	Max	27	34	34	34	34	32

Modified WAI M24-M00 Signed rank (wilcoxon), p-value: <.0001
 Modified WAI M60-M00 Signed rank (wilcoxon), p-value: <.0001

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.1 Absenteeism (%)

5.9.1.1 Absenteeism (%) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	2253	1892	1550	1256	847	557	371	261
	Missing	1032	1393	1735	2029	2438	2728	2914	3024
	Mean	21.0	10.4	10.8	9.3	8.8	7.5	7.7	12.8
	SD	36.6	26.6	27.4	25.6	24.0	23.1	23.2	30.6
	Min	0	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	100	100	100	100	100	100	100	100

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.1 Absenteeism (%)

5.9.1.2 Absenteeism (%) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	1482	1220	969	660	424	287	200
	Missing	1803	2065	2316	2625	2861	2998	3085
	Mean	-7.9	-8.0	-7.3	-6.5	-8.0	-5.2	-5.2
	SD	34.6	37.2	38.3	36.1	34.7	34.6	40.7
	Min	-100	-100	-100	-100	-100	-100	-100
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	100	100	100	100	100	100	100

Absenteeism M24-M00 Signed rank (wilcoxon), p-value: <.0001
 Absenteeism M60-M00 Signed rank (wilcoxon), p-value: 0.0468

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.2 Presenteeism (%)

5.9.2.1 Presenteeism (%) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	2758	2433	2093	1714	1209	804	539	370
	Missing	527	852	1192	1571	2076	2481	2746	2915
	Mean	46.7	34.8	33.9	31.8	31.1	28.6	27.0	25.1
	SD	26.9	24.3	24.3	23.7	23.7	23.3	22.1	21.3
	Min	0	0	0	0	0	0	0	0
	Median	50.0	30.0	30.0	30.0	30.0	20.0	20.0	20.0
	Max	100	100	100	100	100	100	100	100

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.2 Presenteeism (%)

5.9.2.2 Presenteeism (%) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	2157	1852	1513	1084	717	490	343
	Missing	1128	1433	1772	2201	2568	2795	2942
	Mean	-11.3	-11.8	-12.7	-12.9	-15.3	-16.4	-15.2
	SD	25.8	26.7	28.2	28.6	28.8	29.4	27.8
	Min	-100	-100	-100	-100	-100	-100	-90
	Median	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
	Max	90	100	100	100	80	80	90

Presenteeism M24-M00 Signed rank (wilcoxon), p-value: <.0001
 Presenteeism M60-M00 Signed rank (wilcoxon), p-value: <.0001

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.3 Total work productivity impairment (%)

5.9.3.1 Total work productivity impairment (%) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	2026	1793	1458	1183	811	530	356	239
	Missing	1259	1492	1827	2102	2474	2755	2929	3046
	Mean	50.9	37.1	36.0	32.7	33.0	29.8	29.6	28.8
	SD	28.9	26.5	26.7	25.4	26.0	24.8	24.3	24.9
	Min	0	0	0	0	0	0	0	0
	Median	50.0	30.0	30.0	30.0	30.0	20.0	20.0	20.0
	Max	100	100	100	100	100	100	100	100

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.3 Total work productivity impairment (%)

5.9.3.2 Total work productivity impairment (%) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	1313	1073	851	596	382	261	171
	Missing	1972	2212	2434	2689	2903	3024	3114
	Mean	-13.0	-14.4	-16.4	-15.3	-18.8	-16.7	-16.5
	SD	27.7	28.8	30.3	30.6	29.3	31.6	33.8
	Min	-100	-100	-100	-100	-100	-100	-88
	Median	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
	Max	90	100	100	80	80	80	93

Total work productivity impairment M24-M00 Signed rank (wilcoxon), p-value: <.0001
 Total work productivity impairment M60-M00 Signed rank (wilcoxon), p-value: <.0001

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.4 Total activity impairment (%)

5.9.4.1 Total activity impairment (%) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	3248	2783	2444	2025	1434	977	691	514
	Missing	37	502	841	1260	1851	2308	2594	2771
	Mean	51.7	39.5	37.6	35.3	33.9	31.5	31.3	30.4
	SD	25.9	24.7	25.2	24.9	24.4	23.9	23.5	23.2
	Min	0	0	0	0	0	0	0	0
	Median	50.0	40.0	30.0	30.0	30.0	30.0	30.0	30.0
	Max	100	100	100	100	100	100	100	100

Employed patient data set

5. Work disability

5.9 Modified WPAI

5.9.4 Total activity impairment (%)

5.9.4.2 Total activity impairment (%) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	2758	2420	2007	1424	970	687	509
	Missing	527	865	1278	1861	2315	2598	2776
	Mean	-11.9	-12.8	-13.8	-14.3	-15.4	-14.8	-14.8
	SD	26.5	27.5	28.6	28.4	29.7	29.4	28.6
	Min	-100	-100	-100	-100	-100	-100	-100
	Median	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
	Max	90	100	100	80	80	80	80

Total activity impairment M24-M00 Signed rank (wilcoxon), p-value: <.0001
 Total activity impairment M60-M00 Signed rank (wilcoxon), p-value: <.0001

Employed patient data set

6. Work disability by baseline sick leave days

6.1 Employment status over time

6.1.1 Employment status by visit

		Visit														
		M0		M6		M12		M24		M36		M48		M60		
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Sick leave days in past 6 months	Employment status															
	0-5	Full time job (35h and more)	1112	63.8	853	62.5	732	61.9	528	61.5	370	60.2	252	57.4	181	53.9
		Part-time work	632	36.2	455	33.3	379	32.0	249	29.0	161	26.2	110	25.1	77	22.9
		School, education, studying	0	0.0	3	0.2	3	0.3	3	0.3	4	0.7	2	0.5	0	0.0
		Home making, child-rearing	0	0.0	12	0.9	14	1.2	14	1.6	10	1.6	10	2.3	8	2.4
		Unemployed	0	0.0	19	1.4	16	1.4	20	2.3	13	2.1	13	3.0	14	4.2
		Retirement	0	0.0	23	1.7	39	3.3	44	5.1	57	9.3	52	11.8	56	16.7
		Total	1744	100.0	1365	100.0	1183	100.0	858	100.0	615	100.0	439	100.0	336	100.0

Employed patient data set
 6. Work disability by baseline sick leave days
 6.1 Employment status over time
 6.1.1 Employment status by visit

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sick leave days in past 6 months	Employment status														
	>5														
	Full time job (35h and more)	965	68.3	668	65.8	521	63.3	357	62.5	245	64.5	154	59.9	101	55.5
	Part-time work	447	31.7	288	28.4	226	27.5	148	25.9	96	25.3	68	26.5	46	25.3
	School, education, studying	0	0.0	7	0.7	3	0.4	2	0.4	0	0.0	1	0.4	1	0.5
	Home making, child-rearing	0	0.0	9	0.9	7	0.9	7	1.2	2	0.5	3	1.2	3	1.6
	Unemployed	0	0.0	24	2.4	34	4.1	30	5.3	13	3.4	3	1.2	7	3.8
	Retirement	0	0.0	19	1.9	32	3.9	27	4.7	24	6.3	28	10.9	24	13.2
Total	1412	100.0	1015	100.0	823	100.0	571	100.0	380	100.0	257	100.0	182	100.0	

Employed patient data set

6. Work disability by baseline sick leave days

6.1 Employment status over time

6.1.2 Employment status supplemented with disposition information

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sick leave days in past 6 months	Supplemented employment status														
	0-5														
	Full time job (35h and more)	1112	63.8	853	48.9	732	42.0	528	30.3	370	21.2	252	14.4	181	10.4
	Part-time work	632	36.2	455	26.1	379	21.7	249	14.3	161	9.2	110	6.3	77	4.4
	Not employed	0	0.0	57	3.3	72	4.1	81	4.6	84	4.8	77	4.4	78	4.5
	In study but unknown employment status	0	0.0	46	2.6	34	1.9	36	2.1	18	1.0	19	1.1	15	0.9
	Discontinued, lost to follow up or single visit missing	0	0.0	333	19.1	527	30.2	850	48.7	1111	63.7	1286	73.7	1393	79.9
	Total	1744	100.0	1744	100.0	1744	100.0	1744	100.0	1744	100.0	1744	100.0	1744	100.0
>5	Supplemented employment status														
	Full time job (35h and more)	965	68.3	668	47.3	521	36.9	357	25.3	245	17.4	154	10.9	101	7.2
	Part-time work	447	31.7	288	20.4	226	16.0	148	10.5	96	6.8	68	4.8	46	3.3
	Not employed	0	0.0	59	4.2	76	5.4	66	4.7	39	2.8	35	2.5	35	2.5
	In study but unknown employment status	0	0.0	48	3.4	35	2.5	17	1.2	18	1.3	12	0.8	9	0.6

(Continued)

Employed patient data set

6. Work disability by baseline sick leave days

6.1 Employment status over time

6.1.2 Employment status supplemented with disposition information

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sick leave days in past 6 months	Supplemented employment status														
	>5														
	Discontinued, lost to follow up or single visit missing	0	0.0	349	24.7	554	39.2	824	58.4	1014	71.8	1143	80.9	1221	86.5
	Total	1412	100.0	1412	100.0	1412	100.0	1412	100.0	1412	100.0	1412	100.0	1412	100.0

Employed patient data set

6. Work disability by baseline sick leave days

6.2 Mean missed work days

		M00	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months								
	0-5							
	N	1744	1310	1113	788	534	374	265
	Missing	0	434	631	956	1210	1370	1479
	Mean	0.6	4.4	6.2	4.2	4.7	3.2	7.4
	SD	1.4	16.1	21.6	13.0	17.1	9.3	21.8
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	5	180	183	163	183	90	183
	>5							
	N	1412	957	742	502	334	222	150
	Missing	0	455	670	910	1078	1190	1262
	Mean	42.2	22.7	19.7	12.5	10.3	8.4	9.1
	SD	48.3	45.1	42.0	26.6	21.0	17.3	22.5
	Min	6	0	0	0	0	0	0
	Median	21.0	5.0	2.0	3.5	3.0	2.5	2.0
	Max	183	183	183	183	183	183	183

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

6. Work disability by baseline sick leave days

6.2 Mean missed work days

		M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00	
Sick leave days in past 6 months								
	0-5	N	1310	1113	788	534	374	265
		Missing	434	631	956	1210	1370	1479
		Mean	3.8	5.6	3.7	4.1	2.7	6.9
		SD	16.0	21.5	13.0	16.9	9.2	21.7
		Min	-5	-5	-5	-5	-5	-5
		Median	0.0	0.0	0.0	0.0	0.0	0.0
		Max	180	180	163	183	90	179
>5	N	957	742	502	334	222	150	
	Missing	455	670	910	1078	1190	1262	
	Mean	-15.4	-17.0	-20.2	-24.0	-21.7	-23.5	
	SD	44.3	49.7	41.8	42.0	39.3	37.8	
	Min	-183	-183	-183	-180	-183	-183	
	Median	-10.0	-13.0	-12.0	-14.5	-14.0	-14.0	
	Max	171	174	154	155	143	98	

Differences

Employed patient data set

6. Work disability by baseline sick leave days

6.3 Mean missing work days due to rheumatic disease

		M00	M06	M12	M24	M36	M48	M60	
Sick leave days in past 6 months									
	0-5	N	1744	1312	1115	790	536	375	265
		Missing	0	432	629	954	1208	1369	1479
		Mean	0.3	1.8	2.0	1.0	1.4	0.6	1.2
		SD	1.0	11.6	14.1	7.7	10.4	3.0	6.6
		Min	0	0	0	0	0	0	0
		Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Max	5	180	183	138	183	45	90
>5	N	1412	962	749	512	335	225	150	
	Missing	0	450	663	900	1077	1187	1262	
	Mean	28.1	14.7	10.0	6.1	2.7	2.4	2.1	
	SD	45.6	39.8	33.2	22.6	8.2	6.6	9.3	
	Min	0	0	0	0	0	0	0	
	Median	12.0	0.0	0.0	0.0	0.0	0.0	0.0	
	Max	183	183	183	183	90	60	105	

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

6. Work disability by baseline sick leave days

6.4 Mean missing work days due to infection

		M00	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months								
	0-5							
	N	1744	1312	1115	790	536	375	265
	Missing	0	432	629	954	1208	1369	1479
	Mean	0.2	0.8	1.0	0.8	0.8	0.8	0.7
	SD	0.9	3.1	4.7	2.1	2.3	2.4	2.4
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	5	35	120	19	24	25	23
	>5							
	N	1412	962	749	512	335	225	150
	Missing	0	450	663	900	1077	1187	1262
	Mean	3.0	1.9	2.5	1.6	2.2	2.4	1.3
	SD	8.1	6.5	9.4	4.3	5.1	9.6	2.8
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	120	180	50	45	132	15

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

6. Work disability by baseline sick leave days

6.5 Mean missing work days due to joint operations

		M00	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months								
	0-5							
	N	1744	1312	1115	790	536	375	265
	Missing	0	432	629	954	1208	1369	1479
	Mean	0.0	0.8	1.2	1.0	1.0	0.2	0.9
	SD	0.1	8.8	10.4	8.0	9.6	2.6	6.3
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	4	180	180	163	135	45	60
	>5							
	N	1412	962	749	512	335	225	150
	Missing	0	450	663	900	1077	1187	1262
	Mean	4.1	1.5	3.3	2.5	1.3	1.4	2.5
	SD	19.2	11.3	20.6	15.4	8.1	6.9	17.1
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	180	183	183	90	60	183

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

6. Work disability by baseline sick leave days

6.6 Mean missing work days due to other reasons

		M00	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months								
	0-5							
	N	1744	1312	1115	790	536	375	265
	Missing	0	432	629	954	1208	1369	1479
	Mean	0.1	0.9	2.3	1.4	2.0	1.5	3.8
	SD	0.6	4.6	14.1	6.1	11.8	7.0	18.4
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	5	63	180	75	183	90	183
	>5							
	N	1412	962	749	512	335	225	150
	Missing	0	450	663	900	1077	1187	1262
	Mean	6.3	3.7	5.6	2.6	2.9	2.1	2.6
	SD	22.3	18.2	24.4	9.2	12.5	8.0	9.1
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	183	100	150	75	90

Absolute values, for baseline, visit month 6, visit month 12 in the last 6 month. For visit month 24 in the last 12 month here divided by 2.

Employed patient data set

6. Work disability by baseline sick leave days

6.7 Missed work days (%)

6.7.1 Any missed work days

		Visit														
		M0		M6		M12		M24		M36		M48		M60		
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Sick leave days in past 6 months	Any missed work days															
	0-5	Yes	265	15.2	356	27.0	313	28.0	306	38.6	188	34.8	134	35.4	120	44.6
	No	1475	84.8	963	73.0	805	72.0	487	61.4	352	65.2	245	64.6	149	55.4	
	Total	1740	100.0	1319	100.0	1118	100.0	793	100.0	540	100.0	379	100.0	269	100.0	
>5	Any missed work days															
	Yes	1412	100.0	557	57.1	400	53.3	315	62.3	216	63.2	143	64.1	89	59.3	
	No	0	0.0	419	42.9	351	46.7	191	37.7	126	36.8	80	35.9	61	40.7	
	Total	1412	100.0	976	100.0	751	100.0	506	100.0	342	100.0	223	100.0	150	100.0	

Employed patient data set

6. Work disability by baseline sick leave days

6.7 Missed work days (%)

6.7.2 Missed work days <= 5

		Visit														
		M0		M6		M12		M24		M36		M48		M60		
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Sick leave days in past 6 months	Percentage of patients with <= 5 missing work days															
	0-5	Yes	1744	100.0	1093	83.4	896	80.5	640	81.2	443	83.0	310	82.9	211	79.6
		No	0	0.0	217	16.6	217	19.5	148	18.8	91	17.0	64	17.1	54	20.4
		Total	1744	100.0	1310	100.0	1113	100.0	788	100.0	534	100.0	374	100.0	265	100.0
>5	Percentage of patients with <= 5 missing work days															
		Yes	0	0.0	509	53.2	425	57.3	292	58.2	201	60.2	141	63.5	95	63.3
		No	1412	100.0	448	46.8	317	42.7	210	41.8	133	39.8	81	36.5	55	36.7
		Total	1412	100.0	957	100.0	742	100.0	502	100.0	334	100.0	222	100.0	150	100.0

Employed patient data set

6. Work disability by baseline sick leave days

6.8 Modified WAI

		M00	M06	M12	M24	M36	M48	M60	
Sick leave days in past 6 months									
	0-5	N	1217	1186	930	703	469	332	233
		Missing	527	558	814	1041	1275	1412	1511
		Mean	35.2	37.1	37.6	38.2	38.7	39.4	39.2
		SD	6.4	6.6	6.8	6.6	6.5	6.0	6.5
		Min	12	9	14	14	12	20	12
		Median	35.5	38.0	38.5	39.0	40.0	40.0	40.0
		Max	49	49	49	49	49	49	49
>5	N	884	844	606	449	309	195	136	
	Missing	528	568	806	963	1103	1217	1276	
	Mean	28.1	31.8	33.7	34.6	35.0	35.8	35.7	
	SD	7.4	7.9	8.1	7.6	7.7	7.1	7.6	
	Min	7	7	10	7	9	11	17	
	Median	28.0	32.5	34.0	35.0	35.0	36.0	36.0	
	Max	47	48	49	49	49	49	49	

Absolute values

535

The number of sick leave days was reported at baseline for the last 6 month, to accomplish a 12 month time period the sick leave days of visit month 6 were added.

Employed patient data set

6. Work disability by baseline sick leave days

6.8 Modified WAI

		M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
0-5	Sick leave days in past 6 months						
	N	1118	876	607	405	288	207
	Missing	626	868	1137	1339	1456	1537
	Mean	1.8	1.8	2.1	2.2	2.1	1.4
	SD	5.2	5.6	5.7	5.5	5.6	5.9
	Min	-18	-20	-20	-18	-17	-21
	Median	1.5	1.5	2.0	2.0	2.0	1.5
	Max	24	23	18	16	17	20
>5	N	785	563	376	258	162	111
	Missing	627	849	1036	1154	1250	1301
	Mean	3.5	4.9	5.0	5.7	5.4	6.0
	SD	6.6	7.7	7.9	8.4	7.4	7.9
	Min	-18	-19	-20	-20	-16	-14
	Median	3.0	4.0	4.0	5.0	5.0	5.0
	Max	27	34	34	34	34	32

Differences

536

The number of sick leave days was reported at baseline for the last 6 month, to accomplish a 12 month time period the sick leave days of visit month 6 were added.

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.1 Absenteeism (%)

		M00	M03	M06	M12	M24	M36	M48	M60	
Sick leave days in past 6 months										
	0-5	N	1196	1062	862	727	489	334	229	165
		Missing	548	682	882	1017	1255	1410	1515	1579
		Mean	6.6	5.8	6.2	5.8	6.2	4.1	5.4	10.0
		SD	19.4	19.4	20.3	20.7	20.2	17.7	20.5	27.3
		Min	0	0	0	0	0	0	0	0
		Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Max	100	100	100	100	100	100	100	100
>5	N	1012	792	657	502	338	213	135	92	
	Missing	400	620	755	910	1074	1199	1277	1320	
	Mean	37.6	16.1	16.6	14.0	12.4	13.0	11.5	17.3	
	SD	44.0	32.7	33.5	30.4	28.4	29.3	27.1	34.9	
	Min	0	0	0	0	0	0	0	0	
	Median	9.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	Max	100	100	100	100	100	100	100	100	

Absolute values

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.1 Absenteeism (%)

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00	
Sick leave days in past 6 months									
	0-5	N	833	681	564	391	261	180	130
		Missing	911	1063	1180	1353	1483	1564	1614
		Mean	-0.9	-1.1	0.3	0.2	-1.3	0.6	2.8
		SD	23.0	23.9	24.7	25.4	20.8	22.0	33.1
		Min	-100	-100	-100	-100	-100	-91	-100
		Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
		Max	100	100	100	100	100	100	100
>5	N	629	523	390	258	159	103	68	
	Missing	783	889	1022	1154	1253	1309	1344	
	Mean	-16.9	-16.3	-18.4	-16.5	-18.5	-15.1	-20.7	
	SD	44.1	47.7	50.0	46.3	47.7	48.2	49.4	
	Min	-100	-100	-100	-100	-100	-100	-100	
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	Max	100	100	100	100	100	100	100	

Differences

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.2 Presenteeism (%)

		M00	M03	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months									
	0-5								
	N	1606	1393	1217	1024	719	480	328	240
	Missing	138	351	527	720	1025	1264	1416	1504
	Mean	40.7	30.9	30.6	28.1	27.2	25.1	24.7	22.0
	SD	25.5	22.6	23.3	22.3	22.5	21.9	21.7	19.1
	Min	0	0	0	0	0	0	0	0
	Median	40.0	30.0	30.0	20.0	20.0	20.0	20.0	20.0
	Max	100	100	100	100	100	100	100	90
>5	N	1076	981	823	645	461	305	199	124
	Missing	336	431	589	767	951	1107	1213	1288
	Mean	54.9	39.8	38.3	36.9	36.3	33.1	30.6	29.8
	SD	26.4	25.6	24.9	24.7	24.0	24.1	22.4	23.4
	Min	0	0	0	0	0	0	0	0
	Median	60.0	40.0	30.0	30.0	30.0	30.0	30.0	30.0
	Max	100	100	100	100	100	100	100	100

Absolute values

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.2 Presenteeism (%)

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00	
Sick leave days in past 6 months									
	0-5	N	1301	1135	958	675	451	312	233
		Missing	443	609	786	1069	1293	1432	1511
		Mean	-9.0	-9.6	-10.9	-11.9	-13.9	-12.8	-12.8
		SD	23.8	24.9	26.0	27.4	26.8	27.7	25.5
		Min	-100	-100	-90	-90	-90	-90	-80
		Median	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
		Max	90	100	80	80	80	80	90
>5	N	811	681	519	387	252	170	106	
	Missing	601	731	893	1025	1160	1242	1306	
	Mean	-14.7	-15.6	-16.6	-14.8	-18.5	-23.0	-21.4	
	SD	28.6	29.2	31.2	30.7	31.9	31.3	31.4	
	Min	-100	-100	-100	-100	-100	-100	-90	
	Median	-10.0	-10.0	-20.0	-10.0	-20.0	-20.0	-20.0	
	Max	80	100	100	100	80	60	60	

Differences

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.3 Total work productivity impairment (%)

		M00	M03	M06	M12	M24	M36	M48	M60
Sick leave days in past 6 months									
	0-5								
	N	1166	1028	827	694	472	322	221	156
	Missing	578	716	917	1050	1272	1422	1523	1588
	Mean	42.5	32.8	31.5	28.5	28.1	24.8	26.7	26.2
	SD	26.4	24.4	24.9	23.5	24.1	22.1	23.9	23.6
	Min	0	0	0	0	0	0	0	0
	Median	40.0	30.0	30.0	20.0	20.0	20.0	20.0	20.0
	Max	100	100	100	100	100	100	100	100
>5	N	823	731	603	462	319	198	128	81
	Missing	589	681	809	950	1093	1214	1284	1331
	Mean	62.7	42.8	41.7	38.2	39.4	37.7	34.1	33.5
	SD	28.1	28.2	27.9	26.6	26.7	27.1	24.4	27.1
	Min	0	0	0	0	0	0	0	0
	Median	70.0	40.0	40.0	30.0	40.0	30.0	30.0	30.0
	Max	100	100	100	100	100	100	100	100

Absolute values

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.3 Total work productivity impairment (%)

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00	
Sick leave days in past 6 months									
	0-5	N	794	642	534	375	248	176	119
		Missing	950	1102	1210	1369	1496	1568	1625
		Mean	-9.7	-11.8	-12.5	-12.7	-16.2	-13.1	-11.4
		SD	25.1	25.8	27.0	28.8	28.2	29.7	31.6
		Min	-90	-90	-90	-98	-88	-98	-88
		Median	-5.9	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
		Max	90	100	70	80	80	80	93
>5	N	503	421	304	212	131	82	51	
	Missing	909	991	1108	1200	1281	1330	1361	
	Mean	-18.2	-18.4	-23.9	-20.0	-24.2	-25.6	-28.7	
	SD	30.7	32.5	33.8	33.5	30.7	34.2	36.0	
	Min	-100	-100	-100	-100	-100	-100	-80	
	Median	-14.5	-20.0	-20.0	-16.1	-20.0	-22.6	-30.0	
	Max	90	70	80	70	30	70	70	

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.4 Total activity impairment (%)

		M00	M03	M06	M12	M24	M36	M48	M60	
Sick leave days in past 6 months										
	0-5	N	1728	1510	1355	1158	834	584	425	324
		Missing	16	234	389	586	910	1160	1319	1420
		Mean	44.5	34.7	33.0	30.8	29.8	27.7	28.1	27.0
		SD	25.2	23.3	23.7	22.9	23.6	22.4	22.3	21.5
		Min	0	0	0	0	0	0	0	0
		Median	50.0	30.0	30.0	30.0	20.0	20.0	20.0	20.0
		Max	100	100	100	100	100	100	100	90
>5	N	1393	1182	1013	808	556	366	247	178	
	Missing	19	230	399	604	856	1046	1165	1234	
	Mean	59.8	44.9	43.0	41.3	39.4	36.5	35.9	34.9	
	SD	24.2	25.1	26.1	26.1	24.4	25.0	24.2	24.5	
	Min	0	0	0	0	0	0	0	0	
	Median	60.0	40.0	40.0	40.0	40.0	30.0	30.0	30.0	
	Max	100	100	100	100	100	100	100	100	

Absolute values

Employed patient data set

6. Work disability by baseline sick leave days

6.9 Modified WPAI

6.9.4 Total activity impairment (%)

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Sick leave days in past 6 months								
0-5	N	1498	1343	1149	828	580	423	320
	Missing	246	401	595	916	1164	1321	1424
	Mean	-9.7	-10.4	-11.5	-12.1	-12.6	-11.6	-10.4
	SD	24.5	25.7	26.5	27.1	27.7	27.6	25.7
	Min	-100	-100	-90	-100	-100	-80	-80
	Median	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0	-10.0
	Max	90	100	80	80	70	80	80
>5	N	1171	1002	799	552	363	245	177
	Missing	241	410	613	860	1049	1167	1235
	Mean	-14.8	-16.2	-17.6	-18.0	-20.2	-20.6	-23.7
	SD	28.5	29.7	30.9	30.0	32.7	31.6	31.7
	Min	-100	-100	-100	-100	-100	-100	-100
	Median	-10.0	-20.0	-20.0	-20.0	-20.0	-20.0	-20.0
	Max	90	100	90	80	80	70	60

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	3156	19.1730038	38.3516284	0	183.0000000
present_M00	Presenteism (%)	2758	46.6715011	26.9165234	0	100.0000000
wai_M00	Modified WAI	2110	32.1758294	7.7401115	7.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	3282	0.3019500	0.4591737	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3243	0.1122418	0.3157123	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3248	0.1659483	0.3720915	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	3044	0.6363338	0.4811332	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	2834	0.6429076	0.4792269	0	1.0000000
smokejn	Smoker (1=yes)	3228	0.2503098	0.4332585	0	1.0000000
AGE	Age	3285	48.3245053	9.4164716	18.0000000	83.0000000
bmi_M00	Body mass index (kg/m ²)	3239	26.4102992	5.2446266	17.0068027	65.4372397
bradau	Duration of disease (years)	3227	7.8681038	7.2390550	0.0054757	54.3299110
STIFFTM_M00	Morning stiffness (minutes)	3201	53.9934396	70.7215598	0	800.0000000
CRP_M00	CRP (mg/l)	3099	15.8024589	45.7581626	0	978.0000000
BSG_M00	ESR (mm/h)	2917	23.1412410	19.6462003	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	3028	18.7932629	26.6086206	0	483.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3259	5.3620743	2.8510578	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3259	5.3099110	2.5670260	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3265	0.9468369	0.6774310	0	3.0000000
prevbio	Number of previous biologics	3285	0.2910198	0.5765899	0	6.0000000
mtxjn	MTX	3285	0.5519026	0.4973745	0	1.0000000
saspjn	SASP	3285	0.0359209	0.1861212	0	1.0000000
lefjn	Leflunomide	3285	0.1156773	0.3198863	0	1.0000000
nsacoxjn	NSAID, Coxibe	3285	0.2079148	0.4058773	0	1.0000000
anajn	Analgesics	3285	0.0901065	0.2863779	0	1.0000000
glucjn	Glucocorticoides	3285	0.6280061	0.4834104	0	1.0000000
seq1jn	Arterial hypertension	3285	0.2270928	0.4190169	0	1.0000000
seq2jn	Coronary heart disease	3285	0.0164384	0.1271733	0	1.0000000
seq3jn	Hyperlipidemia	3285	0.0474886	0.2127139	0	1.0000000
seq4jn	Diabetes Type I	3285	0.0121766	0.1096903	0	1.0000000
seq5jn	Diabetes Type II	3285	0.0435312	0.2040807	0	1.0000000
seq6jn	Chronic inflammatory disease	3285	0.0182648	0.1339280	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3285	0.0307458	0.1726545	0	1.0000000
seq8jn	Osteoporosis	3285	0.0687976	0.2531481	0	1.0000000
seq9jn	Degenerative joint disease	3285	0.1086758	0.3112794	0	1.0000000
seq10jn	Degenerative spinal disease	3285	0.0861492	0.2806269	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3285	0.0453577	0.2081191	0	1.0000000
wg	Without graduation	3257	0.0110531	0.1045672	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	3257	0.2661959	0.4420358	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	3257	0.4482653	0.4973927	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	3257	0.2744857	0.4463233	0	1.0000000

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	1235	12.9052632	28.4308413	0	183.0000000
present_M00	Presenteism (%)	1235	43.7083708	25.2045363	0	100.0000000
wai_M00	Modified WAI	1235	33.4442871	6.8329935	11.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	1235	0.2957861	0.4563953	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	1235	0.1181744	0.3218976	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	1235	0.1582382	0.3637792	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	1235	0.6608696	0.4570173	0	1.0000000
ccpin_M00	Anti-ccp (1=positive)	1235	0.6877870	0.4353202	0	1.0000000
smokejn	Smoker (1=yes)	1235	0.2324633	0.4210313	0	1.0000000
AGE	Age	1235	47.8210526	9.0094248	20.0000000	78.0000000
bmi_M00	Body mass index (kg/m ²)	1235	26.1214927	5.0001993	17.0403288	53.1462585
bradau	Duration of disease (years)	1235	8.2920553	7.1175791	0.0164271	40.9199179
STIFFTM_M00	Morning stiffness (minutes)	1235	47.8420622	64.9298494	0	720.0000000
CRP_M00	CRP (mg/l)	1233	14.4202676	39.9936403	0	642.0000000
BSG_M00	ESR (mm/h)	1235	21.7255075	17.8727184	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	1235	18.6198980	24.6777463	0	164.0000000
EXH_7DAYS_M00	Fatigue (0-10)	1235	4.9413203	2.8676612	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	1235	4.7879282	2.5914179	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	1235	0.8192834	0.6403303	0	2.7500000
prevbio	Number of previous biologics	1235	0.2429150	0.4823678	0	3.0000000
mtxjn	MTX	1235	0.5935223	0.4913747	0	1.0000000
saspjn	SASP	1235	0.0380567	0.1914106	0	1.0000000
lefjn	Leflunomide	1235	0.1020243	0.3028029	0	1.0000000
nsacoxjn	NSAID, Coxibe	1235	0.2105263	0.4078476	0	1.0000000
anajn	Analgesics	1235	0.0744939	0.2626794	0	1.0000000
glucjn	Glucocorticoides	1235	0.6259109	0.4840828	0	1.0000000
seq1jn	Arterial hypertension	1235	0.2056680	0.4043527	0	1.0000000
seq2jn	Coronary heart disease	1235	0.0137652	0.1165620	0	1.0000000
seq3jn	Hyperlipidemia	1235	0.0510121	0.2201116	0	1.0000000
seq4jn	Diabetes Type I	1235	0.0137652	0.1165620	0	1.0000000
seq5jn	Diabetes Type II	1235	0.0291498	0.1682944	0	1.0000000
seq6jn	Chronic inflammatory disease	1235	0.0170040	0.1293385	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	1235	0.0202429	0.1408872	0	1.0000000
seq8jn	Osteoporosis	1235	0.0615385	0.2404127	0	1.0000000
seq9jn	Degenerative joint disease	1235	0.0971660	0.2963036	0	1.0000000
seq10jn	Degenerative spinal disease	1235	0.0834008	0.2765991	0	1.0000000
seq11jn	Mental illness (e.g. depression)	1235	0.0307692	0.1727618	0	1.0000000
wg	Without graduation	1235	0.0072874	0.0850894	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	1235	0.2153846	0.4112554	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	1235	0.4639676	0.4989020	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	1235	0.3133603	0.4640474	0	1.0000000

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

1235 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Missing work days (last 6 month, M0)	-0.925123	-0.842121	50	0	183	12.905263
Health Assessment questionnaire (HAQ)	2.7881498	4.5707457	27	0	2.75	0.8192834
Hyperlipidemia	6.0485322	9.8482159	27	0	1	0.0510121
Modified WAI	-0.474374	-0.24741	27	11	49	33.444287
Body mass index (kg/m ²)	0.212159	0.3323274	14	17.040329	53.146259	26.121493
Prior joint surgery (1=yes)	3.0142896	4.4077865	12	0	1	0.1582382
CRP (mg/l)	-0.03541	-0.025712	9	0	642	14.420268
Rheumatic factor (1=positive)	-3.361105	-2.157276	9	0	1	0.6608696
Mental illness (e.g. depression)	7.344556	11.522114	9	0	1	0.0307692
Chronic obstructive pulmonary disease	-11.13213	-8.007253	8	0	1	0.0202429
Arterial hypertension	-4.693574	-2.832289	7	0	1	0.205668
Rheumatoid nodules (1=yes)	3.2661502	3.8904548	6	0	1	0.1181744
Leflunomide	3.8452425	4.0268773	4	0	1	0.1020243
Fatigue (0-10)	0.5416683	0.5465139	3	0	10	4.9413203
Presenteism (%)	-0.070294	-0.069128	3	0	100	43.708371
Diabetes Type II	-7.73435	-7.711343	3	0	1	0.0291498
NSAID, Coxibe	2.599551	2.599551	2	0	1	0.2105263
Coronary heart disease	-10.54642	-10.29621	2	0	1	0.0137652
Chronic inflammatory disease	9.0847476	9.2987801	2	0	1	0.017004
Degenerative joint disease	3.7285329	4.0214215	2	0	1	0.097166
ESR (mm/h)	-0.061132	-0.061132	1	1	120	21.725508

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Modell variables for $p:0.001$ with coefficients and R^2

1235 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R^2	Cummulated R^2 (model)	p-value
Intercept	18.79950	.	.	<.0001
Missing work days (last 6 month, M0)	-0.87379	0.61134	0.6113	<.0001
Modified WAI	-0.39027	0.00653	0.6179	<.0001

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Modell variables for p:0.001 with coefficients and R²

1235 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	2.40180	0.0063
Missing work days (last 6 month, M0)	-0.85898	<.0001
Health Assessment questionnaire (HAQ)	3.84846	<.0001

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand varanz	Mean prediction error Number of selected variables	9.220 2.000	8.481 2.000	9.833 2.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	9.225 2.600	8.399 2.000	10.020 3.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	9.283 3.000	8.399 2.000	10.020 5.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	9.562 6.800	8.803 6.000	10.233 7.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	9.682 9.200	9.094 7.000	10.338 11.000
none	0	5	meand varanz	Mean prediction error Number of selected variables	15.372 0.000	13.189 0.000	17.166 0.000
	1	5	meand varanz	Mean prediction error Number of selected variables	9.876 41.000	9.456 41.000	10.525 41.000
stepwise	0.0001	5	meand varanz	Mean prediction error Number of selected variables	9.284 2.000	8.481 2.000	10.152 2.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	9.252 2.400	8.399 2.000	10.152 3.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	9.329 3.000	8.399 2.000	10.251 5.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	9.454 5.600	8.429 4.000	10.233 7.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	9.654 8.800	9.015 7.000	10.351 11.000

Employed patient data set

7. Regression analyses:

7.1 Regression analysis for Missing work days (M24-M0) - lower values are better

Fixed modell

1290 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R ² stepwise is used				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	5.03803	.	.	<.0001
Missing work days (last 6 month, M0)	-0.81548	0.60018	0.6002	<.0001

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	3156	19.1730038	38.3516284	0	183.0000000
present_M00	Presenteeism (%)	2758	46.6715011	26.9165234	0	100.0000000
absent_M00	Absenteeism (%)	2253	20.9862399	36.5510465	0	100.0000000
wai_M00	Modified WAI	2110	32.1758294	7.7401115	7.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	3282	0.3019500	0.4591737	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3243	0.1122418	0.3157123	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3248	0.1659483	0.3720915	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	3044	0.6363338	0.4811332	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	2834	0.6429076	0.4792269	0	1.0000000
smokejn	Smoker (1=yes)	3228	0.2503098	0.4332585	0	1.0000000
AGE	Age	3285	48.3245053	9.4164716	18.0000000	83.0000000
bmi_M00	Body mass index (kg/m ²)	3239	26.4102992	5.2446266	17.0068027	65.4372397
bradau	Duration of disease (years)	3227	7.8681038	7.2390550	0.0054757	54.3299110
STIFFTM_M00	Morning stiffness (minutes)	3201	53.9934396	70.7215598	0	800.0000000
CRP_M00	CRP (mg/l)	3099	15.8024589	45.7581626	0	978.0000000
BSG_M00	ESR (mm/h)	2917	23.1412410	19.6462003	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	3028	18.7932629	26.6086206	0	483.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3259	5.3620743	2.8510578	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3259	5.3099110	2.5670260	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3265	0.9468369	0.6774310	0	3.0000000
prevbio	Number of previous biologics	3285	0.2910198	0.5765899	0	6.0000000
mtxjn	MTX	3285	0.5519026	0.4973745	0	1.0000000
saspjn	SASP	3285	0.0359209	0.1861212	0	1.0000000
lefjn	Leflunomide	3285	0.1156773	0.3198863	0	1.0000000
nsacoxjn	NSAID, Coxibe	3285	0.2079148	0.4058773	0	1.0000000
anajn	Analgesics	3285	0.0901065	0.2863779	0	1.0000000
glucjn	Glucocorticoides	3285	0.6280061	0.4834104	0	1.0000000
seq1jn	Arterial hypertension	3285	0.2270928	0.4190169	0	1.0000000
seq2jn	Coronary heart disease	3285	0.0164384	0.1271733	0	1.0000000
seq3jn	Hyperlipidemia	3285	0.0474886	0.2127139	0	1.0000000
seq4jn	Diabetes Type I	3285	0.0121766	0.1096903	0	1.0000000
seq5jn	Diabetes Type II	3285	0.0435312	0.2040807	0	1.0000000
seq6jn	Chronic inflammatory disease	3285	0.0182648	0.1339280	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3285	0.0307458	0.1726545	0	1.0000000
seq8jn	Osteoporosis	3285	0.0687976	0.2531481	0	1.0000000
seq9jn	Degenerative joint disease	3285	0.1086758	0.3112794	0	1.0000000
seq10jn	Degenerative spinal disease	3285	0.0861492	0.2806269	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3285	0.0453577	0.2081191	0	1.0000000
wg	Without graduation	3257	0.0110531	0.1045672	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	3257	0.2661959	0.4420358	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	3257	0.4482653	0.4973927	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	3257	0.2744857	0.4463233	0	1.0000000

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	639	12.4738510	26.0137810	0	183.0000000
present_M00	Presenteism (%)	639	43.8372093	25.6341528	0	100.0000000
absent_M00	Absenteeism (%)	639	14.7951859	31.0339395	0	100.0000000
wai_M00	Modified WAI	639	33.3058076	6.8972783	14.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	639	0.3103448	0.4626348	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	639	0.1165354	0.3201106	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	639	0.1732283	0.3775538	0	1.0000000
rfljn_M00	Rheumatic factor (1=positive)	639	0.6583333	0.4599276	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	639	0.6806283	0.4418453	0	1.0000000
smokejn	Smoker (1=yes)	639	0.2204724	0.4135894	0	1.0000000
AGE	Age	639	46.8888889	9.0489016	20.0000000	78.0000000
bmi_M00	Body mass index (kg/m ²)	639	26.1279028	4.8671359	17.0403288	51.2110727
bradau	Duration of disease (years)	639	8.6602267	7.4018154	0.0219028	40.9199179
STIFFTM_M00	Morning stiffness (minutes)	639	50.4091627	63.0940114	0	360.0000000
CRP_M00	CRP (mg/l)	638	14.9378723	42.2362541	0	548.0000000
BSG_M00	ESR (mm/h)	639	21.7996604	18.1445070	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	639	18.8887043	25.4559532	0	164.0000000
EXH_7DAYS_M00	Fatigue (0-10)	639	5.0188679	2.8619692	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	639	4.8929134	2.5927068	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	639	0.8314889	0.6532509	0	2.7500000
prevbio	Number of previous biologics	639	0.2331768	0.4722000	0	3.0000000
mtxjn	MTX	639	0.5805947	0.4938483	0	1.0000000
saspjn	SASP	639	0.0453834	0.2083067	0	1.0000000
lefjn	Leflunomide	639	0.1095462	0.3125679	0	1.0000000
nsacoxjn	NSAID, Coxibe	639	0.2206573	0.4150147	0	1.0000000
anajn	Analgesics	639	0.0766823	0.2662952	0	1.0000000
glucjn	Glucocorticoides	639	0.6118936	0.4877008	0	1.0000000
seq1jn	Arterial hypertension	639	0.2081377	0.4062939	0	1.0000000
seq2jn	Coronary heart disease	639	0.0078247	0.0881797	0	1.0000000
seq3jn	Hyperlipidemia	639	0.0500782	0.2182773	0	1.0000000
seq4jn	Diabetes Type I	639	0.0140845	0.1179318	0	1.0000000
seq5jn	Diabetes Type II	639	0.0250391	0.1563663	0	1.0000000
seq6jn	Chronic inflammatory disease	639	0.0187793	0.1358512	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	639	0.0156495	0.1242123	0	1.0000000
seq8jn	Osteoporosis	639	0.0563380	0.2307539	0	1.0000000
seq9jn	Degenerative joint disease	639	0.1001565	0.3004437	0	1.0000000
seq10jn	Degenerative spinal disease	639	0.0813772	0.2736276	0	1.0000000
seq11jn	Mental illness (e.g. depression)	639	0.0266041	0.1610493	0	1.0000000
wg	Without graduation	639	0.0015649	0.0395594	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	639	0.1987480	0.3993706	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	639	0.4679186	0.4993606	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	639	0.3317684	0.4712172	0	1.0000000

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

639 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Absenteeism (%)	-0.93907	-0.869302	50	0	100	14.795186
Health Assessment questionnaire (HAQ)	3.9421555	6.8455897	24	0	2.75	0.8314889
Fatigue (0-10)	0.9704635	1.1892294	14	0	10	5.0188679
Chronic inflammatory disease	16.087449	19.313444	11	0	1	0.0187793
Glucocorticoides	4.4693203	4.6617548	4	0	1	0.6118936
Gender (1=male, 0=female)	-4.487484	-4.487484	4	0	1	0.3103448
Age	0.2565209	0.2565209	3	20	78	46.888889
Analgesics	7.5224263	7.5224263	2	0	1	0.0766823
Rheumatoid nodules (1=yes)	6.4152566	6.4152566	2	0	1	0.1165354
Hyperlipidemia	-8.071914	-8.071914	2	0	1	0.0500782

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Modell variables for $p:0.001$ with coefficients and R^2

639 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R^2	Cummulated R^2 (model)	p-value
Intercept	2.71801	.	.	0.0638
Absenteism (%)	-0.90615	0.58426	0.5843	<.0001
Health Assessment questionnaire (HAQ)	5.09352	0.00806	0.5923	0.0004

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Modell variables for p:0.001 with coefficients and R²

639 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	2.71801	0.0638
Absenteism (%)	-0.90615	<.0001
Health Assessment questionnaire (HAQ)	5.09352	0.0004

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand varanz	Mean prediction error Number of selected variables	13.408 1.200	11.646 1.000	16.124 2.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	13.337 1.600	11.646 1.000	16.124 2.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	13.166 2.000	11.073 2.000	15.841 2.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	13.334 3.200	11.372 2.000	15.764 4.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	13.387 3.800	11.372 2.000	15.764 6.000
none	0	5	meand varanz	Mean prediction error Number of selected variables	20.739 0.000	17.494 0.000	26.796 0.000
	1	5	meand varanz	Mean prediction error Number of selected variables	14.178 42.000	12.815 42.000	16.360 42.000
stepwise	0.0001	5	meand varanz	Mean prediction error Number of selected variables	13.408 1.200	11.646 1.000	16.124 2.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	13.337 1.600	11.646 1.000	16.124 2.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	13.166 2.000	11.073 2.000	15.841 2.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	13.274 2.800	11.073 2.000	15.764 4.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	13.387 3.800	11.372 2.000	15.764 6.000

Employed patient data set

7. Regression analyses:

7.2 Regression analysis for WPAI - Absenteeism (%) (M24-M0) - lower values are better

Fixed modell

660 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R ² stepwise is used				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	3.00060	.	.	0.0422
Absenteism (%)	-0.90618	0.57924	0.5792	<.0001
Health Assessment questionnaire (HAQ)	5.04378	0.00761	0.5868	0.0005

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	3156	19.1730038	38.3516284	0	183.0000000
present_M00	Presenteeism (%)	2758	46.6715011	26.9165234	0	100.0000000
wai_M00	Modified WAI	2110	32.1758294	7.7401115	7.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	3282	0.3019500	0.4591737	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3243	0.1122418	0.3157123	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3248	0.1659483	0.3720915	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	3044	0.6363338	0.4811332	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	2834	0.6429076	0.4792269	0	1.0000000
smokejn	Smoker (1=yes)	3228	0.2503098	0.4332585	0	1.0000000
AGE	Age	3285	48.3245053	9.4164716	18.0000000	83.0000000
bmi_M00	Body mass index (kg/m ²)	3239	26.4102992	5.2446266	17.0068027	65.4372397
bradau	Duration of disease (years)	3227	7.8681038	7.2390550	0.0054757	54.3299110
STIFFTM_M00	Morning stiffness (minutes)	3201	53.9934396	70.7215598	0	800.0000000
CRP_M00	CRP (mg/l)	3099	15.8024589	45.7581626	0	978.0000000
BSG_M00	ESR (mm/h)	2917	23.1412410	19.6462003	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	3028	18.7932629	26.6086206	0	483.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3259	5.3620743	2.8510578	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3259	5.3099110	2.5670260	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3265	0.9468369	0.6774310	0	3.0000000
prevbio	Number of previous biologics	3285	0.2910198	0.5765899	0	6.0000000
mtxjn	MTX	3285	0.5519026	0.4973745	0	1.0000000
saspjn	SASP	3285	0.0359209	0.1861212	0	1.0000000
lefjn	Leflunomide	3285	0.1156773	0.3198863	0	1.0000000
nsacoxjn	NSAID, Coxibe	3285	0.2079148	0.4058773	0	1.0000000
anajn	Analgesics	3285	0.0901065	0.2863779	0	1.0000000
glucjn	Glucocorticoides	3285	0.6280061	0.4834104	0	1.0000000
seq1jn	Arterial hypertension	3285	0.2270928	0.4190169	0	1.0000000
seq2jn	Coronary heart disease	3285	0.0164384	0.1271733	0	1.0000000
seq3jn	Hyperlipidemia	3285	0.0474886	0.2127139	0	1.0000000
seq4jn	Diabetes Type I	3285	0.0121766	0.1096903	0	1.0000000
seq5jn	Diabetes Type II	3285	0.0435312	0.2040807	0	1.0000000
seq6jn	Chronic inflammatory disease	3285	0.0182648	0.1339280	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3285	0.0307458	0.1726545	0	1.0000000
seq8jn	Osteoporosis	3285	0.0687976	0.2531481	0	1.0000000
seq9jn	Degenerative joint disease	3285	0.1086758	0.3112794	0	1.0000000
seq10jn	Degenerative spinal disease	3285	0.0861492	0.2806269	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3285	0.0453577	0.2081191	0	1.0000000
wg	Without graduation	3257	0.0110531	0.1045672	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	3257	0.2661959	0.4420358	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	3257	0.4482653	0.4973927	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	3257	0.2744857	0.4463233	0	1.0000000

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	1046	10.6585839	23.8248357	0	183.0000000
present_M00	Presenteeism (%)	1046	43.4225621	26.4836725	0	100.0000000
wai_M00	Modified WAI	1046	33.9763780	6.5122633	12.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	1046	0.2985646	0.4576284	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	1046	0.1145332	0.3175422	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	1046	0.1666667	0.3714277	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	1046	0.6598361	0.4578560	0	1.0000000
ccpin_M00	Anti-ccp (1=positive)	1046	0.6851852	0.4353061	0	1.0000000
smokejn	Smoker (1=yes)	1046	0.2321773	0.4208050	0	1.0000000
AGE	Age	1046	47.6137667	8.7767615	20.0000000	78.0000000
bmi_M00	Body mass index (kg/m ²)	1046	26.0610060	4.8452885	17.0403288	51.2110727
bradau	Duration of disease (years)	1046	8.4001592	7.2565778	0.0219028	40.9199179
STIFFTM_M00	Morning stiffness (minutes)	1046	46.6017358	64.8420423	0	720.0000000
CRP_M00	CRP (mg/l)	1045	14.1998422	41.6128386	0	642.0000000
BSG_M00	ESR (mm/h)	1046	20.4511435	16.9000497	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	1046	18.8142570	25.0694087	0	164.0000000
EXH_7DAYS_M00	Fatigue (0-10)	1046	4.8853565	2.8455215	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	1046	4.6904532	2.5743742	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	1046	0.7957033	0.6272872	0	2.7500000
prevbio	Number of previous biologics	1046	0.2543021	0.4914149	0	3.0000000
mtxjn	MTX	1046	0.5956023	0.4910099	0	1.0000000
saspjn	SASP	1046	0.0439771	0.2051422	0	1.0000000
lefjn	Leflunomide	1046	0.0975143	0.2967988	0	1.0000000
nsacoxjn	NSAID, Coxibe	1046	0.1969407	0.3978774	0	1.0000000
anajn	Analgesics	1046	0.0726577	0.2596980	0	1.0000000
glucjn	Glucocorticoides	1046	0.6032505	0.4894572	0	1.0000000
seq1jn	Arterial hypertension	1046	0.2112811	0.4084126	0	1.0000000
seq2jn	Coronary heart disease	1046	0.0133843	0.1149688	0	1.0000000
seq3jn	Hyperlipidemia	1046	0.0516252	0.2213751	0	1.0000000
seq4jn	Diabetes Type I	1046	0.0124283	0.1108403	0	1.0000000
seq5jn	Diabetes Type II	1046	0.0277247	0.1642614	0	1.0000000
seq6jn	Chronic inflammatory disease	1046	0.0162524	0.1265051	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	1046	0.0191205	0.1370139	0	1.0000000
seq8jn	Osteoporosis	1046	0.0573614	0.2326431	0	1.0000000
seq9jn	Degenerative joint disease	1046	0.0956023	0.2941857	0	1.0000000
seq10jn	Degenerative spinal disease	1046	0.0841300	0.2777155	0	1.0000000
seq11jn	Mental illness (e.g. depression)	1046	0.0267686	0.1614838	0	1.0000000
wg	Without graduation	1046	0.0076482	0.0871605	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	1046	0.2256214	0.4181908	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	1046	0.4531549	0.4980388	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	1046	0.3135755	0.4641680	0	1.0000000

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

1046 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Presenteeism (%)	-0.966757	-0.890991	50	0	100	43.422562
Fatigue (0-10)	1.1675827	1.7554163	49	0	10	4.8853565
Modified WAI	-0.928542	-0.465463	46	12	49	33.976378
Diploma qualifying for matriculation (Ab	-7.877255	-4.825467	40	0	1	0.3135755
Health Assessment questionnaire (HAQ)	3.6800165	8.9740902	35	0	2.75	0.7957033
Age	0.151096	0.2852738	24	20	78	47.613767
Morning stiffness (minutes)	-0.042598	-0.020361	23	0	720	46.601736
ESR (mm/h)	-0.125956	-0.073316	21	1	120	20.451143
Body mass index (kg/m ²)	0.2528118	0.5657452	16	17.040329	51.211073	26.061006
Analgesics	5.5037963	6.2048806	12	0	1	0.0726577
Rheumatic factor (1=positive)	-3.28469	-2.956466	12	0	1	0.6598361
Secondary school certificate (Hauptschul	6.7919441	8.8908118	10	0	1	0.2256214
Secondary school level 1 (Realschule)	5.5997448	7.0643089	10	0	1	0.4531549
MTX	-3.252623	-3.045602	8	0	1	0.5956023
Prior joint surgery (1=yes)	4.5891236	5.0766994	6	0	1	0.1666667
Anti-ccp (1=positive)	-3.572351	-3.572351	4	0	1	0.6851852
NSAID, Coxibe	-3.748134	-3.666298	4	0	1	0.1969407
Number of previous biologics	2.7557798	3.129522	4	0	3	0.2543021
Leflunomide	-3.976487	-3.896113	2	0	1	0.0975143
Chronic inflammatory disease	9.6224487	9.6486608	2	0	1	0.0162524

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Modell variables for p:0.001 with coefficients and R²

1046 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	44.28477	.	.	<.0001
Presenteeism (%)	-0.95390	0.41287	0.4129	<.0001
Modified WAI	-0.69550	0.03677	0.4496	<.0001
Health Assessment questionnaire (HAQ)	6.19186	0.01299	0.4626	<.0001
Diploma qualifying for matriculation (Abitur)	-6.90256	0.00904	0.4717	<.0001
Fatigue (0-10)	1.34736	0.00967	0.4813	<.0001
Morning stiffness (minutes)	-0.03493	0.00540	0.4867	0.0010

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Modell variables for p:0.001 with coefficients and R²

1046 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	44.28477	<.0001
Presenteeism (%)	-0.95390	<.0001
Modified WAI	-0.69550	<.0001
Diploma qualifying for matriculation (Abitur)	-6.90256	<.0001
Fatigue (0-10)	1.34736	<.0001
Health Assessment questionnaire (HAQ)	6.19186	<.0001
Morning stiffness (minutes)	-0.03493	0.0010

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand varanz	Mean prediction error Number of selected variables	16.502 4.400	15.937 4.000	16.936 5.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	16.531 5.400	16.171 4.000	16.832 6.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	16.408 6.800	15.830 6.000	16.963 8.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	16.369 10.400	16.128 8.000	16.632 12.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	16.303 11.800	15.990 11.000	16.608 13.000
none	0	5	meand varanz	Mean prediction error Number of selected variables	21.979 0.000	20.692 0.000	23.601 0.000
	1	5	meand varanz	Mean prediction error Number of selected variables	16.522 41.000	16.236 41.000	16.813 41.000
stepwise	0.0001	5	meand varanz	Mean prediction error Number of selected variables	16.567 4.000	15.937 4.000	16.936 4.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	16.512 5.000	16.171 4.000	16.832 6.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	16.365 6.600	15.830 6.000	16.963 8.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	16.352 10.000	16.128 8.000	16.632 12.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	16.275 11.200	15.966 10.000	16.608 13.000

Employed patient data set

7. Regression analyses:

7.3 Regression analysis for WPAI - Presenteeism (%) (M24-M0) - lower values are better

Fixed modell

886 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R² stepwise is used				
Variable	Coefficient	Partial R²	Cummulated R² (model)	p-value
Intercept	56.37563	.	.	<.0001
Presenteism (%)	-1.00589	0.41495	0.4150	<.0001
Modified WAI	-0.93937	0.05405	0.4690	<.0001
Health Assessment questionnaire (HAQ)	6.12128	0.00934	0.4783	<.0001
Morning stiffness (minutes)	-0.04700	0.00857	0.4869	<.0001
Diploma qualifying for matriculation (Abitur)	-6.26926	0.00790	0.4948	<.0001
Fatigue (0-10)	1.10872	0.00679	0.5016	0.0006

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	3156	19.1730038	38.3516284	0	183.0000000
present_M00	Presenteism (%)	2758	46.6715011	26.9165234	0	100.0000000
wai_M00	Modified WAI	2110	32.1758294	7.7401115	7.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	3282	0.3019500	0.4591737	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3243	0.1122418	0.3157123	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3248	0.1659483	0.3720915	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	3044	0.6363338	0.4811332	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	2834	0.6429076	0.4792269	0	1.0000000
smokejn	Smoker (1=yes)	3228	0.2503098	0.4332585	0	1.0000000
AGE	Age	3285	48.3245053	9.4164716	18.0000000	83.0000000
bmi_M00	Body mass index (kg/m ²)	3239	26.4102992	5.2446266	17.0068027	65.4372397
bradau	Duration of disease (years)	3227	7.8681038	7.2390550	0.0054757	54.3299110
STIFFTM_M00	Morning stiffness (minutes)	3201	53.9934396	70.7215598	0	800.0000000
CRP_M00	CRP (mg/l)	3099	15.8024589	45.7581626	0	978.0000000
BSG_M00	ESR (mm/h)	2917	23.1412410	19.6462003	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	3028	18.7932629	26.6086206	0	483.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3259	5.3620743	2.8510578	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3259	5.3099110	2.5670260	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3265	0.9468369	0.6774310	0	3.0000000
prevbio	Number of previous biologics	3285	0.2910198	0.5765899	0	6.0000000
mtxjn	MTX	3285	0.5519026	0.4973745	0	1.0000000
saspjn	SASP	3285	0.0359209	0.1861212	0	1.0000000
lefjn	Leflunomide	3285	0.1156773	0.3198863	0	1.0000000
nsacoxjn	NSAID, Coxibe	3285	0.2079148	0.4058773	0	1.0000000
anajn	Analgesics	3285	0.0901065	0.2863779	0	1.0000000
glucjn	Glucocorticoides	3285	0.6280061	0.4834104	0	1.0000000
seq1jn	Arterial hypertension	3285	0.2270928	0.4190169	0	1.0000000
seq2jn	Coronary heart disease	3285	0.0164384	0.1271733	0	1.0000000
seq3jn	Hyperlipidemia	3285	0.0474886	0.2127139	0	1.0000000
seq4jn	Diabetes Type I	3285	0.0121766	0.1096903	0	1.0000000
seq5jn	Diabetes Type II	3285	0.0435312	0.2040807	0	1.0000000
seq6jn	Chronic inflammatory disease	3285	0.0182648	0.1339280	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3285	0.0307458	0.1726545	0	1.0000000
seq8jn	Osteoporosis	3285	0.0687976	0.2531481	0	1.0000000
seq9jn	Degenerative joint disease	3285	0.1086758	0.3112794	0	1.0000000
seq10jn	Degenerative spinal disease	3285	0.0861492	0.2806269	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3285	0.0453577	0.2081191	0	1.0000000
wg	Without graduation	3257	0.0110531	0.1045672	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	3257	0.2661959	0.4420358	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	3257	0.4482653	0.4973927	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	3257	0.2744857	0.4463233	0	1.0000000

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AUDAYS_M00	Missing work days (last 6 month, M0)	952	12.1663158	26.6586027	0	183.0000000
present_M00	Presenteism (%)	952	43.1481481	24.8451997	0	100.0000000
wai_M00	Modified WAI	952	33.6407563	7.2072839	12.0000000	49.0000000
sexjn	Gender (1=male, 0=female)	952	0.3112513	0.4630053	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	952	0.1142857	0.3171527	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	952	0.1553911	0.3613235	0	1.0000000
rfjn_M00	Rheumatic factor (1=positive)	952	0.6674157	0.4557785	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	952	0.6885442	0.4347063	0	1.0000000
smokejn	Smoker (1=yes)	952	0.2333685	0.4220843	0	1.0000000
AGE	Age	952	47.4212185	8.8362895	20.0000000	78.0000000
bmi_M00	Body mass index (kg/m ²)	952	26.1350354	4.8235354	17.0403288	51.2110727
bradau	Duration of disease (years)	952	8.3223276	7.0248466	0.0164271	40.9199179
STIFFTM_M00	Morning stiffness (minutes)	952	48.7904762	66.9639050	0	720.0000000
CRP_M00	CRP (mg/l)	950	15.1394372	42.5058096	0	642.0000000
BSG_M00	ESR (mm/h)	952	21.6217143	17.9932160	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	952	19.1376652	25.6558513	0	164.0000000
EXH_7DAYS_M00	Fatigue (0-10)	952	4.9185185	2.8478276	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	952	4.7513228	2.5364972	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	952	0.8018233	0.6311626	0	2.7500000
prevbio	Number of previous biologics	952	0.2489496	0.4896392	0	3.0000000
mtxjn	MTX	952	0.6092437	0.4881763	0	1.0000000
saspjn	SASP	952	0.0378151	0.1908492	0	1.0000000
lefjn	Leflunomide	952	0.0987395	0.2984687	0	1.0000000
nsacoxjn	NSAID, Coxibe	952	0.2205882	0.4148612	0	1.0000000
anajn	Analgesics	952	0.0777311	0.2678887	0	1.0000000
glucjn	Glucocorticoides	952	0.6250000	0.4843774	0	1.0000000
seq1jn	Arterial hypertension	952	0.2058824	0.4045574	0	1.0000000
seq2jn	Coronary heart disease	952	0.0136555	0.1161170	0	1.0000000
seq3jn	Hyperlipidemia	952	0.0535714	0.2252884	0	1.0000000
seq4jn	Diabetes Type I	952	0.0136555	0.1161170	0	1.0000000
seq5jn	Diabetes Type II	952	0.0273109	0.1630735	0	1.0000000
seq6jn	Chronic inflammatory disease	952	0.0147059	0.1204361	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	952	0.0189076	0.1362702	0	1.0000000
seq8jn	Osteoporosis	952	0.0651261	0.2468778	0	1.0000000
seq9jn	Degenerative joint disease	952	0.0945378	0.2927293	0	1.0000000
seq10jn	Degenerative spinal disease	952	0.0777311	0.2678887	0	1.0000000
seq11jn	Mental illness (e.g. depression)	952	0.0273109	0.1630735	0	1.0000000
wg	Without graduation	952	0.0052521	0.0723188	0	1.0000000
ssc	Secondary school certificate (Hauptschule)	952	0.2058824	0.4045574	0	1.0000000
ssl1	Secondary school level 1 (Realschule)	952	0.4632353	0.4989086	0	1.0000000
abi	Diploma qualifying for matriculation (Abitur)	952	0.3256303	0.4688562	0	1.0000000

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

952 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Age	-0.161613	-0.12046	50	20	78	47.421218
Modified WAI	-0.557199	-0.460029	50	12	49	33.640756
Rheumatic factor (1=positive)	1.2280014	1.8974123	37	0	1	0.6674157
Degenerative joint disease	-3.019474	-1.635743	32	0	1	0.0945378
Morning stiffness (minutes)	0.0084267	0.0127107	31	0	720	48.790476
Arterial hypertension	-2.393421	-0.999726	28	0	1	0.2058824
Gender (1=male, 0=female)	0.8919165	1.4125871	28	0	1	0.3112513
Analgesics	-3.1756	-1.444253	25	0	1	0.0777311
Body mass index (kg/m ²)	-0.177477	-0.087686	21	17.040329	51.211073	26.135035
Hyperlipidemia	-3.032203	-1.68225	14	0	1	0.0535714
Chronic inflammatory disease	-4.034671	-3.162798	13	0	1	0.0147059
Health Assessment questionnaire (HAQ)	-1.037623	-0.766934	10	0	2.75	0.8018233
MTX	0.8192064	0.9697771	9	0	1	0.6092437
Number of previous biologics	-0.95062	-0.732479	9	0	3	0.2489496
Rheumatoid nodules (1=yes)	-1.754233	-1.555777	9	0	1	0.1142857
Chronic obstructive pulmonary disease	-3.095315	-2.519386	7	0	1	0.0189076
Prior joint surgery (1=yes)	-1.471409	-1.345063	6	0	1	0.1553911
Without graduation	8.7070392	9.318942	6	0	1	0.0052521
Secondary school certificate (Hauptschul	-1.261661	-1.050003	5	0	1	0.2058824
ESR (mm/h)	0.0206468	0.0223981	4	1	120	21.621714
Leflunomide	-1.454211	-1.40829	3	0	1	0.0987395
SASP	1.8152602	1.8152602	2	0	1	0.0378151
Smoker (1=yes)	-0.94477	-0.94477	2	0	1	0.2333685

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Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

952 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Fatigue (0-10)	-0.155099	-0.155099	1	0	10	4.9185185
Diploma qualifying for matriculation (Ab	0.8776746	0.8776746	1	0	1	0.3256303
Mental illness (e.g. depression)	-2.250575	-2.250575	1	0	1	0.0273109
Secondary school level 1 (Realschule)	-0.969895	-0.969895	1	0	1	0.4632353

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Modell variables for $p:0.001$ with coefficients and R^2

952 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R^2	Cummulated R^2 (model)	p-value
Intercept	30.14818	.	.	<.0001
Modified WAI	-0.50851	0.21324	0.2132	<.0001
Age	-0.14641	0.03648	0.2497	<.0001
Rheumatic factor (1=positive)	1.56578	0.01348	0.2632	0.0002
Degenerative joint disease	-2.48639	0.01166	0.2749	0.0002
Body mass index (kg/m ²)	-0.14101	0.00955	0.2844	0.0004

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Modell variables for p:0.001 with coefficients and R²

952 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	25.23738	<.0001
Modified WAI	-0.47901	<.0001
Age	-0.14489	<.0001
Arterial hypertension	-1.87315	0.0001
Rheumatic factor (1=positive)	1.58667	0.0001
Analgesics	-2.46373	0.0004
Morning stiffness (minutes)	0.01006	0.0005

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand varanz	Mean prediction error Number of selected variables	4.572 2.800	4.271 2.000	4.760 3.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	4.567 4.800	4.262 4.000	4.790 5.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	4.527 7.400	4.082 6.000	4.775 8.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	4.512 11.400	4.209 9.000	4.778 14.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	4.490 14.800	4.126 12.000	4.826 19.000
none	0	5	meand varanz	Mean prediction error Number of selected variables	5.139 0.000	5.015 0.000	5.297 0.000
	1	5	meand varanz	Mean prediction error Number of selected variables	4.426 41.000	4.045 41.000	4.721 41.000
stepwise	0.0001	5	meand varanz	Mean prediction error Number of selected variables	4.572 2.800	4.271 2.000	4.760 3.000
	0.001	5	meand varanz	Mean prediction error Number of selected variables	4.542 4.600	4.262 4.000	4.790 5.000
	0.01	5	meand varanz	Mean prediction error Number of selected variables	4.526 7.400	4.082 6.000	4.775 8.000
	0.05	5	meand varanz	Mean prediction error Number of selected variables	4.504 10.600	4.122 9.000	4.778 12.000
	0.1	5	meand varanz	Mean prediction error Number of selected variables	4.485 14.400	4.126 12.000	4.826 17.000

Employed patient data set

7. Regression analyses:

7.4 Regression analysis for modified WAI (M24-M0)

Fixed modell

906 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R ² stepwise is used				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	27.72471	.	.	<.0001
Modified WAI	-0.50224	0.23811	0.2381	<.0001
Age	-0.18091	0.04440	0.2825	<.0001
Rheumatic factor (1=positive)	1.67854	0.01329	0.2958	<.0001

Appendix 7 Statistical Tables for Clinical Outcomes (FAS)

**Long-term Documentation of the
Safety, Effectiveness, and Effects on
Quality of Life and Work Productivity in
Patients with Rheumatoid Arthritis
during HUMIRA® (Adalimumab)
Therapy in Routine Clinical Practice
(AGIL) and Supplementary
Documentation to Record
Cardiovascular and Metabolic Risk
Factors (AGIL-CV)**

**Final analysis
Appendix: Statistical Tables for
Clinical Outcomes (FAS)**

March, 05 2018

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FAS patient data set

1. General parameters

1.1 Exclusion criteria for FAS evaluation

	n	%
Exclusion criterias		
Patient base	7229	100.0
At least one of the following criteria lead to exclusion:	2763	38.2
Patients with DAS28 <= 3.2 (baseline)	1097	15.2
Patients without DAS28 measurement (baseline)	1097	15.2
Patients without post baseline information (no visit dates)	556	7.7
Patients with prior Humira therapy	362	5.0

FAS patient data set

1. General parameters

1.2 Gender

	Gender				Total	
	Male		Female			
	n	%	n	%	n	%
Total	1157	25.9	3306	74.1	4463	100.0

FAS patient data set
1. General parameters
1.3 Age (years)
1.3.1 Age - total

	Total
N	4464
Missing	2
Mean	55.1
SD	13.0
Min	15
Median	55.0
Max	90

FAS patient data set

1. General parameters

1.3 Age (years)

1.3.2 Age by gender

	Missing	Male	Female
N	2	1157	3305
Missing	1	0	1
Mean	54.0	55.6	55.0
SD	9.9	11.9	13.4
Min	47	15	18
Median	54.0	55.0	56.0
Max	61	85	90

FAS patient data set
1. General parameters
1.4 Height (cm)
1.4.1 Height - total

	Total
N	4435
Missing	31
Mean	168.3
SD	9.0
Min	130
Median	168.0
Max	214

FAS patient data set

1. General parameters

1.4 Height (cm)

1.4.2 Height by gender

	Missing	Male	Female
N	2	1152	3281
Missing	1	5	25
Mean	164.0	177.7	165.0
SD	1.4	7.4	6.9
Min	163	150	130
Median	164.0	178.0	165.0
Max	165	214	190

FAS patient data set
1. General parameters
1.5 Weight (kg)
1.5.1 Weight - total

	Total
N	4437
Missing	29
Mean	76.9
SD	17.1
Min	36
Median	75.0
Max	177

FAS patient data set

- 1. General parameters
- 1.5 Weight (kg)
- 1.5.2 Weight by gender

	Missing	Male	Female
N	2	1153	3282
Missing	1	4	24
Mean	58.0	86.1	73.7
SD	4.2	15.8	16.3
Min	55	50	36
Median	58.0	84.0	70.0
Max	61	155	177

FAS patient data set
1. General parameters
1.6 BMI (kg/m²)
1.6.1 BMI - total

	Total
N	4433
Missing	33
Mean	27.1
SD	5.6
Min	14
Median	26.2
Max	65

FAS patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.2 BMI by gender

	Missing	Male	Female
N	2	1152	3279
Missing	1	5	27
Mean	21.6	27.2	27.1
SD	1.9	4.6	5.9
Min	20	18	14
Median	21.6	26.5	26.0
Max	23	45	65

FAS patient data set
 1. General parameters
 1.7 Smoking habits

	Smoking habits				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1000	22.7	3398	77.3	4398	100.0

FAS patient data set

1. General parameters

1.8 Duration of disease (years)

1.8.1 Duration - total

	Total
N	4416
Missing	50
Mean	9.2
SD	8.7
Min	0
Median	6.6
Max	61

	Duration of disease (grouped)																		Total	
	< 2 years		2 - 4 years		4 - 6 years		6 - 8 years		8 - 10 years		10 - 15 years		15 - 20 years		20 - 30 years		> 30 years			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	834	18.9	718	16.3	524	11.9	412	9.3	406	9.2	665	15.1	360	8.2	329	7.5	168	3.8	4416	100.0

FAS patient data set
 1. General parameters
 1.9 Erosive changes

	Erosive changes				Total	
	Yes		No			
	n	%	n	%	n	%
Total	2183	61.6	1358	38.4	3541	100.0

FAS patient data set

1. General parameters

1.10 Indications for receiving adalimumab therapy

	n	%
Indications for current adalimumab therapy		
Patient base	4466	100.0
High disease activity	3728	83.5
Lack of effectiveness of previous therapy	3143	70.4
Intolerance of previous therapy	1267	28.4
Rapid radiologic progression	694	15.5
Other	90	2.0

FAS patient data set

- 1. General parameters
- 1.11 Humira therapy
- 1.11.1 Dose (mg) at baseline

	Dose				Total	
	40mg each 14 days		Other			
	n	%	n	%	n	%
Total	4415	99.0	45	1.0	4460	100.0

FAS patient data set

1. General parameters

1.11 Humira therapy

1.11.2 Exposure (years) of study drug

	Total
N	4453
Missing	13
Mean	2.11
SD	1.71
Min	0.0
Median	1.60
Max	6.4

FAS patient data set

1. General parameters

1.12 Physician global assessment of disease activity

	Total
N	4459
Missing	7
Mean	6.0
SD	1.9
Min	0
Median	6.0
Max	10

FAS patient data set

1. General parameters

1.13 Morning stiffness

1.13.1 Patients with morning stiffness(%)

	Morning stiffness				Total	
	Yes		No			
	n	%	n	%	n	%
Total	3684	83.5	727	16.5	4411	100.0

FAS patient data set

1. General parameters

1.13 Morning stiffness

1.13.2 Morning stiffness (minutes)

	Total
N	4370
Missing	96
Mean	65.3
SD	72.8
Min	0
Median	60.0
Max	800

FAS patient data set

1. General parameters

1.14 Rheumatic nodules

	Rheumatic nodules				Total	
	Yes		No			
	n	%	n	%	n	%
Total	686	15.5	3728	84.5	4414	100.0

FAS patient data set

1. General parameters

1.15 Prior joint surgery

	Prior joint surgery				Total	
	Yes		No			
	n	%	n	%	n	%
Total	989	22.3	3440	77.7	4429	100.0

FAS patient data set

1. General parameters

1.16 Joint involvement

		TJC (M0)	SJC (M0)
Total	N	4466	4466
	Missing	0	0
	Mean	8.8	6.0
	SD	6.7	5.4
	Min	0	0
	Median	8.0	5.0
	Max	28	28

FAS patient data set

1. General parameters

1.17 Laboratory

1.17.1 Rheumatic factor

	Rheumatic Factor				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	2786	65.8	1451	34.2	4237	100.0

FAS patient data set
 1. General parameters
 1.17 Laboratory
 1.17.2 Anti-CCP

	Anti-ccp				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	2604	66.0	1339	34.0	3943	100.0

FAS patient data set
1. General parameters
1.17 Laboratory
1.17.3 CRP (mg/l)

	Total
N	4353
Missing	113
Mean	19.3
SD	50.7
Min	0
Median	7.0
Max	913

FAS patient data set
1. General parameters
1.17 Laboratory
1.17.4 ESR (mm/h)
1.17.4.1 ESR - total

	Total
N	4466
Missing	0
Mean	29.5
SD	21.9
Min	1
Median	24.0
Max	138

FAS patient data set

- 1. General parameters
- 1.17 Laboratory
- 1.17.4 ESR (mm/h)
- 1.17.4.2 ESR by gender

	Missing	Male	Female
N	3	1157	3306
Missing	0	0	0
Mean	8.3	31.0	29.0
SD	6.7	23.7	21.2
Min	4	1	1
Median	5.0	24.0	24.0
Max	16	138	131

FAS patient data set

1. General parameters

1.17 Laboratory

1.17.5 Hemoglobin (g/dl)

	Total
N	4288
Missing	178
Mean	17.7
SD	24.2
Min	0
Median	13.0
Max	434

FAS patient data set
 1. General parameters
 1.17 Laboratory
 1.17.6 Hepatitis B

	Hepatitis B				Total	
	Yes		No			
	n	%	n	%	n	%
Total	22	0.6	3639	99.4	3661	100.0

FAS patient data set
 1. General parameters
 1.17 Laboratory
 1.17.7 Hepatitis C

	Hepatitis C				Total	
	Yes		No			
	n	%	n	%	n	%
Total	12	0.3	3635	99.7	3647	100.0

FAS patient data set

1. General parameters

1.17 Laboratory

1.17.8 Latent tuberculosis

	Latent tuberculosis				Total	
	Yes		No			
	n	%	n	%	n	%
Total	176	4.0	4179	96.0	4355	100.0

FAS patient data set

1. General parameters

1.18 School leaving certificate

	School leaving certificate								Total	
	Without graduation		Secondary school certificate (Hauptschule)		Secondary school level I certificate (Realschulabschluss - mittlere Reife)		Diploma from German secondary school qualifying for university admission or matriculation (Abitur)			
	n	%	n	%	n	%	n	%	n	%
Total	99	2.2	1537	34.8	1841	41.6	944	21.4	4421	100.0

FAS patient data set

1. General parameters

1.19 Professional education

	n	%
Professional education		
Patient base	4466	100.0
Alternance training (School and on-the-job training)	1949	43.6
Off-the-job training	880	19.7
Technical college / Master craftsman training	630	14.1
University of applied science	322	7.2
Semiskilled	318	7.1
University	316	7.1
None	310	6.9

FAS patient data set
 1. General parameters
 1.20 Employment

	Employment												Total	
	Full time job (35h and more)		Part-time work		School, education, studying		Home making, child-rearing		Unemployed		Retirement			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	1346	30.6	705	16.0	79	1.8	208	4.7	325	7.4	1735	39.4	4398	100.0

FAS patient data set

1. General parameters

1.21 Early retirement due to rheumatic disease (only patients in retirement)

	Retirement due to rheumatic disease				Total	
	Yes		No			
	n	%	n	%	n	%
Total	669	39.3	1032	60.7	1701	100.0

FAS patient data set

1. General parameters

1.22 Occupational status (only patients with occupation)

	Occupational status								Total	
	Salaried		Civil servant		Leading function		Freelancer			
	n	%	n	%	n	%	n	%	n	%
Total	1668	83.1	71	3.5	97	4.8	171	8.5	2007	100.0

FAS patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.1 Household

	Household								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	3335	74.7	704	15.8	178	4.0	249	5.6	4466	100.0

	Household				Total	
	Yes		No			
	n	%	n	%	n	%
Total	3335	82.6	704	17.4	4039	100.0

Without not applicable and missings

	Total
N	3368
Missing	1098
Mean	56.9
SD	64.3
Min	0
Median	30.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

FAS patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.2 Parenting

	Parenting								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	338	7.6	957	21.4	1875	42.0	1296	29.0	4466	100.0

	Parenting				Total	
	Yes		No			
	n	%	n	%	n	%
Total	338	26.1	957	73.9	1295	100.0

Without not applicable and missings

	Total
N	1220
Missing	3246
Mean	15.1
SD	41.6
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

FAS patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.3 Education

	Education								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	167	3.7	843	18.9	2056	46.0	1400	31.3	4466	100.0

	Education				Total	
	Yes		No			
	n	%	n	%	n	%
Total	167	16.5	843	83.5	1010	100.0

Without not applicable and missings

	Total
N	975
Missing	3491
Mean	8.3
SD	31.6
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

FAS patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.4 Recreational (free-time)

	Recreational(free-time)								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	3041	68.1	656	14.7	205	4.6	564	12.6	4466	100.0

	Recreational(free-time)				Total	
	Yes		No			
	n	%	n	%	n	%
Total	3041	82.3	656	17.7	3697	100.0

Without not applicable and missings

	Total
N	3101
Missing	1365
Mean	59.1
SD	65.6
Min	0
Median	30.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

FAS patient data set

1. General parameters

1.24 Missed work days in the last 6 month

	M00				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1284	51.1	1231	48.9	2515	100.0

Missed work days in the last 6 month (% of patients)

	Total
N	2470
Missing	1996
Mean	22.0
SD	43.8
Min	0
Median	0.0
Max	183

Number of missed work days in the last 6 month

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.1 Number of visits at the rheumatologist

	Total
N	4344
Missing	122
Mean	3.3
SD	3.1
Min	0
Median	3.0
Max	57

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.2 Number of visits at the general practitioner

	Total
N	4344
Missing	122
Mean	4.0
SD	4.6
Min	0
Median	3.0
Max	68

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.3 Number of visits at the orthopaedic specialist

	Total
N	4344
Missing	122
Mean	0.9
SD	2.2
Min	0
Median	0.0
Max	31

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.4 Number of visits at other medical specialists

	Total
N	4344
Missing	122
Mean	1.2
SD	2.4
Min	0
Median	0.0
Max	78

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.5 Number of hospitalizations

	Total
N	4344
Missing	122
Mean	0.4
SD	1.5
Min	0
Median	0.0
Max	34

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.6 Total duration of hospitalizations (days)

	Total
N	4344
Missing	122
Mean	2.3
SD	7.3
Min	0
Median	0.0
Max	183

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.7 Number of convalescent cares, stationary rehabilitations

	Total
N	4344
Missing	122
Mean	0.2
SD	1.6
Min	0
Median	0.0
Max	42

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.8 Total duration of convalescent cares, stationary rehabilitations (days)

	Total
N	4344
Missing	122
Mean	1.6
SD	7.2
Min	0
Median	0.0
Max	183

FAS patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.9 Number of physical therapies, for example physiotherapy

	Total
N	4344
Missing	122
Mean	3.9
SD	9.7
Min	0
Median	0.0
Max	98

FAS patient data set
1. General parameters
1.26 Modified WAI

	Total
N	1461
Missing	3005
Mean	30.6
SD	7.5
Min	7
Median	31.0
Max	49

FAS patient data set

1. General parameters

1.27 WPAI

1.27.1 Presenteeism (%)

	Total
N	1888
Missing	2578
Mean	51.9
SD	25.9
Min	0
Median	50.0
Max	100

FAS patient data set

1. General parameters

1.27 WPAI

1.27.2 Absenteeism (%)

	Total
N	1481
Missing	2985
Mean	23.8
SD	38.2
Min	0
Median	0.0
Max	100

FAS patient data set

1. General parameters

1.27 WPAI

1.27.3 Total work productivity impairment (%)

	Total
N	1325
Missing	3141
Mean	56.2
SD	27.7
Min	0
Median	59.3
Max	100

FAS patient data set

1. General parameters

1.27 WPAI

1.27.4 Total activity impairment (%)

	Total
N	4402
Missing	64
Mean	59.2
SD	22.8
Min	0
Median	60.0
Max	100

FAS patient data set

1. General parameters

1.28 Patient global assessment of disease activity

	Total
N	4466
Missing	0
Mean	6.1
SD	2.2
Min	0
Median	6.0
Max	10

FAS patient data set
1. General parameters
1.29 Fatigue

	Total
N	4449
Missing	17
Mean	5.8
SD	2.7
Min	0
Median	6.0
Max	10

FAS patient data set
1. General parameters
1.30 Pain

	Total
N	4455
Missing	11
Mean	6.1
SD	2.3
Min	0
Median	6.0
Max	10

FAS patient data set
1. General parameters
1.31 HAQ-DI

	Total
N	4449
Missing	17
Mean	1.30
SD	0.70
Min	0.0
Median	1.38
Max	3.0

FAS patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.1 Mobility

	Mobility						Total	
	No problems		Some problems		Confined to bed			
	n	%	n	%	n	%	n	%
Total	1662	37.8	2728	62.0	8	0.2	4398	100.0

FAS patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.2 Self-care

	Self-care						Total	
	No problems		Some problems		Unable to wash or dress myself			
	n	%	n	%	n	%	n	%
Total	2599	59.1	1680	38.2	115	2.6	4394	100.0

FAS patient data set

1. General parameters

1.32 EQ-5D

1.32.3 Usual activities (e.g., work, study, housework, family or leisure activities)

	Usual activities						Total	
	No problems		Some problems		Unable to perform			
	n	%	n	%	n	%	n	%
Total	953	21.7	3236	73.6	206	4.7	4395	100.0

FAS patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.4 Pain/discomfort

	Pain/discomfort						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	147	3.3	2965	67.4	1288	29.3	4400	100.0

FAS patient data set

1. General parameters

1.32 EQ-5D

1.32.5 Anxiety/depression

	Anxiety/depression						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	2159	49.1	1961	44.6	275	6.3	4395	100.0

FAS patient data set
1. General parameters
1.32 EQ-5D
1.32.6 Mean EQ VAS

	Total
N	4405
Missing	61
Mean	48.9
SD	20.8
Min	0
Median	50.0
Max	100

FAS patient data set
1. General parameters
1.33 DAS28

	Total
N	4466
Missing	0
Mean	5.13
SD	1.14
Min	3.2
Median	5.06
Max	8.9

FAS patient data set

1. General parameters

1.34 Participation in Abbott Care

	Participation in Abbott Care service program				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1380	34.9	2571	65.1	3951	100.0

FAS patient data set

2. Concomitant diseases

	n	%
Previous concomitant diseases		
Patient base	4466	100.0
Total	3096	69.3
Arterial hypertension	1584	35.5
Other disease	1443	32.3
Degenerative joint disease	833	18.7
Degenerative spinal disease	684	15.3
Osteoporosis	664	14.9
Diabetes Type II	395	8.8
Hyperlipidemia	367	8.2
Mental illness (e.g. depression)	301	6.7
Coronary heart disease	246	5.5
Chronic obstructive pulmonary disease	223	5.0
Chronic inflammatory disease	91	2.0
Diabetes Type I	63	1.4

FAS patient data set

3.Previous and concomitant medication

3.1 Previous documented DMARDs

	n	%
Previous documented DMARDs		
Patient base	4466	100.0
MTX	2853	63.9
Leflunomide	2530	56.7
Glucocorticoides	1914	42.9
NSAID, Coxibe	1565	35.0
SASP	1389	31.1
Analgesics	1036	23.2
Other	697	15.6

FAS patient data set

3.Previous and concomitant medication

3.2 Documented DMARDs at baseline

	n	%
Documented DMARDs at baseline		
Patient base	4466	100.0
Glucocorticoides	3042	68.1
MTX	2385	53.4
NSAID, Coxibe	985	22.1
Leflunomide	534	12.0
Analgesics	489	10.9
Other	169	3.8
SASP	161	3.6

FAS patient data set

3.Previous and concomitant medication

3.3 Documented DMARDs during study, baseline included

	n	%
Concomitant DMARDs		
Total	4172	93.4
Glucocorticoids	3277	73.4
MTX	2616	58.6
NSAIDs, Coxibe	1080	24.2
Leflunomide	581	13.0
Analgesics	558	12.5
Other	439	9.8
SASP	184	4.1

FAS patient data set

3.Previous and concomitant medication

3.4 Glucocorticoid dosage at baseline and maximum dosage during study

		Glucocorticode dosage at baseline mg/d	Maximum Glucocorticode dosage during study mg/d
Total	N	3014	3256
	Missing	1452	1210
	Mean	7.7	9.2
	SD	5.8	8.0
	Min	1	1
	Median	5.0	5.0
	Max	103	103

FAS patient data set

3.Previous and concomitant medication

3.5 MTX dosage at baseline and maximum dosage during study

		MTX dosage at baseline mg/w	Maximum MTX dosage during study mg/w
Total	N	2336	2577
	Missing	2130	1889
	Mean	14.8	14.8
	SD	7.0	6.9
	Min	1	1
	Median	15.0	15.0
	Max	215	215

FAS patient data set

3.Previous and concomitant medication

3.6 Previous biologic therapies

3.6.1 Percentage previous biologics

	n	%
Documented previous biologics at baseline		
Patient base	4466	100.0
Etanercept	828	18.5
Infliximab	138	3.1
Tocilizumab	125	2.8
Certolizumab	96	2.1
Golimumab	92	2.1
Rituximab	57	1.3
Abatacept	56	1.3
Other	47	1.1

FAS patient data set

3.Previous and concomitant medication

3.6 Previous biologic therapies

3.6.2 Mean duration of previous biologics (month)

		Infliximab	Etanercept	Golimumab	Certolizumab	Abatacept	Rituximab	Tocilizumab
Total	N	137	816	92	95	55	54	125
	Missing	4329	3650	4374	4371	4411	4412	4341
	Mean	29.5	30.2	15.2	9.9	11.1	20.9	12.1
	SD	33.3	34.4	22.4	10.6	11.5	24.1	12.5
	Min	1	1	1	1	1	1	1
	Median	13.0	14.5	7.0	6.0	7.0	9.5	8.0
	Max	177	196	169	62	62	96	75

FAS patient data set

3.Previous and concomitant medication

3.7 Number of previous biologics

	Number of previous biologics						Total	
	0		1		≥2			
	n	%	n	%	n	%	n	%
Total	3288	73.6	981	22.0	197	4.4	4466	100.0

FAS patient data set

3.Previous and concomitant medication

3.8 Main reasons for discontinuing the previous biologic therapy

	Reason for discontinuing the previous biologic therapy						Total	
	Lack of effectiveness		Lack of tolerance		Other reason			
	n	%	n	%	n	%	n	%
Total	890	71.7	233	18.8	119	9.6	1242	100.0

FAS patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.1 Withdrawal reasons by visit

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
FAS	Adverse drug reaction	67	1.6	46	1.2	35	1.2	25	1.1	5	0.3	8	0.7	1	0.1
	Lack of effectiveness	219	5.1	249	6.7	237	7.8	177	8.1	81	5.4	29	2.7	13	1.6
	Other reason	89	2.1	111	3.0	138	4.5	124	5.7	90	6.0	52	4.9	49	6.2
	Unknown Reason	5	0.1	11	0.3	12	0.4	8	0.4	5	0.3	3	0.3	0	0.0
	Ongoing patients at the end of visit	3936	91.2	3300	88.8	2618	86.1	1842	84.7	1318	87.9	975	91.4	726	92.0
	Total	4316	100.0	3717	100.0	3040	100.0	2176	100.0	1499	100.0	1067	100.0	789	100.0

FAS patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.2 Disposition of patients (cumulated withdrawal rates)

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
FAS	Adverse drug reaction	67	1.5	113	2.5	148	3.3	173	3.9	178	4.0	186	4.2	187	4.2
	Lack of effectiveness	219	4.9	468	10.5	705	15.8	882	19.7	963	21.6	992	22.2	1005	22.5
	Other reason	89	2.0	200	4.5	338	7.6	462	10.3	552	12.4	604	13.5	653	14.6
	Unknown Reason	5	0.1	16	0.4	28	0.6	36	0.8	41	0.9	44	1.0	44	1.0
	Lost to follow up (cummulated)	0	0.0	243	5.4	550	12.3	988	22.1	1347	30.2	1611	36.1	1851	41.4
	Ongoing patients at the end of visit	3936	88.1	3300	73.9	2618	58.6	1842	41.2	1318	29.5	975	21.8	726	16.3
	Single visit missing (a later visit is following)	150	3.4	126	2.8	79	1.8	83	1.9	67	1.5	54	1.2	0	0.0
	Total	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0

FAS patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

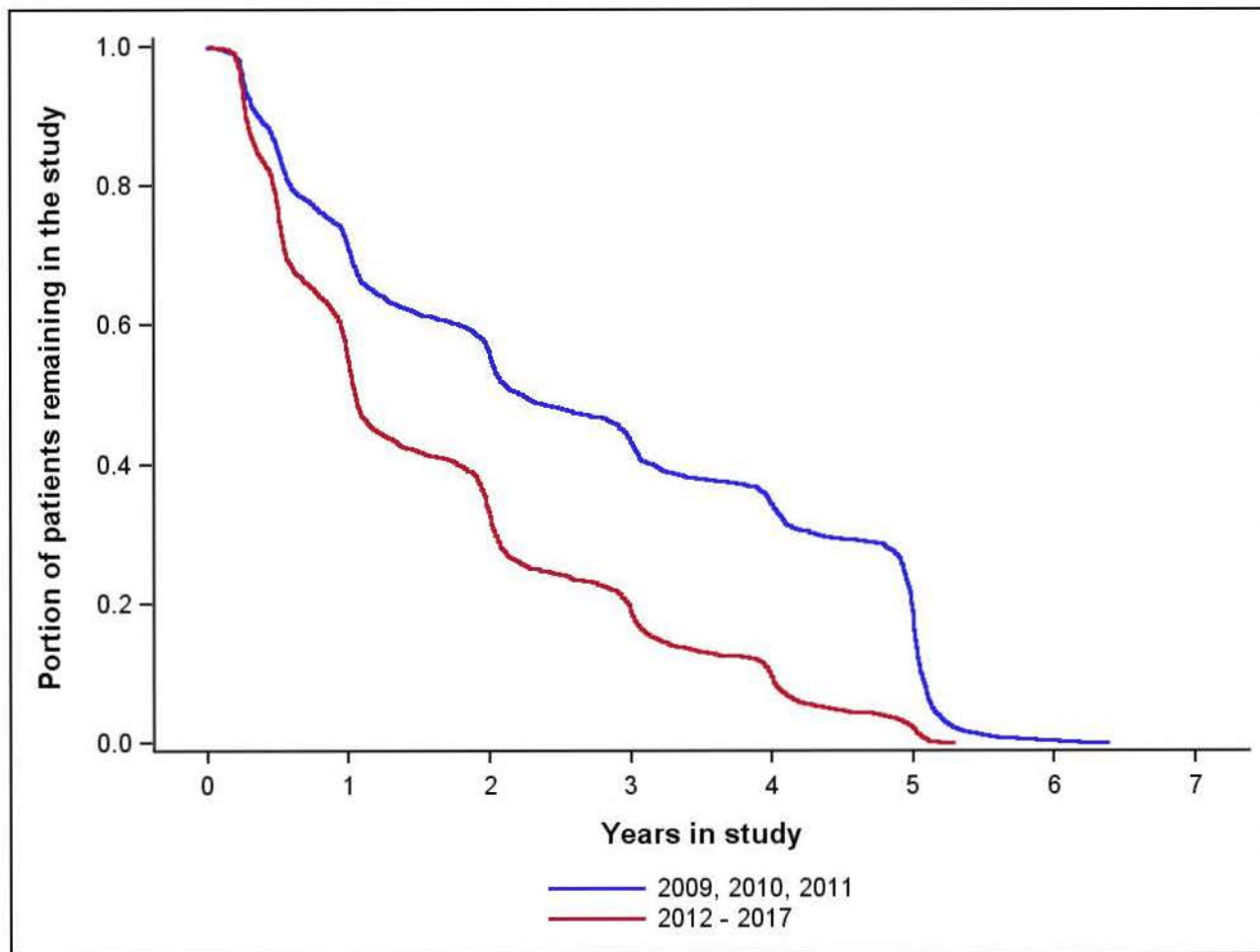
4.3 Disposition of patients (shortened)

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
FAS	Cummulative documented withdrawals	380	8.5	797	17.8	1219	27.3	1553	34.8	1734	38.8	1826	40.9	1889	42.3
	Ongoing patients at the end of visit	3936	88.1	3300	73.9	2618	58.6	1842	41.2	1318	29.5	975	21.8	726	16.3
	Single visit missing (a later visit is following)	150	3.4	126	2.8	79	1.8	83	1.9	67	1.5	54	1.2	0	0.0
	Lost to follow up (cummulated)	0	0.0	243	5.4	550	12.3	988	22.1	1347	30.2	1611	36.1	1851	41.4
	Total	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0	4466	100.0

FAS patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.4 Total duration of study (Kaplan-Meier, computed by visit dates) by year of baseline



FAS patient data set

5. Clinical outcomes - FAS

5.1 DAS28

5.1.1 DAS28 - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4466	3749	3229	2621	1818	1250	912	650
	Missing	0	717	1237	1845	2648	3216	3554	3816
	Mean	5.13	3.81	3.55	3.38	3.21	3.10	3.01	2.93
	SD	1.14	1.38	1.36	1.35	1.32	1.27	1.21	1.22
	Min	3.2	0.0	0.3	0.0	0.0	0.0	0.5	0.0
	Median	5.06	3.76	3.45	3.23	3.07	2.94	2.79	2.78
	Max	8.9	8.5	8.5	8.6	8.1	7.9	7.6	7.6

FAS patient data set

5. Clinical outcomes - FAS

5.1 DAS28

5.1.2 DAS28 - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	3749	3229	2621	1818	1250	912	650
	Missing	717	1237	1845	2648	3216	3554	3816
	Mean	-1.34	-1.56	-1.71	-1.84	-1.94	-2.01	-2.15
	SD	1.39	1.46	1.55	1.57	1.61	1.59	1.63
	Min	-6.4	-6.4	-7.4	-6.9	-7.6	-7.1	-7.1
	Median	-1.27	-1.51	-1.68	-1.81	-1.93	-2.03	-2.07
	Max	3.7	3.6	2.7	3.5	2.8	2.8	2.0

DAS28 M24-M00 Signed rank (wilcoxon), p-value: <.0001
 DAS28 M60-M00 Signed rank (wilcoxon), p-value: <.0001

FAS patient data set

5. Clinical outcomes - FAS

5.1 DAS28

5.1.3 DAS28 - remission and dcrit

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	DAS28 remission (< 2.6)																
Total	Yes	0	0.0	768	20.5	844	26.1	799	30.5	672	37.0	492	39.4	391	42.9	294	45.2
	No	4466	100.0	2981	79.5	2385	73.9	1822	69.5	1146	63.0	758	60.6	521	57.1	356	54.8
	Total	4466	100.0	3749	100.0	3229	100.0	2621	100.0	1818	100.0	1250	100.0	912	100.0	650	100.0

		Visit													
		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Dcrit (improvement of 1.8 or more)														
Total	Yes	1342	35.8	1386	42.9	1214	46.3	911	50.1	674	53.9	507	55.6	388	59.7
	No	2407	64.2	1843	57.1	1407	53.7	907	49.9	576	46.1	405	44.4	262	40.3
	Total	3749	100.0	3229	100.0	2621	100.0	1818	100.0	1250	100.0	912	100.0	650	100.0

FAS patient data set

5. Clinical outcomes - FAS

5.2 TJC

5.2.1 TJC - absolute values

		TJC (M0)	M03	M06	M12	M24	M36	M48	M60
Total	N	4466	4280	3657	2969	2095	1456	1040	752
	Missing	0	186	809	1497	2371	3010	3426	3714
	Mean	8.8	4.6	3.8	3.3	2.8	2.5	2.2	2.2
	SD	6.7	5.8	5.3	4.9	4.6	4.4	4.0	3.9
	Min	0	0	0	0	0	0	0	0
	Median	8.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
	Max	28	28	28	28	28	28	28	28

FAS patient data set

5. Clinical outcomes - FAS

5.2 TJC

5.2.2 TJC - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4280	3657	2969	2095	1456	1040	752
	Missing	186	809	1497	2371	3010	3426	3714
	Mean	-4.3	-4.9	-5.3	-5.6	-5.9	-6.1	-6.4
	SD	6.2	6.5	6.7	6.5	6.7	6.7	6.5
	Min	-28	-28	-28	-28	-28	-28	-28
	Median	-3.0	-4.0	-4.0	-5.0	-5.0	-5.0	-5.0
	Max	26	28	24	24	28	28	17

TJC M24-M00 Signed rank (wilcoxon), p-value: <.0001
 TJC M60-M00 Signed rank (wilcoxon), p-value: <.0001

FAS patient data set

5. Clinical outcomes - FAS

5.3 SJC

5.3.1 SJC - absolute values

		SJC (M0)	M03	M06	M12	M24	M36	M48	M60
Total	N	4466	4280	3657	2969	2095	1456	1040	752
	Missing	0	186	809	1497	2371	3010	3426	3714
	Mean	6.0	2.9	2.2	1.9	1.6	1.4	1.2	1.1
	SD	5.4	4.1	3.5	3.4	3.0	2.6	2.4	2.7
	Min	0	0	0	0	0	0	0	0
	Median	5.0	1.0	1.0	0.0	0.0	0.0	0.0	0.0
	Max	28	28	26	27	26	23	28	24

FAS patient data set

5. Clinical outcomes - FAS

5.3 SJC

5.3.2 TJC - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4280	3657	2969	2095	1456	1040	752
	Missing	186	809	1497	2371	3010	3426	3714
	Mean	-3.2	-3.8	-4.1	-4.4	-4.8	-5.0	-5.5
	SD	4.9	5.2	5.4	5.6	5.7	5.7	6.1
	Min	-27	-28	-28	-27	-27	-27	-27
	Median	-2.0	-3.0	-3.0	-3.0	-4.0	-4.0	-4.0
	Max	22	26	21	20	19	19	11

SJC M24-M00 Signed rank (wilcoxon), p-value: <.0001
 SJC M60-M00 Signed rank (wilcoxon), p-value: <.0001

FAS patient data set

5. Clinical outcomes - FAS

5.4 Physician global assessment of disease activity

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4459	4280	3660	2958	2088	1450	1041	747
	Missing	7	186	806	1508	2378	3016	3425	3719
	Mean	6.0	3.7	3.3	3.0	2.7	2.5	2.3	2.2
	SD	1.9	2.1	2.1	2.1	2.0	1.9	1.8	1.7
	Min	0	0	0	0	0	0	0	0
	Median	6.0	3.0	3.0	3.0	2.0	2.0	2.0	2.0
	Max	10	10	10	10	10	10	10	9

Absolute values

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4274	3655	2954	2085	1448	1039	746
	Missing	192	811	1512	2381	3018	3427	3720
	Mean	-2.3	-2.7	-2.9	-3.1	-3.3	-3.3	-3.4
	SD	2.4	2.5	2.6	2.6	2.6	2.5	2.4
	Min	-10	-10	-10	-10	-10	-10	-9
	Median	-2.0	-3.0	-3.0	-3.0	-3.0	-4.0	-4.0
	Max	8	8	7	7	6	7	6

Differences

FAS patient data set

5. Clinical outcomes - FAS

5.5 Patient global assessment of disease activity

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4407	4178	3582	2902	2042	1417	1013	737
	Missing	59	288	884	1564	2424	3049	3453	3729
	Mean	6.1	4.5	4.2	4.0	3.7	3.6	3.4	3.4
	SD	2.2	2.3	2.4	2.4	2.3	2.4	2.3	2.3
	Min	0	0	0	0	0	0	0	0
	Median	6.0	4.0	4.0	4.0	3.0	3.0	3.0	3.0
	Max	10	10	10	10	10	10	10	10

Absolute values

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4128	3538	2870	2021	1406	1005	730
	Missing	338	928	1596	2445	3060	3461	3736
	Mean	-1.6	-1.8	-1.9	-2.1	-2.2	-2.3	-2.2
	SD	2.8	2.9	2.9	2.9	2.9	2.8	2.9
	Min	-10	-10	-10	-10	-10	-10	-10
	Median	-2.0	-2.0	-2.0	-2.0	-2.0	-2.0	-2.0
	Max	9	10	10	8	7	6	6

Differences

FAS patient data set

5. Clinical outcomes - FAS

5.6 Fatigue

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4449	4180	3580	2901	2046	1418	1005	732
	Missing	17	286	886	1565	2420	3048	3461	3734
	Mean	5.8	4.4	4.2	4.0	3.8	3.5	3.5	3.4
	SD	2.7	2.7	2.7	2.7	2.7	2.6	2.6	2.7
	Min	0	0	0	0	0	0	0	0
	Median	6.0	4.0	4.0	4.0	3.0	3.0	3.0	3.0
	Max	10	10	10	10	10	10	10	10

Absolute values

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4163	3571	2893	2041	1414	1005	731
	Missing	303	895	1573	2425	3052	3461	3735
	Mean	-1.3	-1.5	-1.5	-1.7	-1.9	-1.8	-1.9
	SD	2.9	3.0	3.1	3.0	3.0	3.1	3.1
	Min	-10	-10	-10	-10	-10	-10	-9
	Median	-1.0	-1.0	-1.0	-2.0	-2.0	-2.0	-2.0
	Max	9	9	10	10	10	10	8

Differences

FAS patient data set

5. Clinical outcomes - FAS

5.7 Pain

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4455	4178	3582	2901	2045	1415	1004	730
	Missing	11	288	884	1565	2421	3051	3462	3736
	Mean	6.1	4.4	4.2	3.9	3.7	3.5	3.3	3.3
	SD	2.3	2.5	2.5	2.5	2.4	2.4	2.4	2.4
	Min	0	0	0	0	0	0	0	0
	Median	6.0	4.0	4.0	4.0	3.0	3.0	3.0	3.0
	Max	10	10	10	10	10	10	10	10

Absolute values

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4167	3574	2895	2039	1411	1002	730
	Missing	299	892	1571	2427	3055	3464	3736
	Mean	-1.7	-1.8	-1.9	-2.1	-2.2	-2.3	-2.2
	SD	2.7	2.7	2.8	2.7	2.8	2.9	2.9
	Min	-10	-10	-10	-10	-10	-10	-9
	Median	-2.0	-2.0	-2.0	-2.0	-2.0	-2.0	-2.0
	Max	9	8	8	6	7	7	7

Differences

FAS patient data set

5. Clinical outcomes - FAS

5.8 Morning stiffness

5.8.1 Patients with morning stiffness(%)

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Morning stiffness																
Total	Yes	3684	83.5	2670	62.9	2085	57.4	1533	52.0	989	47.6	648	44.8	429	41.4	296	39.7
	No	727	16.5	1577	37.1	1547	42.6	1415	48.0	1090	52.4	798	55.2	606	58.6	450	60.3
	Total	4411	100.0	4247	100.0	3632	100.0	2948	100.0	2079	100.0	1446	100.0	1035	100.0	746	100.0

FAS patient data set

5. Clinical outcomes - FAS

5.8 Morning stiffness

5.8.2 Morning stiffness (minutes)

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4370	4222	3617	2931	2070	1439	1034	743
	Missing	96	244	849	1535	2396	3027	3432	3723
	Mean	65.3	34.6	27.4	24.2	20.9	19.0	15.0	15.2
	SD	72.8	55.6	44.3	43.5	39.8	41.0	29.8	32.7
	Min	0	0	0	0	0	0	0	0
	Median	60.0	15.0	10.0	5.0	0.0	0.0	0.0	0.0
	Max	800	720	420	400	420	600	300	360

FAS patient data set

5. Clinical outcomes - FAS

5.9 Inflammatory markers

5.9.1 CRP (mg/l)

5.9.1.1 CRP (mg/l) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4353	3928	3356	2744	1954	1348	973	690
	Missing	113	538	1110	1722	2512	3118	3493	3776
	Mean	19.3	12.4	11.9	11.9	12.8	11.6	8.4	5.5
	SD	50.7	37.0	39.0	48.1	51.4	51.4	30.3	9.4
	Min	0	0	0	0	0	0	0	0
	Median	7.0	4.0	4.0	3.0	3.0	3.0	3.0	3.0
	Max	913	743	833	996	951	928	420	99

FAS patient data set

5. Clinical outcomes - FAS

5.9 Inflammatory markers

5.9.1 CRP (mg/l)

5.9.1.2 CRP (mg/l) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	3858	3296	2693	1918	1319	950	678
	Missing	608	1170	1773	2548	3147	3516	3788
	Mean	-7.1	-7.3	-7.5	-8.0	-8.6	-5.8	-7.8
	SD	45.2	49.1	59.4	64.0	65.9	47.5	39.3
	Min	-773	-818	-818	-812	-811	-818	-818
	Median	-1.0	-2.0	-2.0	-2.0	-2.0	-2.0	-2.0
	Max	425	732	847	742	923	417	65

FAS patient data set

5. Clinical outcomes - FAS

5.9 Inflammatory markers

5.9.2 ESR (mm/h)

5.9.2.1 ESR (mm/h) - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4466	3893	3321	2705	1891	1299	953	673
	Missing	0	573	1145	1761	2575	3167	3513	3793
	Mean	29.5	22.7	21.5	20.8	20.0	19.6	19.5	18.9
	SD	21.9	19.6	18.2	18.1	17.5	17.0	17.6	16.9
	Min	1	1	1	1	1	1	1	1
	Median	24.0	17.0	16.0	16.0	15.0	14.0	14.0	14.0
	Max	138	126	120	146	117	106	120	105

FAS patient data set

5. Clinical outcomes - FAS

5.9 Inflammatory markers

5.9.2 ESR (mm/h)

5.9.2.2 ESR (mm/h) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	3893	3321	2705	1891	1299	953	673
	Missing	573	1145	1761	2575	3167	3513	3793
	Mean	-7.1	-7.9	-8.5	-9.0	-8.9	-9.3	-9.9
	SD	20.5	20.6	21.6	22.2	22.1	22.7	22.5
	Min	-136	-94	-101	-111	-111	-111	-108
	Median	-4.0	-5.0	-6.0	-6.0	-6.0	-6.0	-6.0
	Max	118	105	113	72	64	94	66

FAS patient data set

5. Clinical outcomes - FAS

5.9 Inflammatory markers

5.9.3 Hemoglobin (g/dl)

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4288	3939	3386	2763	1937	1352	984	703
	Missing	178	527	1080	1703	2529	3114	3482	3763
	Mean	17.7	17.0	17.3	17.7	18.0	15.9	15.3	14.8
	SD	24.2	25.3	25.4	22.7	30.4	17.6	15.5	13.7
	Min	0	0	0	0	0	0	1	4
	Median	13.0	13.0	14.0	14.0	14.0	14.0	14.0	14.0
	Max	434	920	840	169	960	152	150	161

Absolute values

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	3821	3282	2680	1878	1306	957	684
	Missing	645	1184	1786	2588	3160	3509	3782
	Mean	-0.6	-0.4	-0.2	0.2	-2.8	-3.8	-3.0
	SD	27.6	28.7	29.1	35.4	29.5	32.1	25.6
	Min	-279	-277	-281	-419	-419	-418	-147
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	837	832	155	947	139	135	141

Differences

FAS patient data set

5. Clinical outcomes - FAS

5.10 HAQ-DI

5.10.1 HAQ-DI - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4449	4143	3546	2881	2019	1403	994	728
	Missing	17	323	920	1585	2447	3063	3472	3738
	Mean	1.30	1.08	1.02	0.98	0.94	0.94	0.90	0.92
	SD	0.70	0.73	0.74	0.74	0.74	0.73	0.72	0.71
	Min	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Median	1.38	1.00	1.00	1.00	0.88	0.88	0.88	0.88
	Max	3.0	3.0	3.0	3.0	3.0	3.0	3.0	2.9

Absolute values

FAS patient data set

5. Clinical outcomes - FAS

5.10 HAQ-DI

5.10.2 HAQ-DI - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4130	3537	2873	2014	1400	992	727
	Missing	336	929	1593	2452	3066	3474	3739
	Mean	-0.22	-0.24	-0.27	-0.28	-0.30	-0.32	-0.28
	SD	0.51	0.54	0.58	0.60	0.62	0.61	0.63
	Min	-2.5	-2.8	-2.5	-2.6	-2.6	-2.6	-2.3
	Median	-0.13	-0.13	-0.25	-0.25	-0.25	-0.25	-0.25
	Max	2.1	2.0	2.3	1.8	1.5	1.6	1.8

FAS patient data set
 5. Clinical outcomes - FAS
 5.11 EQ-5D
 5.11.1 Mobility

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Mobility																
Total	No problems	1662	37.8	2072	50.3	1937	55.0	1644	57.6	1190	58.9	843	60.2	614	61.9	447	61.1
	Some problems	2728	62.0	2034	49.4	1575	44.7	1200	42.0	824	40.8	554	39.5	376	37.9	282	38.5
	Confined to bed	8	0.2	12	0.3	12	0.3	12	0.4	6	0.3	4	0.3	2	0.2	3	0.4
	Total	4398	100.0	4118	100.0	3524	100.0	2856	100.0	2020	100.0	1401	100.0	992	100.0	732	100.0

FAS patient data set
 5. Clinical outcomes - FAS
 5.11 EQ-5D
 5.11.2 Self-care

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Self-care																
Total	No problems	2599	59.1	2792	67.8	2476	70.3	2088	73.1	1484	73.5	1038	74.1	729	73.5	506	69.1
	Some problems	1680	38.2	1226	29.8	972	27.6	706	24.7	503	24.9	338	24.1	243	24.5	208	28.4
	Unable to wash or dress myself	115	2.6	98	2.4	75	2.1	62	2.2	33	1.6	25	1.8	20	2.0	18	2.5
	Total	4394	100.0	4116	100.0	3523	100.0	2856	100.0	2020	100.0	1401	100.0	992	100.0	732	100.0

FAS patient data set

5. Clinical outcomes - FAS

5.11 EQ-5D

5.11.3 Usual activities (e.g., work, study, housework, family or leisure activities)

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Usual activities																
Total	No problems	953	21.7	1463	35.5	1431	40.6	1303	45.6	958	47.4	677	48.3	503	50.7	353	48.2
	Some problems	3236	73.6	2511	61.0	1989	56.5	1455	50.9	1015	50.2	696	49.7	464	46.8	362	49.5
	Unable to perform	206	4.7	142	3.4	103	2.9	98	3.4	47	2.3	28	2.0	25	2.5	17	2.3
	Total	4395	100.0	4116	100.0	3523	100.0	2856	100.0	2020	100.0	1401	100.0	992	100.0	732	100.0

FAS patient data set
 5. Clinical outcomes - FAS
 5.11 EQ-5D
 5.11.4 Pain/discomfort

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Pain/discomfort																
Total	None	147	3.3	585	14.2	587	16.7	582	20.4	478	23.7	383	27.3	298	30.0	225	30.7
	Moderate	2965	67.4	2932	71.2	2508	71.2	1989	69.6	1381	68.4	917	65.5	631	63.6	461	63.0
	Extreme	1288	29.3	601	14.6	429	12.2	285	10.0	161	8.0	101	7.2	63	6.4	46	6.3
	Total	4400	100.0	4118	100.0	3524	100.0	2856	100.0	2020	100.0	1401	100.0	992	100.0	732	100.0

FAS patient data set
 5. Clinical outcomes - FAS
 5.11 EQ-5D
 5.11.5 Anxiety/depression

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Anxiety/depression																
Total	None	2159	49.1	2328	56.6	2141	60.8	1791	62.8	1349	66.8	977	69.8	705	71.1	526	71.9
	Moderate	1961	44.6	1601	38.9	1238	35.1	956	33.5	607	30.0	395	28.2	265	26.7	190	26.0
	Extreme	275	6.3	187	4.5	144	4.1	107	3.7	64	3.2	28	2.0	22	2.2	16	2.2
	Total	4395	100.0	4116	100.0	3523	100.0	2854	100.0	2020	100.0	1400	100.0	992	100.0	732	100.0

FAS patient data set

5. Clinical outcomes - FAS

5.11 EQ-5D

5.11.6 Mean EQ VAS

5.11.6.1 Mean EQ VAS - absolute values

		M00	M03	M06	M12	M24	M36	M48	M60
Total	N	4405	4116	3522	2850	2013	1407	994	730
	Missing	61	350	944	1616	2453	3059	3472	3736
	Mean	48.9	58.9	61.2	63.4	65.6	67.2	68.4	68.6
	SD	20.8	21.5	21.7	21.9	21.4	21.5	20.9	21.8
	Min	0	0	0	0	1	0	0	9
	Median	50.0	60.0	61.0	65.0	70.0	70.0	70.0	71.0
	Max	100	100	100	100	100	100	100	100

FAS patient data set

5. Clinical outcomes - FAS

5.11 EQ-5D

5.11.6 Mean EQ VAS

5.11.6.2 Mean EQ VAS - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00	M48 - M00	M60 - M00
Total	N	4073	3480	2815	1990	1393	986	725
	Missing	393	986	1651	2476	3073	3480	3741
	Mean	10.0	11.7	12.9	14.9	16.2	15.8	14.9
	SD	24.0	24.9	25.8	25.4	25.4	25.2	25.4
	Min	-82	-89	-80	-73	-76	-65	-70
	Median	10.0	10.0	11.0	15.0	17.0	16.0	15.0
	Max	100	100	90	95	95	85	90

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.1 Number of visits at the rheumatologist

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3408	2774	1946	1357	960	703
	Missing	122	4466	1058	1692	2520	3109	3506	3763
	Mean	3.3	.	2.5	2.2	1.9	1.8	1.9	1.8
	SD	3.1	.	2.7	2.0	1.5	1.4	1.4	1.6
	Min	0	.	0	0	0	0	0	0
	Median	3.0	.	2.0	2.0	2.0	2.0	2.0	2.0
	Max	57	.	62	31	26	25	22	32

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.2 Number of visits at the general practitioner

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3407	2774	1946	1357	960	703
	Missing	122	4466	1059	1692	2520	3109	3506	3763
	Mean	4.0	.	2.9	2.6	2.1	2.1	1.9	1.8
	SD	4.6	.	4.4	3.2	2.5	3.0	2.4	2.5
	Min	0	.	0	0	0	0	0	0
	Median	3.0	.	2.0	2.0	1.5	1.5	1.5	1.5
	Max	68	.	99	40	26	50	46	45

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.3 Number of visits at the orthopaedic specialist

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3408	2774	1946	1357	960	703
	Missing	122	4466	1058	1692	2520	3109	3506	3763
	Mean	0.9	.	0.6	0.7	0.5	0.5	0.5	0.5
	SD	2.2	.	1.9	1.6	1.3	1.3	1.0	1.9
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	31	.	48	24	23	28	9	45

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.4 Number of visits at other medical specialists

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3407	2774	1946	1357	960	703
	Missing	122	4466	1059	1692	2520	3109	3506	3763
	Mean	1.2	.	0.9	0.9	0.8	0.8	0.8	0.8
	SD	2.4	.	1.8	1.8	1.4	1.5	1.5	1.5
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.5	0.5
	Max	78	.	26	20	25	30	30	27

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.5 Number of hospitalizations

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3408	2774	1946	1357	960	703
	Missing	122	4466	1058	1692	2520	3109	3506	3763
	Mean	0.4	.	0.2	0.2	0.1	0.1	0.1	0.1
	SD	1.5	.	1.0	1.1	0.5	0.4	0.7	0.4
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	34	.	28	28	11	5	21	7

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.6 Total duration of hospitalizations (days)

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3407	2773	1946	1357	960	703
	Missing	122	4466	1059	1693	2520	3109	3506	3763
	Mean	2.3	.	1.1	1.1	0.8	0.7	0.7	0.5
	SD	7.3	.	4.4	4.8	3.5	3.1	3.5	2.4
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	.	90	92	63	60	75	33

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.7 Number of convalescent cares, stationary rehabilitations

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3408	2774	1946	1357	960	703
	Missing	122	4466	1058	1692	2520	3109	3506	3763
	Mean	0.2	.	0.1	0.1	0.1	0.1	0.0	0.1
	SD	1.6	.	1.4	1.2	0.6	0.5	0.5	0.8
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	42	.	30	25	14	11	14	15

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.8 Total duration of convalescent cares, stationary rehabilitations (days)

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3407	2773	1946	1357	960	703
	Missing	122	4466	1059	1693	2520	3109	3506	3763
	Mean	1.6	.	1.0	1.0	0.6	0.5	0.5	0.5
	SD	7.2	.	4.9	6.0	2.7	2.6	2.5	2.4
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	.	45	183	25	30	26	21

FAS patient data set

5. Clinical outcomes - FAS

5.12 Number of physician visits and number and duration of hospitalizations

5.12.9 Number of physical therapies, for example physiotherapy

		M00	M00	M06	M12	M24	M36	M48	M60
Total	N	4344	0	3408	2774	1946	1357	960	703
	Missing	122	4466	1058	1692	2520	3109	3506	3763
	Mean	3.9	.	3.0	3.0	2.0	1.9	1.8	1.8
	SD	9.7	.	8.8	8.5	5.9	6.0	5.5	5.4
	Min	0	.	0	0	0	0	0	0
	Median	0.0	.	0.0	0.0	0.0	0.0	0.0	0.0
	Max	98	.	99	99	50	50	50	48

FAS patient data set

5. Clinical outcomes - FAS

5.13 Impairment of non-occupational activities

5.13.1 Household, without not applicable and missing patients

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Household														
Total	Yes	3335	82.6	1890	60.9	1411	55.9	1004	55.7	681	54.8	494	55.9	357	55.3
	No	704	17.4	1213	39.1	1115	44.1	799	44.3	562	45.2	389	44.1	288	44.7
	Total	4039	100.0	3103	100.0	2526	100.0	1803	100.0	1243	100.0	883	100.0	645	100.0

		M00	M06	M12	M24	M36	M48	M60
Total	N	3368	2666	2199	1572	1093	784	574
	Missing	1098	1800	2267	2894	3373	3682	3892
	Mean	56.9	27.7	22.4	20.6	18.2	19.2	16.1
	SD	64.3	50.6	46.1	46.3	43.7	46.1	39.8
	Min	0	0	0	0	0	0	0
	Median	30.0	3.0	0.0	0.0	0.0	0.5	0.0
	Max	183	183	183	183	183	183	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account.

FAS patient data set

5. Clinical outcomes - FAS

5.13 Impairment of non-occupational activities

5.13.2 Parenting, without not applicable and missing patients

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Parenting														
Total	Yes	338	26.1	155	13.9	89	9.7	74	11.0	38	8.7	30	9.8	15	7.6
	No	957	73.9	958	86.1	827	90.3	598	89.0	401	91.3	276	90.2	183	92.4
	Total	1295	100.0	1113	100.0	916	100.0	672	100.0	439	100.0	306	100.0	198	100.0

		M00	M06	M12	M24	M36	M48	M60
Total	N	1220	1068	896	654	435	300	195
	Missing	3246	3398	3570	3812	4031	4166	4271
	Mean	15.1	4.7	3.1	2.8	1.9	3.0	1.6
	SD	41.6	23.1	18.1	18.4	13.6	19.7	8.2
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	183	183	183	183	60

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account.

FAS patient data set

5. Clinical outcomes - FAS

5.13 Impairment of non-occupational activities

5.13.3 Education, without not applicable and missing patients

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Education														
Total	Yes	167	16.5	61	6.8	53	6.9	27	4.8	17	4.5	11	4.2	7	4.1
	No	843	83.5	838	93.2	716	93.1	538	95.2	364	95.5	251	95.8	162	95.9
	Total	1010	100.0	899	100.0	769	100.0	565	100.0	381	100.0	262	100.0	169	100.0

		M00	M06	M12	M24	M36	M48	M60
Total	N	975	887	750	558	379	257	168
	Missing	3491	3579	3716	3908	4087	4209	4298
	Mean	8.3	2.5	1.6	1.1	1.0	0.9	1.4
	SD	31.6	17.1	13.3	10.1	10.1	11.5	12.6
	Min	0	0	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Max	183	183	180	183	183	183	150

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account.

FAS patient data set

5. Clinical outcomes - FAS

5.13 Impairment of non-occupational activities

5.13.4 Recreational (free-time), without not applicable and missing patients

		Visit													
		M0		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Recreational (free-time)														
Total	Yes	3041	82.3	1699	60.1	1227	54.0	895	55.1	615	53.6	459	56.4	321	54.0
	No	656	17.7	1127	39.9	1045	46.0	729	44.9	533	46.4	355	43.6	273	46.0
	Total	3697	100.0	2826	100.0	2272	100.0	1624	100.0	1148	100.0	814	100.0	594	100.0

		M00	M06	M12	M24	M36	M48	M60
Total	N	3101	2467	2000	1426	1016	728	532
	Missing	1365	1999	2466	3040	3450	3738	3934
	Mean	59.1	28.3	23.0	19.5	18.5	19.1	16.3
	SD	65.6	50.9	47.4	45.0	44.9	46.0	41.7
	Min	0	0	0	0	0	0	0
	Median	30.0	4.0	0.0	0.0	0.0	0.5	0.0
	Max	183	183	183	183	183	183	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account.

FAS patient data set

5. Clinical outcomes - FAS

5.14 Patient assessment of adalimumab therapy

		Visit													
		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Patient assessment														
Total	Considerably better	1428	35.6	1366	39.6	1304	46.3	1023	51.6	704	51.5	539	55.5	384	53.6
	Better	1468	36.6	1369	39.7	1050	37.3	735	37.1	552	40.4	370	38.1	278	38.8
	About the same	771	19.2	516	14.9	342	12.2	181	9.1	91	6.7	54	5.6	40	5.6
	Worse	277	6.9	171	5.0	107	3.8	38	1.9	18	1.3	5	0.5	8	1.1
	Noticeably worse	63	1.6	30	0.9	11	0.4	6	0.3	1	0.1	3	0.3	6	0.8
	Total	4007	100.0	3452	100.0	2814	100.0	1983	100.0	1366	100.0	971	100.0	716	100.0

FAS patient data set
 5. Clinical outcomes - FAS
 5.15 Participation in Abbott Care

		Visit															
		M0		M3		M6		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Abbott Care																
Total	No	2571	65.1	2270	64.9	2068	62.6	1708	63.5	1253	66.3	885	67.5	642	68.8	489	71.2
	Yes	1380	34.9	1226	35.1	1234	37.4	980	36.5	636	33.7	426	32.5	291	31.2	198	28.8
	Total	3951	100.0	3496	100.0	3302	100.0	2688	100.0	1889	100.0	1311	100.0	933	100.0	687	100.0

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
das_M00	DAS28	4466	5.1333074	1.1449191	3.2008121	8.8507843
sexjn	Gender (1=male, 0=female)	4463	0.2592427	0.4382681	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	4414	0.1554146	0.3623405	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	4429	0.2233010	0.4165055	0	1.0000000
rfnj_M00	Rheumatic factor (1=positive)	4237	0.6575407	0.4745883	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	3943	0.6604109	0.4736299	0	1.0000000
smokejn	Smoker (1=yes)	4398	0.2273761	0.4191851	0	1.0000000
AGE	Age	4464	55.1314964	12.9941283	15.0000000	90.0000000
bmi_M00	Body mass index (kg/m ²)	4433	27.1108687	5.5523542	14.1868512	65.0137741
bradau	Duration of disease (years)	4416	9.2019289	8.7389332	0.0054757	60.5475702
STIFFTM_M00	Morning stiffness (minutes)	4370	65.3075515	72.8235445	0	800.0000000
CRP_M00	CRP (mg/l)	4353	19.3420859	50.6794998	0	913.0000000
BSG_M00	ESR (mm/h)	4466	29.5497089	21.8744328	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	4288	17.6930970	24.1972404	0	434.0000000
EXH_7DAYS_M00	Fatigue (0-10)	4449	5.7727579	2.6702489	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	4455	6.0637486	2.2656875	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	4449	1.2984659	0.7024280	0	3.0000000
prevbio	Number of previous biologics	4466	0.3222123	0.6147381	0	6.0000000
mtxjn	MTX	4466	0.5340349	0.4988961	0	1.0000000
saspjn	SASP	4466	0.0360502	0.1864358	0	1.0000000
lefjn	Lefunomide	4466	0.1195701	0.3244945	0	1.0000000
nsacoxjn	NSAID, Coxibe	4466	0.2205553	0.4146675	0	1.0000000
anajn	Analgesics	4466	0.1094940	0.3122929	0	1.0000000
glucjn	Glucocorticoides	4466	0.6811464	0.4660843	0	1.0000000
seq1jn	Arterial hypertension	4466	0.3546798	0.4784698	0	1.0000000
seq2jn	Coronary heart disease	4466	0.0550828	0.2281674	0	1.0000000
seq3jn	Hyperlipidemia	4466	0.0821764	0.2746641	0	1.0000000
seq4jn	Diabetes Type I	4466	0.0141066	0.1179436	0	1.0000000
seq5jn	Diabetes Type II	4466	0.0884460	0.2839743	0	1.0000000
seq6jn	Chronic inflammatory disease	4466	0.0203762	0.1412992	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	4466	0.0499328	0.2178306	0	1.0000000
seq8jn	Osteoporosis	4466	0.1486789	0.3558115	0	1.0000000
seq9jn	Degenerative joint disease	4466	0.1865204	0.3895696	0	1.0000000
seq10jn	Degenerative spinal disease	4466	0.1531572	0.3601793	0	1.0000000
seq11jn	Mental illness (e.g. depression)	4466	0.0673981	0.2507383	0	1.0000000

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
das_M00	DAS28	3218	5.1086060	1.1475381	3.2008121	8.8507843
sexjn	Gender (1=male, 0=female)	3218	0.2681182	0.4428418	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3218	0.1513819	0.3565777	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3218	0.2180451	0.4113106	0	1.0000000
rfnj_M00	Rheumatic factor (1=positive)	3218	0.6657963	0.4603574	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	3218	0.6705508	0.4409924	0	1.0000000
smokejn	Smoker (1=yes)	3218	0.2324188	0.4193439	0	1.0000000
AGE	Age	3218	55.1047560	12.9058870	15.0000000	90.0000000
bmi_M00	Body mass index (kg/m ²)	3218	26.9632182	5.5006978	14.1868512	60.9733701
bradau	Duration of disease (years)	3218	9.3514025	8.5631048	0.0054757	60.5475702
STIFFTM_M00	Morning stiffness (minutes)	3218	64.4495093	69.3503172	0	720.0000000
CRP_M00	CRP (mg/l)	3210	19.4150493	53.5648346	0	913.0000000
BSG_M00	ESR (mm/h)	3218	29.1817899	21.4866684	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	3218	17.8439716	24.1054599	0	434.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3218	5.6447491	2.6663501	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3218	5.9401869	2.2486494	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3218	1.2617471	0.6908608	0	3.0000000
prevbio	Number of previous biologics	3218	0.3138595	0.6074355	0	6.0000000
mtxjn	MTX	3218	0.5518956	0.4973768	0	1.0000000
saspjn	SASP	3218	0.0341827	0.1817265	0	1.0000000
lefjn	Lefunomide	3218	0.1180858	0.3227598	0	1.0000000
nsacoxjn	NSAID, Coxibe	3218	0.2175264	0.4126277	0	1.0000000
anajn	Analgesics	3218	0.1053449	0.3070451	0	1.0000000
glucjn	Glucocorticoides	3218	0.6765071	0.4678817	0	1.0000000
seq1jn	Arterial hypertension	3218	0.3458670	0.4757240	0	1.0000000
seq2jn	Coronary heart disease	3218	0.0497203	0.2174003	0	1.0000000
seq3jn	Hyperlipidemia	3218	0.0807955	0.2725632	0	1.0000000
seq4jn	Diabetes Type I	3218	0.0127408	0.1121714	0	1.0000000
seq5jn	Diabetes Type II	3218	0.0814170	0.2735170	0	1.0000000
seq6jn	Chronic inflammatory disease	3218	0.0211311	0.1438438	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3218	0.0487881	0.2154582	0	1.0000000
seq8jn	Osteoporosis	3218	0.1538222	0.3608343	0	1.0000000
seq9jn	Degenerative joint disease	3218	0.1867620	0.3897809	0	1.0000000
seq10jn	Degenerative spinal disease	3218	0.1584835	0.3652505	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3218	0.0680547	0.2518789	0	1.0000000

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

3218 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Body mass index (kg/m ²)	0.0163424	0.0249551	50	14.186851	60.97337	26.963218
DAS28	-0.733264	-0.659348	50	3.2008121	8.8507843	5.108606
Health Assessment questionnaire (HAQ)	0.2341947	0.3313196	50	0	3	1.2617471
MTX	-0.326421	-0.248081	50	0	1	0.5518956
Number of previous biologics	0.181591	0.220165	50	0	6	0.3138595
Age	0.0052805	0.0092278	46	15	90	55.104756
Analgesics	0.202553	0.2947597	30	0	1	0.1053449
Rheumatoid nodules (1=yes)	0.1256861	0.2050349	26	0	1	0.1513819
Leflunomide	0.1385596	0.2282058	19	0	1	0.1180858
Gender (1=male, 0=female)	-0.19783	-0.111241	19	0	1	0.2681182
ESR (mm/h)	0.0023754	0.0033721	14	1	120	29.18179
SASP	-0.359368	-0.279524	10	0	1	0.0341827
Arterial hypertension	0.1009775	0.1203433	6	0	1	0.345867
Chronic obstructive pulmonary disease	0.2063647	0.2335285	6	0	1	0.0487881
Diabetes Type II	0.1951264	0.1972701	4	0	1	0.081417
Smoker (1=yes)	0.1192086	0.1192591	3	0	1	0.2324188
Morning stiffness (minutes)	0.0006695	0.0006695	2	0	720	64.449509

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Modell variables for p:0.001 with coefficients and R²

3218 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	0.68287	.	.	<.0001
DAS28	-0.68658	0.22413	0.2241	<.0001
Health Assessment questionnaire (HAQ)	0.27593	0.02991	0.2540	<.0001
MTX	-0.29030	0.01091	0.2649	<.0001
Number of previous biologics	0.20102	0.00746	0.2724	<.0001
Body mass index (kg/m ²)	0.02071	0.00674	0.2791	<.0001
Age	0.00783	0.00433	0.2835	<.0001
Analgesics	0.23977	0.00248	0.2859	0.0009

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Modell variables for $p:0.001$ with coefficients and R^2
 3218 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	0.68287	<.0001
DAS28	-0.68658	<.0001
Health Assessment questionnaire (HAQ)	0.27593	<.0001
MTX	-0.29030	<.0001
Number of previous biologics	0.20102	<.0001
Body mass index (kg/m ²)	0.02071	<.0001
Age	0.00783	<.0001
Analgesics	0.23977	0.0009

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand	Mean prediction error	1.005	0.949	1.045
			varanz	Number of selected variables	5.600	5.000	6.000
	0.001	5	meand	Mean prediction error	1.002	0.941	1.038
			varanz	Number of selected variables	6.200	6.000	7.000
	0.01	5	meand	Mean prediction error	1.002	0.940	1.032
varanz			Number of selected variables	8.200	7.000	10.000	
0.05	5	meand	Mean prediction error	1.002	0.940	1.032	
		varanz	Number of selected variables	11.000	9.000	12.000	
none	0	5	meand	Mean prediction error	1.175	1.131	1.247
			varanz	Number of selected variables	0.000	0.000	0.000
stepwise	0.0001	5	meand	Mean prediction error	1.005	0.949	1.045
			varanz	Number of selected variables	5.600	5.000	6.000
0.001	5	meand	Mean prediction error	1.002	0.941	1.038	
		varanz	Number of selected variables	6.200	6.000	7.000	
0.01	5	meand	Mean prediction error	1.002	0.940	1.032	
		varanz	Number of selected variables	8.400	7.000	10.000	
0.05	5	meand	Mean prediction error	1.001	0.940	1.031	
		varanz	Number of selected variables	10.600	9.000	12.000	
0.1	5	meand	Mean prediction error	0.999	0.936	1.028	
		varanz	Number of selected variables	12.600	12.000	13.000	

FAS patient data set

6. Regression analysis for DAS28 (M6-M0)

Fixed modell

3196 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R ² stepwise is used				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	0.68622	.	.	<.0001
DAS28	-0.68831	0.22628	0.2263	<.0001
Health Assessment questionnaire (HAQ)	0.27091	0.02920	0.2555	<.0001
MTX	-0.28603	0.01061	0.2661	<.0001
Number of previous biologics	0.19937	0.00737	0.2735	<.0001
Body mass index (kg/m ²)	0.02076	0.00684	0.2803	<.0001
Age	0.00797	0.00448	0.2848	<.0001
Analgesics	0.24520	0.00257	0.2874	0.0007

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Data overview

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
das_M00	DAS28	4466	5.1333074	1.1449191	3.2008121	8.8507843
sexjn	Gender (1=male, 0=female)	4463	0.2592427	0.4382681	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	4414	0.1554146	0.3623405	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	4429	0.2233010	0.4165055	0	1.0000000
rfnj_M00	Rheumatic factor (1=positive)	4237	0.6575407	0.4745883	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	3943	0.6604109	0.4736299	0	1.0000000
smokejn	Smoker (1=yes)	4398	0.2273761	0.4191851	0	1.0000000
AGE	Age	4464	55.1314964	12.9941283	15.0000000	90.0000000
bmi_M00	Body mass index (kg/m ²)	4433	27.1108687	5.5523542	14.1868512	65.0137741
bradau	Duration of disease (years)	4416	9.2019289	8.7389332	0.0054757	60.5475702
STIFFTM_M00	Morning stiffness (minutes)	4370	65.3075515	72.8235445	0	800.0000000
CRP_M00	CRP (mg/l)	4353	19.3420859	50.6794998	0	913.0000000
BSG_M00	ESR (mm/h)	4466	29.5497089	21.8744328	1.0000000	138.0000000
HB_M00	Hemoglobin (g/dl)	4288	17.6930970	24.1972404	0	434.0000000
EXH_7DAYS_M00	Fatigue (0-10)	4449	5.7727579	2.6702489	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	4455	6.0637486	2.2656875	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	4449	1.2984659	0.7024280	0	3.0000000
prevbio	Number of previous biologics	4466	0.3222123	0.6147381	0	6.0000000
mtxjn	MTX	4466	0.5340349	0.4988961	0	1.0000000
saspjn	SASP	4466	0.0360502	0.1864358	0	1.0000000
lefjn	Lefunomide	4466	0.1195701	0.3244945	0	1.0000000
nsacoxjn	NSAID, Coxibe	4466	0.2205553	0.4146675	0	1.0000000
anajn	Analgesics	4466	0.1094940	0.3122929	0	1.0000000
glucjn	Glucocorticoides	4466	0.6811464	0.4660843	0	1.0000000
seq1jn	Arterial hypertension	4466	0.3546798	0.4784698	0	1.0000000
seq2jn	Coronary heart disease	4466	0.0550828	0.2281674	0	1.0000000
seq3jn	Hyperlipidemia	4466	0.0821764	0.2746641	0	1.0000000
seq4jn	Diabetes Type I	4466	0.0141066	0.1179436	0	1.0000000
seq5jn	Diabetes Type II	4466	0.0884460	0.2839743	0	1.0000000
seq6jn	Chronic inflammatory disease	4466	0.0203762	0.1412992	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	4466	0.0499328	0.2178306	0	1.0000000
seq8jn	Osteoporosis	4466	0.1486789	0.3558115	0	1.0000000
seq9jn	Degenerative joint disease	4466	0.1865204	0.3895696	0	1.0000000
seq10jn	Degenerative spinal disease	4466	0.1531572	0.3601793	0	1.0000000
seq11jn	Mental illness (e.g. depression)	4466	0.0673981	0.2507383	0	1.0000000

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Patients with less than 4 missing values and only variables with more than 80 % data

Remaining missing values are replaced with the mean

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
das_M00	DAS28	3526	5.1162341	1.1470270	3.2008121	8.8507843
sexjn	Gender (1=male, 0=female)	3526	0.2648311	0.4411180	0	1.0000000
modsjn_M00	Rheumatoid nodules (1=yes)	3526	0.1594037	0.3641259	0	1.0000000
jointopjn_M00	Prior joint surgery (1=yes)	3526	0.2197143	0.4125822	0	1.0000000
rfnj_M00	Rheumatic factor (1=positive)	3526	0.6621864	0.4609373	0	1.0000000
ccpjn_M00	Anti-ccp (1=positive)	3526	0.6686979	0.4426756	0	1.0000000
smokejn	Smoker (1=yes)	3526	0.2305699	0.4181396	0	1.0000000
AGE	Age	3526	54.9951773	12.9469722	15.0000000	90.0000000
bmi_M00	Body mass index (kg/m ²)	3526	26.9903000	5.5496408	14.1868512	65.0137741
bradau	Duration of disease (years)	3526	9.3280605	8.6065711	0.0054757	60.5475702
STIFFTM_M00	Morning stiffness (minutes)	3526	65.0439053	71.4231806	0	720.0000000
CRP_M00	CRP (mg/l)	3517	19.4101513	52.9427639	0	913.0000000
BSG_M00	ESR (mm/h)	3526	29.1599546	21.4608586	1.0000000	120.0000000
HB_M00	Hemoglobin (g/dl)	3526	17.8806718	24.2705125	0	434.0000000
EXH_7DAYS_M00	Fatigue (0-10)	3526	5.6627808	2.6695051	0	10.0000000
PAIN_7DAYS_M00	Pain (0-10)	3526	5.9622052	2.2499156	0	10.0000000
haq_M00	Health Assessment questionnaire (HAQ)	3526	1.2639221	0.6943840	0	3.0000000
prevbio	Number of previous biologics	3526	0.3131027	0.6064277	0	6.0000000
mtxjn	MTX	3526	0.5482133	0.4977406	0	1.0000000
saspjn	SASP	3526	0.0340329	0.1813394	0	1.0000000
lefjn	Lefunomide	3526	0.1162791	0.3206047	0	1.0000000
nsacoxjn	NSAID, Coxibe	3526	0.2178106	0.4128165	0	1.0000000
anajn	Analgesics	3526	0.1046512	0.3061468	0	1.0000000
glucjn	Glucocorticoides	3526	0.6766875	0.4678072	0	1.0000000
seq1jn	Arterial hypertension	3526	0.3499716	0.4770283	0	1.0000000
seq2jn	Coronary heart disease	3526	0.0516166	0.2212830	0	1.0000000
seq3jn	Hyperlipidemia	3526	0.0822462	0.2747784	0	1.0000000
seq4jn	Diabetes Type I	3526	0.0133296	0.1146979	0	1.0000000
seq5jn	Diabetes Type II	3526	0.0836642	0.2769228	0	1.0000000
seq6jn	Chronic inflammatory disease	3526	0.0204197	0.1414512	0	1.0000000
seq7jn	Chronic obstructive pulmonary disease	3526	0.0484969	0.2148442	0	1.0000000
seq8jn	Osteoporosis	3526	0.1505956	0.3577050	0	1.0000000
seq9jn	Degenerative joint disease	3526	0.1883154	0.3910193	0	1.0000000
seq10jn	Degenerative spinal disease	3526	0.1565513	0.3634288	0	1.0000000
seq11jn	Mental illness (e.g. depression)	3526	0.0660805	0.2484581	0	1.0000000

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

3526 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Age	0.0049212	0.0060873	50	15	90	54.995177
Body mass index (kg/m ²)	0.0118785	0.0143671	50	14.186851	65.013774	26.9903
Duration of disease (years)	0.0039187	0.0068784	50	0.0054757	60.54757	9.3280605
Health Assessment questionnaire (HAQ)	-0.319461	-0.274094	50	0	3	1.2639221
Number of previous biologics	0.0559521	0.0990189	48	0	6	0.3131027
Morning stiffness (minutes)	-0.00074	-0.000378	45	0	720	65.043905
MTX	-0.087014	-0.042018	38	0	1	0.5482133
Gender (1=male, 0=female)	-0.111843	-0.069133	38	0	1	0.2648311
Chronic obstructive pulmonary disease	0.1097755	0.1567933	34	0	1	0.0484969
Prior joint surgery (1=yes)	0.0469572	0.0981276	32	0	1	0.2197143
Leflunomide	0.0503207	0.1214309	25	0	1	0.1162791
Smoker (1=yes)	0.0537467	0.0815775	24	0	1	0.2305699
Pain (0-10)	-0.018123	-0.008576	22	0	10	5.9622052
SASP	-0.172638	-0.098488	22	0	1	0.0340329
Analgesics	0.065051	0.0842618	20	0	1	0.1046512
Rheumatic factor (1=positive)	-0.060602	-0.038232	16	0	1	0.6621864
CRP (mg/l)	-0.000689	-0.00034	12	0	913	19.410151
Arterial hypertension	0.0407076	0.0454462	8	0	1	0.3499716
Diabetes Type II	0.0681463	0.0836853	8	0	1	0.0836642
Hemoglobin (g/dl)	0.0008316	0.0008545	6	0	434	17.880672
ESR (mm/h)	-0.000805	-0.00078	4	1	120	29.159955
Degenerative spinal disease	0.0463438	0.0487641	4	0	1	0.1565513
Mental illness (e.g. depression)	0.0661505	0.0670406	4	0	1	0.0660805

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FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Most important variables influencing the dependent variable

How often the variable was selected in 50 different models ("Number of models")

3526 patients were used for modelling.

Variable	Coefficient (Min)	Coefficient (Max)	Number of models	Minimum	Maximum	Means
Fatigue (0-10)	0.0078623	0.0078623	2	0	10	5.6627808
Osteoporosis	0.0523443	0.0532682	2	0	1	0.1505956
Anti-ccp (1=positive)	-0.036682	-0.036682	1	0	1	0.6686979

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Modell variables for p:0.001 with coefficients and R²

3526 patients were used for modelling

Stepwise				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	-0.50694	.	.	<.0001
Health Assessment questionnaire (HAQ)	-0.30715	0.09627	0.0963	<.0001
Age	0.00543	0.02413	0.1204	<.0001
Body mass index (kg/m ²)	0.01329	0.01603	0.1364	<.0001
Duration of disease (years)	0.00453	0.01280	0.1492	<.0001
Number of previous biologics	0.07344	0.00754	0.1568	<.0001
Morning stiffness (minutes)	-0.00058165	0.00608	0.1628	<.0001
MTX	-0.06617	0.00433	0.1672	<.0001
Gender (1=male, 0=female)	-0.07890	0.00375	0.1709	<.0001
Chronic obstructive pulmonary disease	0.13779	0.00291	0.1738	0.0004
Prior joint surgery (1=yes)	0.07410	0.00287	0.1767	0.0005

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Modell variables for p:0.001 with coefficients and R²

3526 patients were used for modelling

Backward		
Variable	Coefficient	p-value
Intercept	-0.50694	<.0001
Health Assessment questionnaire (HAQ)	-0.30715	<.0001
Body mass index (kg/m ²)	0.01329	<.0001
Age	0.00543	<.0001
Number of previous biologics	0.07344	<.0001
Morning stiffness (minutes)	-0.00058165	<.0001
Duration of disease (years)	0.00453	<.0001
Gender (1=male, 0=female)	-0.07890	<.0001
MTX	-0.06617	<.0001
Chronic obstructive pulmonary disease	0.13779	0.0004
Prior joint surgery (1=yes)	0.07410	0.0005

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Validation overview

The MEANS Procedure

selection	pvalue	N Obs	Variable	Label	Mean	Minimum	Maximum
backward	0.0001	5	meand	Mean prediction error	0.388	0.382	0.394
			varanz	Number of selected variables	6.400	6.000	8.000
	0.001	5	meand	Mean prediction error	0.386	0.379	0.393
			varanz	Number of selected variables	8.600	7.000	10.000
	0.01	5	meand	Mean prediction error	0.385	0.377	0.394
varanz			Number of selected variables	11.600	9.000	14.000	
0.05	5	meand	Mean prediction error	0.383	0.374	0.394	
		varanz	Number of selected variables	16.200	14.000	18.000	
0.1	5	meand	Mean prediction error	0.382	0.371	0.394	
		varanz	Number of selected variables	19.000	18.000	20.000	
none	0	5	meand	Mean prediction error	0.411	0.403	0.416
			varanz	Number of selected variables	0.000	0.000	0.000
1	5	meand	Mean prediction error	0.382	0.370	0.393	
		varanz	Number of selected variables	35.000	35.000	35.000	
stepwise	0.0001	5	meand	Mean prediction error	0.388	0.382	0.394
			varanz	Number of selected variables	6.400	6.000	8.000
	0.001	5	meand	Mean prediction error	0.386	0.379	0.393
			varanz	Number of selected variables	8.600	7.000	10.000
	0.01	5	meand	Mean prediction error	0.385	0.377	0.394
varanz			Number of selected variables	11.600	9.000	14.000	
0.05	5	meand	Mean prediction error	0.383	0.374	0.394	
		varanz	Number of selected variables	16.200	14.000	18.000	
0.1	5	meand	Mean prediction error	0.383	0.374	0.394	
		varanz	Number of selected variables	18.400	16.000	20.000	

FAS patient data set

7. Regression analysis for HAQ (M6-M0)

Fixed modell

3395 patients were used for modelling, only patients with complete data set for these variables were used

Fixed modell - for partial R ² stepwise is used				
Variable	Coefficient	Partial R ²	Cummulated R ² (model)	p-value
Intercept	-0.51382	.	.	<.0001
Health Assessment questionnaire (HAQ)	-0.30656	0.09673	0.0967	<.0001
Age	0.00558	0.02561	0.1223	<.0001
Body mass index (kg/m ²)	0.01312	0.01598	0.1383	<.0001
Duration of disease (years)	0.00452	0.01297	0.1513	<.0001
Morning stiffness (minutes)	-0.00061523	0.00716	0.1585	<.0001
Number of previous biologics	0.06971	0.00647	0.1649	<.0001
Gender (1=male, 0=female)	-0.07893	0.00419	0.1691	<.0001
Chronic obstructive pulmonary disease	0.14404	0.00336	0.1725	0.0003
Prior joint surgery (1=yes)	0.07634	0.00312	0.1756	0.0004
MTX	-0.05563	0.00257	0.1782	0.0011

Appendix 8 Statistical Tables for CV Substudy (AGIL-CV)

**Long-term Documentation of the
Safety, Effectiveness, and Effects on
Quality of Life and Work Productivity in
Patients with Rheumatoid Arthritis
during HUMIRA® (Adalimumab)
Therapy in Routine Clinical Practice
(AGIL) and Supplementary
Documentation to Record
Cardiovascular and Metabolic Risk
Factors (AGIL-CV)**

**Final analysis
Appendix: Statistical Tables for
CV Substudy (AGIL-CV)**

March, 06 2018

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AGIL-CV patient data set

1. General parameters

1.1 Exclusion criteria for AGIL-CV evaluation

	n	%
Exclusion criterias		
Patient base	7229	100.0
Patients in AGIL only	6969	96.4

AGIL-CV patient data set
1. General parameters
1.2 Gender

	Gender				Total	
	Male		Female			
	n	%	n	%	n	%
Total	74	28.5	186	71.5	260	100.0

AGIL-CV patient data set

1. General parameters

1.3 Age (years)

1.3.1 Age - total

	Total
N	258
Missing	2
Mean	53.6
SD	8.6
Min	20
Median	54.0
Max	76

AGIL-CV patient data set

1. General parameters

1.3 Age (years)

1.3.2 Age by gender

	Male	Female
N	73	185
Missing	1	1
Mean	53.3	53.7
SD	7.7	8.9
Min	33	20
Median	54.0	54.0
Max	76	75

AGIL-CV patient data set

1. General parameters

1.4 Height (cm)

1.4.1 Height - total

	Total
N	246
Missing	14
Mean	168.8
SD	9.0
Min	147
Median	168.0
Max	193

AGIL-CV patient data set

1. General parameters

1.4 Height (cm)

1.4.2 Height by gender

	Male	Female
N	71	175
Missing	3	11
Mean	178.3	165.0
SD	7.3	6.5
Min	163	147
Median	178.0	165.0
Max	193	180

AGIL-CV patient data set

1. General parameters

1.5 Weight (kg)

1.5.1 Weight - total

	Total
N	248
Missing	12
Mean	78.6
SD	17.2
Min	43
Median	77.0
Max	125

AGIL-CV patient data set

1. General parameters

1.5 Weight (kg)

1.5.2 Weight by gender

	Male	Female
N	71	177
Missing	3	9
Mean	88.9	74.5
SD	14.8	16.4
Min	60	43
Median	87.0	72.0
Max	122	125

AGIL-CV patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.1 BMI - total

	Total
N	246
Missing	14
Mean	27.5
SD	5.4
Min	17
Median	26.8
Max	46

AGIL-CV patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.2 BMI by gender

	Male	Female
N	71	175
Missing	3	11
Mean	28.0	27.4
SD	4.5	5.8
Min	20	17
Median	27.4	26.5
Max	40	46

AGIL-CV patient data set

1. General parameters

1.7 Smoking habits

	Smoking habits				Total	
	Yes		No			
	n	%	n	%	n	%
Total	73	29.9	171	70.1	244	100.0

AGIL-CV patient data set
 1. General parameters
 1.8 Duration of disease (years)
 1.8.1 Duration - total

	Total
N	241
Missing	19
Mean	6.9
SD	7.0
Min	0
Median	4.3
Max	39

	Duration of disease (grouped)																		Total	
	< 2 years		2 - 4 years		4 - 6 years		6 - 8 years		8 - 10 years		10 - 15 years		15 - 20 years		20 - 30 years		> 30 years			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	68	28.2	48	19.9	31	12.9	15	6.2	16	6.6	32	13.3	20	8.3	8	3.3	3	1.2	241	100.0

AGIL-CV patient data set

1. General parameters

1.9 Erosive changes

	Erosive changes				Total	
	Yes		No			
	n	%	n	%	n	%
Total	80	46.5	92	53.5	172	100.0

AGIL-CV patient data set

1. General parameters

1.10 Indications for receiving adalimumab therapy

	n	%
Indications for current adalimumab therapy		
Patient base	260	100.0
High disease activity	221	85.0
Lack of effectiveness of previous therapy	171	65.8
Intolerance of previous therapy	77	29.6
Rapid radiologic progression	22	8.5
Other	4	1.5

AGIL-CV patient data set
 1. General parameters
 1.11 Humira therapy
 1.11.1 Dose (mg) at baseline

	Dose				Total	
	40mg each 14 days		Other			
	n	%	n	%	n	%
Total	256	99.6	1	0.4	257	100.0

AGIL-CV patient data set

1. General parameters

1.11 Humira therapy

1.11.2 Exposure (years) of study drug

	Total
N	256
Missing	4
Mean	1.35
SD	1.10
Min	0.0
Median	1.02
Max	4.1

AGIL-CV patient data set

1. General parameters

1.12 Physician global assessment of disease activity

	Total
N	252
Missing	8
Mean	6.3
SD	1.8
Min	0
Median	6.0
Max	10

AGIL-CV patient data set

1. General parameters

1.13 Morning stiffness

1.13.1 Patients with morning stiffness(%)

	Morning stiffness				Total	
	Yes		No			
	n	%	n	%	n	%
Total	208	82.9	43	17.1	251	100.0

AGIL-CV patient data set

1. General parameters

1.13 Morning stiffness

1.13.2 Morning stiffness (minutes)

	Total
N	249
Missing	11
Mean	64.3
SD	73.3
Min	0
Median	45.0
Max	360

AGIL-CV patient data set
 1. General parameters
 1.14 Rheumatic nodules

	Rheumatic nodules				Total	
	Yes		No			
	n	%	n	%	n	%
Total	29	11.5	223	88.5	252	100.0

AGIL-CV patient data set

1. General parameters

1.15 Prior joint surgery

	Prior joint surgery				Total	
	Yes		No			
	n	%	n	%	n	%
Total	58	23.0	194	77.0	252	100.0

AGIL-CV patient data set
 1. General parameters
 1.16 Joint involvement

		M00	M00
Total	N	251	251
	Missing	9	9
	Mean	7.8	4.7
	SD	6.3	4.1
	Min	0	0
	Median	7.0	4.0
	Max	28	25

AGIL-CV patient data set
 1. General parameters
 1.17 Laboratory
 1.17.1 Rheumatic factor

	Rheumatic Factor				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	139	56.5	107	43.5	246	100.0

AGIL-CV patient data set
 1. General parameters
 1.17 Laboratory
 1.17.2 Anti-CCP

	Anti-ccp				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	136	56.9	103	43.1	239	100.0

AGIL-CV patient data set

1. General parameters

1.17 Laboratory

1.17.3 CRP (mg/l)

	Total
N	231
Missing	29
Mean	14.0
SD	34.7
Min	0
Median	6.0
Max	430

AGIL-CV patient data set

1. General parameters

1.17 Laboratory

1.17.4 ESR (mm/h)

1.17.4.1 ESR - total

	Total
N	237
Missing	23
Mean	27.8
SD	22.2
Min	1
Median	23.0
Max	104

AGIL-CV patient data set

1. General parameters

1.17 Laboratory

1.17.4 ESR (mm/h)

1.17.4.2 ESR by gender

	Male	Female
N	69	168
Missing	5	18
Mean	30.7	26.6
SD	26.7	20.0
Min	1	2
Median	21.0	23.5
Max	90	104

AGIL-CV patient data set
1. General parameters
1.17 Laboratory
1.17.5 Hemoglobin (g/dl)

	Total
N	243
Missing	17
Mean	14.0
SD	10.2
Min	8
Median	13.0
Max	143

AGIL-CV patient data set
1. General parameters
1.17 Laboratory
1.17.6 Hepatitis B

	Hepatitis B				Total	
	Yes		No			
	n	%	n	%	n	%
Total	0	0.0	208	100.0	208	100.0

AGIL-CV patient data set
1. General parameters
1.17 Laboratory
1.17.7 Hepatitis C

	Hepatitis C				Total	
	Yes		No			
	n	%	n	%	n	%
Total	0	0.0	206	100.0	206	100.0

AGIL-CV patient data set
 1. General parameters
 1.17 Laboratory
 1.17.8 Latent tuberculosis

	Latent tuberculosis				Total	
	Yes		No			
	n	%	n	%	n	%
Total	9	3.6	243	96.4	252	100.0

AGIL-CV patient data set

1. General parameters

1.18 School leaving certificate

	School leaving certificate								Total	
	Without graduation		Secondary school certificate (Hauptschule)		Secondary school level I certificate (Realschulabschluss - mittlere Reife)		Diploma from German secondary school qualifying for university admission or matriculation (Abitur)			
	n	%	n	%	n	%	n	%	n	%
Total	3	1.2	79	31.2	126	49.8	45	17.8	253	100.0

AGIL-CV patient data set

1. General parameters

1.19 Professional education

	n	%
Professional education		
Patient base	260	100.0
Alternance training (School and on-the-job training)	115	44.2
Off-the-job training	52	20.0
Technical college / Master craftsman training	43	16.5
Semiskilled	17	6.5
University of applied science	16	6.2
None	11	4.2
University	11	4.2

AGIL-CV patient data set

1. General parameters

1.20 Employment

	Employment												Total	
	Full time job (35h and more)		Part-time work		School, education, studying		Home making, child-rearing		Unemployed		Retirement			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	96	37.9	45	17.8	2	0.8	12	4.7	39	15.4	59	23.3	253	100.0

AGIL-CV patient data set

1. General parameters

1.21 Early retirement due to rheumatic disease (only patients in retirement)

	Retirement due to rheumatic disease				Total	
	Yes		No			
	n	%	n	%	n	%
Total	22	44.9	27	55.1	49	100.0

AGIL-CV patient data set

1. General parameters

1.22 Occupational status (only patients with occupation)

	Occupational status								Total	
	Salaried		Civil servant		Leading function		Freelancer			
	n	%	n	%	n	%	n	%	n	%
Total	118	83.7	7	5.0	6	4.3	10	7.1	141	100.0

AGIL-CV patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.1 Household

	Household								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	194	74.6	35	13.5	13	5.0	18	6.9	260	100.0

	Household				Total	
	Yes		No			
	n	%	n	%	n	%
Total	194	84.7	35	15.3	229	100.0

Without not applicable and missings

	Total
N	198
Missing	62
Mean	65.8
SD	65.4
Min	0
Median	40.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

AGIL-CV patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.2 Parenting

	Parenting								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	25	9.6	52	20.0	112	43.1	71	27.3	260	100.0

	Parenting				Total	
	Yes		No			
	n	%	n	%	n	%
Total	25	32.5	52	67.5	77	100.0

Without not applicable and missings

	Total
N	76
Missing	184
Mean	19.1
SD	44.9
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

AGIL-CV patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.3 Education

	Education								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	8	3.1	44	16.9	131	50.4	77	29.6	260	100.0

	Education				Total	
	Yes		No			
	n	%	n	%	n	%
Total	8	15.4	44	84.6	52	100.0

Without not applicable and missings

	Total
N	52
Missing	208
Mean	8.8
SD	35.1
Min	0
Median	0.0
Max	180

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

AGIL-CV patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.4 Recreational (free-time)

	Recreational(free-time)								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	169	65.0	37	14.2	18	6.9	36	13.8	260	100.0

	Recreational(free-time)				Total	
	Yes		No			
	n	%	n	%	n	%
Total	169	82.0	37	18.0	206	100.0

Without not applicable and missings

	Total
N	181
Missing	79
Mean	72.3
SD	70.8
Min	0
Median	40.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

AGIL-CV patient data set

1. General parameters

1.24 Missed work days in the last 6 month

	M00				Total	
	Yes		No			
	n	%	n	%	n	%
Total	89	57.4	66	42.6	155	100.0

Missed work days in the last 6 month (% of patients)

	Total
N	155
Missing	105
Mean	28.5
SD	48.7
Min	0
Median	7.0
Max	182

Number of missed work days in the last 6 month

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.1 Number of visits at the rheumatologist

	Total
N	251
Missing	9
Mean	2.8
SD	1.7
Min	0
Median	2.0
Max	10

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.2 Number of visits at the general practitioner

	Total
N	251
Missing	9
Mean	4.4
SD	5.4
Min	0
Median	3.0
Max	46

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.3 Number of visits at the orthopedic specialist

	Total
N	251
Missing	9
Mean	0.9
SD	1.6
Min	0
Median	0.0
Max	10

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.4 Number of visits at other medical specialists

	Total
N	251
Missing	9
Mean	1.2
SD	1.9
Min	0
Median	0.0
Max	14

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.5 Number of hospitalizations

	Total
N	251
Missing	9
Mean	0.5
SD	1.9
Min	0
Median	0.0
Max	19

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.6 Total duration of hospitalizations (days)

	Total
N	251
Missing	9
Mean	2.2
SD	5.8
Min	0
Median	0.0
Max	40

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.7 Number of convalescent cares, stationary rehabilitations

	Total
N	251
Missing	9
Mean	0.2
SD	1.5
Min	0
Median	0.0
Max	21

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.8 Total duration of convalescent cares, stationary rehabilitations (days)

	Total
N	251
Missing	9
Mean	1.9
SD	6.5
Min	0
Median	0.0
Max	30

AGIL-CV patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.9 Number of physical therapies, for example physiotherapy

	Total
N	251
Missing	9
Mean	3.9
SD	8.8
Min	0
Median	0.0
Max	48

AGIL-CV patient data set
1. General parameters
1.26 Modified WAI

	Total
N	93
Missing	167
Mean	30.5
SD	6.7
Min	14
Median	30.0
Max	46

AGIL-CV patient data set
1. General parameters
1.27 WPAI
1.27.1 Presenteeism (%)

	Total
N	121
Missing	139
Mean	53.7
SD	27.1
Min	0
Median	50.0
Max	100

AGIL-CV patient data set
1. General parameters
1.27 WPAI
1.27.2 Absenteeism (%)

	Total
N	128
Missing	132
Mean	27.1
SD	41.4
Min	0
Median	0.0
Max	100

AGIL-CV patient data set

1. General parameters

1.27 WPAI

1.27.3 Total work productivity impairment (%)

	Total
N	115
Missing	145
Mean	57.9
SD	29.7
Min	0
Median	60.0
Max	100

AGIL-CV patient data set

1. General parameters

1.27 WPAI

1.27.4 Total activity impairment (%)

	Total
N	244
Missing	16
Mean	60.2
SD	23.8
Min	0
Median	60.0
Max	100

AGIL-CV patient data set

1. General parameters

1.28 Patient global assessment of disease activity

	Total
N	246
Missing	14
Mean	6.0
SD	2.5
Min	0
Median	6.0
Max	10

AGIL-CV patient data set

1. General parameters

1.29 Fatigue

	Total
N	246
Missing	14
Mean	6.1
SD	2.7
Min	0
Median	7.0
Max	10

AGIL-CV patient data set
1. General parameters
1.30 Pain

	Total
N	247
Missing	13
Mean	6.4
SD	2.4
Min	0
Median	7.0
Max	10

AGIL-CV patient data set
1. General parameters
1.31 HAQ-DI

	Total
N	247
Missing	13
Mean	1.24
SD	0.74
Min	0.0
Median	1.13
Max	2.9

AGIL-CV patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.1 Mobility

	Mobility						Total	
	No problems		Some problems		Confined to bed			
	n	%	n	%	n	%	n	%
Total	110	43.8	141	56.2	0	0.0	251	100.0

AGIL-CV patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.2 Self-care

	Self-care						Total	
	No problems		Some problems		Unable to wash or dress myself			
	n	%	n	%	n	%	n	%
Total	164	65.3	82	32.7	5	2.0	251	100.0

AGIL-CV patient data set

1. General parameters

1.32 EQ-5D

1.32.3 Usual activities (e.g., work, study, housework, family or leisure activities)

	Usual activities						Total	
	No problems		Some problems		Unable to perform			
	n	%	n	%	n	%	n	%
Total	59	23.6	175	70.0	16	6.4	250	100.0

AGIL-CV patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.4 Pain/discomfort

	Pain/discomfort						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	12	4.8	167	66.5	72	28.7	251	100.0

AGIL-CV patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.5 Anxiety/depression

	Anxiety/depression						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	115	45.8	111	44.2	25	10.0	251	100.0

AGIL-CV patient data set
1. General parameters
1.32 EQ-5D
1.32.6 Mean EQ VAS

	Total
N	251
Missing	9
Mean	50.2
SD	21.3
Min	4
Median	50.0
Max	98

AGIL-CV patient data set
1. General parameters
1.33 DAS28

	Total
N	224
Missing	36
Mean	4.85
SD	1.32
Min	0.9
Median	4.95
Max	8.3

AGIL-CV patient data set
 1. General parameters
 1.34 Participation in Abbott Care

	Participation in Abbott Care service program				Total	
	Yes		No			
	n	%	n	%	n	%
Total	104	49.8	105	50.2	209	100.0

AGIL-CV patient data set
2. Concomitant diseases

	n	%
Previous concomitant diseases		
Patient base	260	100.0
Total	204	78.5
Other disease	123	47.3
Arterial hypertension	98	37.7
Degenerative joint disease	79	30.4
Degenerative spinal disease	42	16.2
Mental illness (e.g. depression)	32	12.3
Osteoporosis	29	11.2
Hyperlipidemia	26	10.0
Diabetes Type II	24	9.2
Chronic obstructive pulmonary disease	21	8.1
Coronary heart disease	11	4.2
Diabetes Type I	9	3.5
Chronic inflammatory disease	8	3.1

AGIL-CV patient data set
 3.Previous and concomitant medication
 3.1 Previous documented DMARDs

	n	%
Previous documented DMARDs		
Patient base	260	100.0
MTX	144	55.4
Leflunomide	136	52.3
Glucocorticoides	94	36.2
NSAID, Coxibe	92	35.4
SASP	62	23.8
Analgesics	61	23.5
Other	33	12.7

AGIL-CV patient data set
 3.Previous and concomitant medication
 3.2 Documented DMARDs at baseline

	n	%
Documented DMARDs at baseline		
Patient base	260	100.0
Glucocorticoides	176	67.7
MTX	151	58.1
NSAID, Coxibe	56	21.5
Analgesics	26	10.0
Leflunomide	21	8.1
Other	12	4.6
SASP	7	2.7

AGIL-CV patient data set

3.Previous and concomitant medication

3.3 Documented DMARDs during study, baseline included

	n	%
Concomitant DMARDs		
Total	246	94.6
Glucocorticoids	191	73.5
MTX	162	62.3
NSAIDs, Coxibe	66	25.4
Analgesics	30	11.5
Other	27	10.4
Leflunomide	24	9.2
SASP	8	3.1

AGIL-CV patient data set

3.Previous and concomitant medication

3.4 Glucocorticoid dosage at baseline and maximum dosage during study

		Glucocorticode dosage at baseline mg/d	Maximum Glucocorticode dosage during study mg/d
Total	N	175	190
	Missing	85	70
	Mean	7.7	9.1
	SD	5.3	7.9
	Min	1	1
	Median	5.0	7.5
	Max	40	60

AGIL-CV patient data set

3.Previous and concomitant medication

3.5 MTX dosage at baseline and maximum dosage during study

		MTX dosage at baseline mg/w	Maximum MTX dosage during study mg/w
Total	N	151	162
	Missing	109	98
	Mean	15.1	15.2
	SD	5.8	5.9
	Min	3	3
	Median	15.0	15.0
	Max	28	28

AGIL-CV patient data set
 3.Previous and concomitant medication
 3.6 Previous biologic therapies
 3.6.1 Percentage previous biologics

	n	%
Documented previous biologics at baseline		
Patient base	260	100.0
Etanercept	32	12.3
Certolizumab	17	6.5
Other	8	3.1
Tocilizumab	8	3.1
Abatacept	4	1.5
Golimumab	4	1.5
Rituximab	3	1.2
Infliximab	2	0.8

AGIL-CV patient data set

3.Previous and concomitant medication

3.6 Previous biologic therapies

3.6.2 Mean duration of previous biologics (month)

		Infliximab	Etanercept	Golimumab	Certolizumab	Abatacept	Rituximab	Tocilizumab
Total	N	2	31	4	17	4	3	8
	Missing	258	229	256	243	256	257	252
	Mean	13.0	33.4	14.8	8.2	10.0	13.0	25.6
	SD	0.0	40.1	17.6	5.5	7.4	6.6	23.0
	Min	13	1	4	3	5	7	3
	Median	13.0	14.0	7.0	7.0	7.0	12.0	19.5
	Max	13	140	41	19	21	20	62

AGIL-CV patient data set
 3.Previous and concomitant medication
 3.7 Number of previous biologics

	Number of previous biologics						Total	
	0		1		>=2			
	n	%	n	%	n	%	n	%
Total	195	75.0	53	20.4	12	4.6	260	100.0

AGIL-CV patient data set

3.Previous and concomitant medication

3.8 Main reasons for discontinuing the previous biologic therapy

	Reason for discontinuing the previous biologic therapy						Total	
	Lack of effectiveness		Lack of tolerance		Other reason			
	n	%	n	%	n	%	n	%
Total	47	77.0	10	16.4	4	6.6	61	100.0

AGIL-CV patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.1 Withdrawal reasons by visit

		Visit									
		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	Withdrawal										
Patients in AGIL CV - substudy	Adverse drug reaction	10	4.1	3	1.5	2	1.3	3	3.1	0	0.0
	Lack of effectiveness	18	7.4	19	9.8	16	10.5	11	11.2	1	2.1
	Other reason	8	3.3	5	2.6	7	4.6	10	10.2	9	19.1
	Unknown Reason	0	0.0	1	0.5	0	0.0	0	0.0	1	2.1
	Ongoing patients at the end of visit	206	85.1	166	85.6	127	83.6	74	75.5	36	76.6
	Total	242	100.0	194	100.0	152	100.0	98	100.0	47	100.0

This table is based on the attended visits and the withdrawal reasons documented on final visit
There are no multiple answers in this table. It was asked for the most important reason.

AGIL-CV patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.2 Disposition of patients (cumulated withdrawal rates)

		Visit									
		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	Withdrawal										
Patients in AGIL CV - substudy	Adverse drug reaction	10	3.8	13	5.0	15	5.8	18	6.9	18	6.9
	Lack of effectiveness	18	6.9	37	14.2	53	20.4	64	24.6	65	25.0
	Other reason	8	3.1	13	5.0	20	7.7	30	11.5	39	15.0
	Unknown Reason	0	0.0	1	0.4	1	0.4	1	0.4	2	0.8
	Lost to follow up (cumulated)	10	3.8	22	8.5	40	15.4	65	25.0	92	35.4
	Ongoing patients at the end of visit	206	79.2	166	63.8	127	48.8	74	28.5	36	13.8
	Single visit missing (a later visit is following)	8	3.1	8	3.1	4	1.5	8	3.1	8	3.1
	Total	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0

This table is based on the attended visits and the withdrawal reasons documented on final visit
There are no multiple answers in this table. It was asked for the most important reason.

AGIL-CV patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.3 Disposition of patients (shortened)

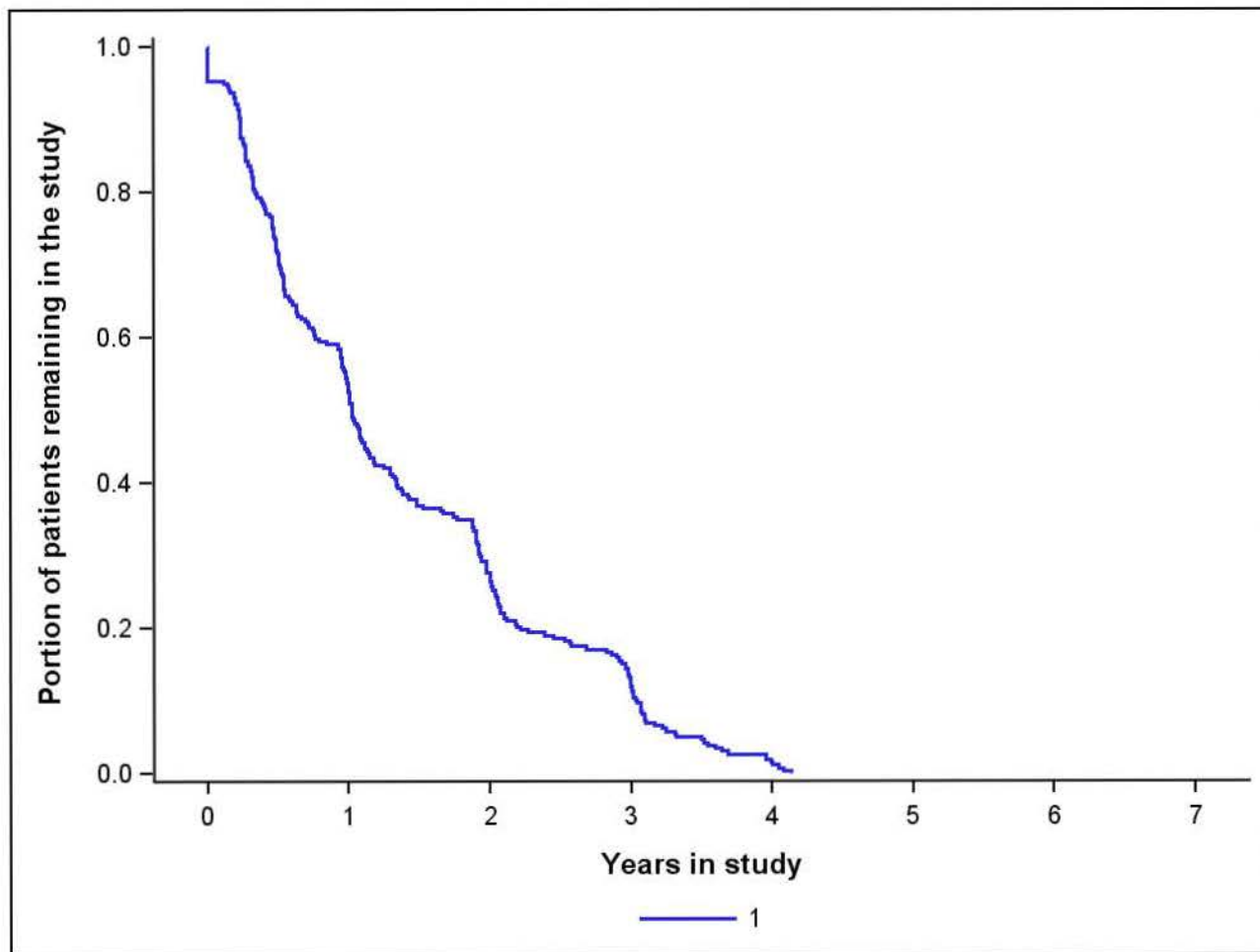
		Visit									
		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	Withdrawal										
Patients in AGIL CV - substudy	Cummulative documented withdrawals	36	13.8	64	24.6	89	34.2	113	43.5	124	47.7
	Ongoing patients at the end of visit	206	79.2	166	63.8	127	48.8	74	28.5	36	13.8
	Single visit missing (a later visit is following)	8	3.1	8	3.1	4	1.5	8	3.1	8	3.1
	Lost to follow up (cummulated)	10	3.8	22	8.5	40	15.4	65	25.0	92	35.4
	Total	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0

This table is based on the attended visits and the withdrawal reasons documented on final visit
 Withdrawal reasons are cumulated, ongoing patients and single visit missing are not cumulated

AGIL-CV patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.4 Total duration of study (Kaplan-Meier, computed by visit dates)



AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.1 Abdominal girth (cm)

	Total
N	237
Missing	23
Mean	96.3
SD	15.5
Min	62
Median	96.0
Max	145

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.2 Hip circumference (cm)

	Total
N	237
Missing	23
Mean	107.2
SD	12.7
Min	80
Median	106.0
Max	160

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.3 Weight (kg)

5.1.3.1 Weight - total

	Total
N	248
Missing	12
Mean	78.6
SD	17.2
Min	43
Median	77.0
Max	125

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.3 Weight (kg)

5.1.3.2 Weight by gender

	Male	Female
N	71	177
Missing	3	9
Mean	88.9	74.5
SD	14.8	16.4
Min	60	43
Median	87.0	72.0
Max	122	125

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.4 BMI (kg/m²)

5.1.4.1 BMI - total

	Total
N	246
Missing	14
Mean	27.5
SD	5.4
Min	17
Median	26.8
Max	46

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.4 BMI (kg/m²)

5.1.4.2 BMI by gender

	Male	Female
N	71	175
Missing	3	11
Mean	28.0	27.4
SD	4.5	5.8
Min	20	17
Median	27.4	26.5
Max	40	46

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.5 Vital signs

5.1.5.1 Systolic blood pressure (mmHg)

	Total
N	253
Missing	7
Mean	132.4
SD	18.1
Min	90
Median	130.0
Max	215

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.5 Vital signs

5.1.5.2 Diastolic blood pressure (mmHg)

	Total
N	253
Missing	7
Mean	83.5
SD	11.0
Min	57
Median	81.0
Max	140

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.5 Vital signs

5.1.5.3 Pulse (beats/min)

	Total
N	245
Missing	15
Mean	73.7
SD	10.5
Min	49
Median	72.0
Max	106

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.6 Alcohol consumption

5.1.6.1 Overall alcohol consumption

	Alcohol consumption				Total	
	Yes		No			
	n	%	n	%	n	%
Total	69	27.3	184	72.7	253	100.0

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.6 Alcohol consumption

5.1.6.2 Units per week (only patients with alcohol consumption)

	Total
N	65
Missing	4
Mean	4.5
SD	5.2
Min	1
Median	2.0
Max	28

AGIL-CV patient data set
 5. AGIL-CV
 5.1 Additional general parameters
 5.1.7 Family history
 5.1.7.1 Parent with diabetes mellitus

	Parent with diabetes mellitus				Total	
	Yes		No			
	n	%	n	%	n	%
Total	67	27.3	178	72.7	245	100.0

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.7 Family history

5.1.7.2 Parent with obesity

	Parent with obesity				Total	
	Yes		No			
	n	%	n	%	n	%
Total	53	21.8	190	78.2	243	100.0

AGIL-CV patient data set

5. AGIL-CV

5.1 Additional general parameters

5.1.7 Family history

5.1.7.3 Parent with heart attack before the age of 60

	Parent with heart attack before the age of 60				Total	
	Yes		No			
	n	%	n	%	n	%
Total	38	15.6	205	84.4	243	100.0

AGIL-CV patient data set

5. AGIL-CV

5.2 Cardiovascular events

5.2.1 Myocardial infarction - new events by visit

		Visit											
		M00		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	New myocardial infarctions												
Patients in AGIL CV - substudy	Yes	6	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	245	97.6	234	100.0	188	100.0	147	100.0	89	100.0	45	100.0
	Total	251	100.0	234	100.0	188	100.0	147	100.0	89	100.0	45	100.0

AGIL-CV patient data set

5. AGIL-CV

5.2 Cardiovascular events

5.2.2 Patients with ever reported myocardial infarction

		Visit											
		M00		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	Patients with myocardial infarction												
Patients in AGIL CV - substudy	Yes	6	2.3	6	2.3	6	2.3	6	2.3	6	2.3	6	2.3
	No	254	97.7	254	97.7	254	97.7	254	97.7	254	97.7	254	97.7
	Total	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0

AGIL-CV patient data set
 5. AGIL-CV
 5.2 Cardiovascular events
 5.2.3 Stroke - new events by visit

		Visit											
		M00		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	New stroke												
Patients in AGIL CV - substudy	Yes	9	3.6	0	0.0	1	0.5	0	0.0	1	1.1	1	2.2
	No	242	96.4	234	100.0	187	99.5	147	100.0	88	98.9	44	97.8
	Total	251	100.0	234	100.0	188	100.0	147	100.0	89	100.0	45	100.0

AGIL-CV patient data set
 5. AGIL-CV
 5.2 Cardiovascular events
 5.2.4 Patients with ever reported stroke

		Visit											
		M00		M03		M06		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
Patients in AGIL-CV	Patients with stroke												
Patients in AGIL CV - substudy	Yes	9	3.5	9	3.5	10	3.8	10	3.8	11	4.2	12	4.6
	No	251	96.5	251	96.5	250	96.2	250	96.2	249	95.8	248	95.4
	Total	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0	260	100.0

AGIL-CV patient data set
 5. AGIL-CV
 5.3 Laboratory
 5.3.1 Fasting glucose (mg/dl)

	Total
N	137
Missing	123
Mean	94.9
SD	37.3
Min	5
Median	91.0
Max	293

Absolute values as documented

	Total
N	137
Missing	123
Mean	96.9
SD	34.8
Min	27
Median	91.9
Max	293

Absolute values - values < 20 were multiplied with 18.018 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set
 5. AGIL-CV
 5.3 Laboratory
 5.3.2 Fasting tryglycerides

Absolute values as documented	Total
N	183
Missing	77
Mean	135.3
SD	86.1
Min	1
Median	114.0
Max	463

Absolute values as documented

	Total
N	183
Missing	77
Mean	139.4
SD	83.1
Min	18
Median	115.0
Max	463

Absolute values - values < 30 were multiplied with 88.496 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set
 5. AGIL-CV
 5.3 Laboratory
 5.3.3 Fasting LDL

	Total
N	191
Missing	69
Mean	134.9
SD	49.9
Min	3
Median	132.0
Max	271

Absolute values as documented

	Total
N	191
Missing	69
Mean	138.8
SD	44.4
Min	41
Median	133.0
Max	271

Absolute values - values < 16 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set
 5. AGIL-CV
 5.3 Laboratory
 5.3.4 Fasting HDL

	Total
N	194
Missing	66
Mean	61.2
SD	29.3
Min	1
Median	58.9
Max	262

Absolute values as documented

	Total
N	194
Missing	66
Mean	63.6
SD	27.3
Min	23
Median	60.0
Max	262

Absolute values - values < 18 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set
 5. AGIL-CV
 5.3 Laboratory
 5.3.5 Fasting total cholesterol

	Total
N	203
Missing	57
Mean	213.4
SD	63.1
Min	4
Median	214.0
Max	370

Absolute values as documented

	Total
N	203
Missing	57
Mean	223.0
SD	60.4
Min	60
Median	215.0
Max	701

Absolute values - values < 20 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set
5. AGIL-CV
5.3 Laboratory
5.3.6 CRP

	Total
N	231
Missing	29
Mean	14.0
SD	34.7
Min	0
Median	6.0
Max	430

Absolute values as documented

AGIL-CV patient data set

5. AGIL-CV

5.4 Concomitant symptoms to rheumatoid arthritis at baseline

	n	%
Concomitant symptoms to rheumatoid arthritis		
Patient base	260	100.0
None of in the CRF mentioned extraarticular manifestations	252	96.9
Missing information	5	1.9
Glomerulonephritis	1	0.4
Polyneuropathy	1	0.4
Pronounced cutane vasculitis	1	0.4
Scleritis	1	0.4

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.1 Abdominal girth (cm)

6.1.1.1 Abdominal girth (cm) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	237	212	174	134	84	41
	Missing	23	48	86	126	176	219
	Mean	96.3	96.1	96.1	97.2	98.3	101.9
	SD	15.5	16.0	15.8	15.8	18.9	14.8
	Min	62	62	62	66	43	68
	Median	96.0	96.0	96.0	97.5	99.0	104.0
	Max	145	166	150	132	173	130

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.1 Abdominal girth (cm)

6.1.1.2 Abdominal girth (cm) - differences

		M03-M00	M06-M00	M12-M00	M24-M00	M36-M00
Total	N	198	165	126	79	38
	Missing	62	95	134	181	222
	Mean	0.6	0.7	1.6	1.2	3.7
	SD	7.7	6.0	6.4	11.6	7.8
	Min	-26	-27	-23	-42	-8
	Median	0.0	0.0	1.0	0.0	1.0
	Max	84	25	26	73	28

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.2 Hip circumference (cm)

6.1.2.1 Hip circumference (cm) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	237	211	173	134	84	41
	Missing	23	49	87	126	176	219
	Mean	107.2	106.9	107.8	107.9	108.5	109.1
	SD	12.7	12.1	13.2	13.0	14.3	16.4
	Min	80	82	82	73	84	70
	Median	106.0	106.0	105.0	105.5	106.0	109.0
	Max	160	144	165	144	146	144

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.2 Hip circumference (cm)

6.1.2.2 Hip circumference (cm) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	197	164	126	79	38
	Missing	63	96	134	181	222
	Mean	0.0	1.2	1.1	0.2	0.3
	SD	6.6	9.0	8.0	7.2	8.0
	Min	-71	-74	-62	-21	-26
	Median	0.0	0.0	0.0	0.0	0.5
	Max	27	60	30	29	15

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.3 Weight (kg)

6.1.3.1 Weight (kg) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	248	223	181	143	86	42
	Missing	12	37	79	117	174	218
	Mean	78.6	79.0	78.6	79.2	80.6	82.1
	SD	17.2	17.2	17.3	18.0	19.1	19.3
	Min	43	44	46	44	48	56
	Median	77.0	77.0	77.0	78.0	78.0	80.5
	Max	125	130	133	135	133	134

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.3 Weight (kg)

6.1.3.2 Weight (kg) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	212	172	135	80	41
	Missing	48	88	125	180	219
	Mean	0.2	0.3	0.9	-0.1	1.0
	SD	3.3	3.5	4.5	5.9	5.2
	Min	-17	-17	-17	-35	-16
	Median	0.0	0.0	1.0	0.0	1.0
	Max	12	12	19	13	13

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.4 BMI (kg/m²)

6.1.4.1 BMI (kg/m²) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	246	210	170	134	80	41
	Missing	14	50	90	126	180	219
	Mean	27.5	27.5	27.4	27.7	27.9	27.8
	SD	5.4	5.3	5.4	5.5	5.8	5.8
	Min	17	18	19	19	17	19
	Median	26.8	26.8	26.9	27.1	27.0	26.7
	Max	46	46	46	45	47	49

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.4 BMI (kg/m²)

6.1.4.2 BMI (kg/m²) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	210	170	134	80	41
	Missing	50	90	126	180	219
	Mean	0.1	0.1	0.3	-0.0	0.3
	SD	1.2	1.2	1.6	2.1	1.8
	Min	-6	-6	-6	-13	-5
	Median	0.0	0.0	0.3	0.0	0.4
	Max	4	4	7	5	5

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.1 Systolic blood pressure (mmHg)

6.1.5.1.1 Systolic blood pressure (mmHg) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	253	218	181	139	84	41
	Missing	7	42	79	121	176	219
	Mean	132.4	131.8	131.6	129.8	130.7	130.4
	SD	18.1	17.4	18.3	15.5	13.7	11.9
	Min	90	80	90	80	100	97
	Median	130.0	130.0	130.0	130.0	130.0	130.0
	Max	215	217	215	187	179	158

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.1 Systolic blood pressure (mmHg)

6.1.5.1.2 Systolic blood pressure (mmHg) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	211	176	134	81	40
	Missing	49	84	126	179	220
	Mean	-0.6	-0.4	-1.7	-1.3	2.4
	SD	15.0	18.0	16.5	16.7	15.4
	Min	-63	-59	-50	-50	-20
	Median	0.0	0.0	-1.0	0.0	-0.5
	Max	48	70	46	48	39

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.1 Systolic blood pressure (mmHg)

6.1.5.1.3 Systolic blood pressure (mmHg) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	48	45	45	46	35	19
	Missing	1	4	4	3	14	30
	Mean	131.2	129.7	128.2	125.7	129.3	130.4
	SD	13.1	12.1	15.2	12.7	13.3	13.8
	Min	110	110	100	94	107	97
	Median	130.0	130.0	130.0	125.0	130.0	130.0
	Max	167	162	194	152	168	158
Moderate response	N	26	23	21	24	17	10
	Missing	0	3	5	2	9	16
	Mean	138.8	135.3	129.0	133.1	136.1	137.2
	SD	15.7	17.1	11.7	16.2	11.8	10.4
	Min	108	98	108	109	115	120
	Median	135.0	132.0	130.0	131.5	135.0	139.0
	Max	170	170	146	172	160	151

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.1 Systolic blood pressure (mmHg)

6.1.5.1.3 Systolic blood pressure (mmHg) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	32	29	29	29	9	2
	Missing	0	3	3	3	23	30
	Mean	131.7	129.9	130.1	132.7	127.0	125.5
	SD	15.3	13.0	15.1	12.2	14.9	3.5
	Min	100	110	103	110	110	123
	Median	130.0	130.0	128.0	130.0	123.0	125.5
	Max	162	155	160	165	154	128

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.1 Systolic blood pressure (mmHg)

6.1.5.1.4 Systolic blood pressure (mmHg) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement >= 1.8 at M12							
Yes	N	52	48	47	49	41	22
	Missing	1	5	6	4	12	31
	Mean	134.0	130.4	128.1	128.6	131.1	132.2
	SD	14.4	13.3	15.1	14.8	13.3	13.9
	Min	110	98	100	94	107	97
	Median	130.0	130.0	129.0	128.0	132.0	134.0
	Max	170	162	194	172	168	158
No	N	54	49	48	50	20	9
	Missing	0	5	6	4	34	45
	Mean	132.4	131.8	129.8	130.5	130.3	132.4
	SD	15.0	14.3	13.7	12.8	13.7	9.6
	Min	100	110	103	100	110	121
	Median	130.0	130.0	130.0	130.0	129.0	130.0
	Max	170	170	160	165	160	147

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.2 Diastolic blood pressure (mmHg)

6.1.5.2.1 Diastolic blood pressure (mmHg) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	253	217	181	139	84	41
	Missing	7	43	79	121	176	219
	Mean	83.5	82.0	81.7	80.6	81.3	79.9
	SD	11.0	10.9	10.5	9.4	9.3	7.6
	Min	57	60	51	60	60	67
	Median	81.0	80.0	80.0	80.0	80.0	80.0
	Max	140	134	113	104	115	101

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.2 Diastolic blood pressure (mmHg)

6.1.5.2.2 Diastolic blood pressure (mmHg) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	210	176	134	81	40
	Missing	50	84	126	179	220
	Mean	-1.1	-0.9	-2.5	-1.6	-3.2
	SD	10.0	10.0	10.2	11.1	9.0
	Min	-26	-25	-36	-35	-30
	Median	0.0	0.0	0.0	0.0	-5.0
	Max	48	30	27	30	18

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.2 Diastolic blood pressure (mmHg)

6.1.5.2.3 Diastolic blood pressure (mmHg) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	48	45	45	46	35	19
	Missing	1	4	4	3	14	30
	Mean	83.1	81.3	81.6	80.0	82.0	80.9
	SD	8.6	8.0	7.7	8.5	8.5	9.7
	Min	70	60	60	64	70	67
	Median	80.0	80.0	83.0	80.0	80.0	80.0
	Max	108	99	105	103	112	101
Moderate response	N	26	23	21	24	17	10
	Missing	0	3	5	2	9	16
	Mean	85.3	85.7	84.0	82.5	83.3	80.1
	SD	6.0	15.4	11.3	9.4	12.3	4.8
	Min	77	62	70	67	65	74
	Median	85.0	84.0	82.0	80.0	80.0	79.0
	Max	102	134	113	102	115	90

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.2 Diastolic blood pressure (mmHg)

6.1.5.2.3 Diastolic blood pressure (mmHg) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	32	29	29	29	9	2
	Missing	0	3	3	3	23	30
	Mean	83.6	80.8	80.0	81.3	78.9	75.0
	SD	11.5	10.7	10.0	9.9	9.4	2.8
	Min	63	65	65	63	60	73
	Median	82.0	80.0	78.0	80.0	80.0	75.0
	Max	115	103	102	103	96	77

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.2 Diastolic blood pressure (mmHg)

6.1.5.2.4 Diastolic blood pressure (mmHg) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement >= 1.8 at M12							
Yes	N	52	48	47	49	41	22
	Missing	1	5	6	4	12	31
	Mean	84.0	81.9	82.0	81.5	81.6	81.2
	SD	8.2	9.0	8.3	9.0	7.7	8.9
	Min	70	60	60	64	70	67
	Median	80.0	80.0	83.0	80.0	80.0	80.0
	Max	108	105	105	103	103	101
No	N	54	49	48	50	20	9
	Missing	0	5	6	4	34	45
	Mean	83.6	82.5	81.3	80.4	82.6	78.0
	SD	9.8	12.7	10.3	9.2	13.2	5.8
	Min	63	65	65	63	60	70
	Median	82.5	80.0	80.0	80.0	80.0	78.0
	Max	115	134	113	103	115	90

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.3 Pulse (beats/min)

6.1.5.3.1 Pulse (beats/min) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	245	212	174	132	83	41
	Missing	15	48	86	128	177	219
	Mean	73.7	73.2	74.8	73.0	73.9	73.5
	SD	10.5	10.7	11.4	9.2	8.8	10.9
	Min	49	50	47	48	60	55
	Median	72.0	72.0	74.5	72.0	72.0	72.0
	Max	106	110	131	100	98	103

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.3 Pulse (beats/min)

6.1.5.3.2 Pulse (beats/min) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	202	168	125	79	39
	Missing	58	92	135	181	221
	Mean	-0.3	0.5	-0.3	0.7	-1.4
	SD	10.0	10.3	11.4	9.1	11.0
	Min	-30	-42	-42	-28	-27
	Median	0.0	0.0	0.0	0.0	-2.0
	Max	42	47	28	23	17

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.3 Pulse (beats/min)

6.1.5.3.3 Pulse (beats/min) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	48	44	44	45	35	19
	Missing	1	5	5	4	14	30
	Mean	74.2	70.9	74.9	74.1	74.5	74.4
	SD	9.9	9.2	10.8	10.6	9.0	13.2
	Min	55	51	56	55	60	56
	Median	72.0	72.0	73.0	74.0	72.0	72.0
	Max	99	92	96	100	98	103
Moderate response	N	26	23	21	24	17	10
	Missing	0	3	5	2	9	16
	Mean	75.4	75.0	72.2	73.2	72.8	71.3
	SD	10.1	11.0	9.0	8.7	9.8	10.0
	Min	58	52	56	57	61	55
	Median	77.0	76.0	75.0	72.0	70.0	70.5
	Max	99	109	86	88	87	87

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.3 Pulse (beats/min)

6.1.5.3.3 Pulse (beats/min) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	29	26	25	26	9	2
	Missing	3	6	7	6	23	30
	Mean	72.9	73.3	72.5	71.4	73.0	78.0
	SD	13.2	10.6	11.8	9.8	9.3	1.4
	Min	49	50	47	48	60	77
	Median	72.0	74.0	71.0	72.0	72.0	78.0
	Max	106	95	100	88	88	79

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.5 Vital signs

6.1.5.3 Pulse (beats/min)

6.1.5.3.4 Pulse (beats/min) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement >= 1.8 at M12							
Yes	N	52	47	46	48	41	22
	Missing	1	6	7	5	12	31
	Mean	75.2	72.3	74.5	74.3	74.5	74.7
	SD	10.0	9.3	10.6	10.2	9.4	12.8
	Min	56	51	56	55	60	56
	Median	73.5	72.0	73.5	75.0	72.0	71.0
	Max	99	92	96	100	98	103
No	N	51	46	44	47	20	9
	Missing	3	8	10	7	34	45
	Mean	73.0	72.9	72.6	71.9	72.3	70.9
	SD	11.7	11.0	10.9	9.5	8.7	8.8
	Min	49	50	47	48	60	55
	Median	72.0	73.5	73.5	72.0	71.0	74.0
	Max	106	109	100	90	88	80

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.6 Smoking

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Smoking												
Total	Yes	73	29.9	61	26.2	54	28.7	43	29.3	29	32.6	14	31.1
	No	171	70.1	172	73.8	134	71.3	104	70.7	60	67.4	31	68.9
	Total	244	100.0	233	100.0	188	100.0	147	100.0	89	100.0	45	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.7 Alcohol consumption

6.1.7.1 Overall alcohol consumption

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Smoking												
Total	Yes	69	27.3	45	19.3	39	20.7	29	19.7	25	28.1	10	22.2
	No	184	72.7	188	80.7	149	79.3	118	80.3	64	71.9	35	77.8
	Total	253	100.0	233	100.0	188	100.0	147	100.0	89	100.0	45	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.1 Additional general parameters

6.1.7 Alcohol consumption

6.1.7.2 Units per week

		M00	M03	M06	M12	M24	M36
Total	N	65	45	38	28	25	10
	Missing	195	215	222	232	235	250
	Mean	4.5	4.9	4.1	4.5	4.2	4.2
	SD	5.2	6.7	5.4	5.3	4.9	3.8
	Min	1	1	1	1	1	1
	Median	2.0	2.0	2.0	2.0	2.0	2.0
	Max	28	28	28	21	20	11

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.1 Fasting glucose (mg/dl)

6.2.1.1 Fasting glucose (mg/dl) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	137	127	101	79	45	17
	Missing	123	133	159	181	215	243
	Mean	94.9	89.6	101.4	93.6	94.7	99.9
	SD	37.3	27.4	41.0	19.1	27.4	34.9
	Min	5	5	54	61	6	59
	Median	91.0	87.0	90.1	90.0	91.0	96.0
	Max	293	196	405	153	162	185

Absolute values - as documented

		M00	M03	M06	M12	M24	M36
Total	N	137	127	101	79	45	17
	Missing	123	133	159	181	215	243
	Mean	96.9	93.9	101.4	93.6	97.0	99.9
	SD	34.8	28.2	41.0	19.1	23.9	34.9
	Min	27	20	54	61	64	59
	Median	91.9	88.3	90.1	90.0	92.0	96.0
	Max	293	270	405	153	162	185

Absolute values - values < 20 were multiplied with 18.018 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.1 Fasting glucose (mg/dl)

6.2.1.2 Fasting glucose (mg/dl) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	94	78	61	36	15
	Missing	166	182	199	224	245
	Mean	-4.4	1.1	-7.0	-0.3	1.0
	SD	29.3	32.8	26.8	30.4	41.0
	Min	-89	-106	-99	-106	-90
	Median	-2.0	0.0	-4.0	1.5	-7.0
	Max	101	88	57	76	55

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.1 Fasting glucose (mg/dl)

6.2.1.3 Fasting glucose (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	33	29	27	28	18	9
	Missing	16	20	22	21	31	40
	Mean	91.5	93.4	91.3	91.1	90.1	99.6
	SD	19.6	25.3	19.0	19.6	20.7	35.0
	Min	49	64	61	61	64	66
	Median	88.0	90.0	87.0	90.5	87.5	93.0
	Max	149	189	156	151	145	185
Moderate response	N	12	12	8	12	8	3
	Missing	14	14	18	14	18	23
	Mean	110.2	99.8	110.4	94.7	97.4	77.2
	SD	48.6	34.6	44.3	23.0	16.8	23.6
	Min	73	71	64	71	76	59
	Median	92.4	88.0	99.5	91.0	95.3	68.0
	Max	225	196	191	153	120	104

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.1 Fasting glucose (mg/dl)

6.2.1.3 Fasting glucose (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	17	20	17	19	8	1
	Missing	15	12	15	13	24	31
	Mean	99.7	91.3	92.3	97.5	98.5	102.0
	SD	24.2	13.0	21.6	17.6	31.2	.
	Min	66	74	57	73	71	102
	Median	94.6	88.3	90.0	90.0	94.5	102.0
	Max	163	122	149	139	162	102

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.1 Fasting glucose (mg/dl)

6.2.1.4 Fasting glucose (mg/dl) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement >= 1.8 at M12							
Yes	N	33	30	27	32	20	11
	Missing	20	23	26	21	33	42
	Mean	93.8	93.9	91.6	91.5	91.1	96.3
	SD	26.1	24.9	20.9	19.5	20.6	33.6
	Min	49	64	61	61	64	59
	Median	89.0	89.1	87.0	91.5	88.0	93.0
	Max	194	189	156	151	145	185
No	N	29	31	25	27	14	2
	Missing	25	23	29	27	40	52
	Mean	101.4	94.0	97.8	96.8	97.6	85.0
	SD	31.7	23.7	29.7	19.6	25.2	24.0
	Min	66	68	57	73	71	68
	Median	92.0	88.6	90.0	90.0	94.5	85.0
	Max	225	196	191	153	162	102

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.2 Fasting tryglicerides (mg/dl)

6.2.2.1 Fasting tryglicerides (mg/dl) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	183	130	115	88	57	23
	Missing	77	130	145	172	203	237
	Mean	135.3	134.0	132.2	141.1	126.4	144.0
	SD	86.1	86.9	81.9	93.8	63.2	71.1
	Min	1	1	27	16	23	44
	Median	114.0	118.5	111.0	123.5	111.0	141.0
	Max	463	519	515	751	333	319

Absolute values - as documented

		M00	M03	M06	M12	M24	M36
Total	N	183	130	115	88	57	23
	Missing	77	130	145	172	203	237
	Mean	139.4	137.8	132.2	141.1	126.4	144.0
	SD	83.1	84.3	81.9	93.8	63.2	71.1
	Min	18	14	27	16	23	44
	Median	115.0	119.5	111.0	123.5	111.0	141.0
	Max	463	519	515	751	333	319

Absolute values - values < 14 were multiplied with 88.496 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.2 Fasting tryglicerides (mg/dl)

6.2.2.2 Fasting tryglicerides (mg/dl) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	97	90	68	45	17
	Missing	163	170	192	215	243
	Mean	-5.3	3.3	16.3	-2.6	-2.9
	SD	67.4	60.1	82.3	81.3	101.8
	Min	-339	-217	-247	-390	-317
	Median	0.0	0.0	10.0	1.0	14.0
	Max	213	176	358	150	176

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.2 Fasting tryglicerides (mg/dl)

6.2.2.3 Fasting tryglicerides (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	36	29	30	31	25	10
	Missing	13	20	19	18	24	39
	Mean	135.4	123.8	130.2	142.4	114.1	127.7
	SD	89.2	66.7	75.8	81.7	58.4	68.4
	Min	19	35	34	47	23	44
	Median	112.0	118.0	108.0	115.0	99.0	123.5
	Max	463	309	368	309	263	240
Moderate response	N	18	13	10	17	10	5
	Missing	8	13	16	9	16	21
	Mean	152.5	159.0	112.4	189.5	159.6	154.6
	SD	99.3	117.1	39.9	156.4	54.9	31.7
	Min	57	68	42	80	85	109
	Median	109.5	128.0	126.5	150.0	146.5	157.0
	Max	393	519	157	751	284	191

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.2 Fasting tryglicerides (mg/dl)

6.2.2.3 Fasting tryglicerides (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	21	20	21	19	9	3
	Missing	11	12	11	13	23	29
	Mean	124.3	138.2	132.9	115.9	133.7	142.0
	SD	75.5	59.8	60.6	51.6	77.8	118.8
	Min	18	14	27	16	79	67
	Median	105.0	132.5	123.9	120.0	106.0	80.0
	Max	336	226	277	227	333	279

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.2 Fasting tryglicerides (mg/dl)

6.2.2.4 Fasting tryglicerides (mg/dl) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement ≥ 1.8 at M12							
Yes	N	39	29	30	34	27	12
	Missing	14	24	23	19	26	41
	Mean	145.1	142.3	133.0	168.8	125.6	141.1
	SD	94.6	96.5	73.0	126.6	55.0	58.9
	Min	19	35	53	52	52	44
	Median	114.0	120.0	112.5	135.0	113.0	151.5
	Max	463	519	368	751	263	240
No	N	36	33	31	33	17	6
	Missing	18	21	23	21	37	48
	Mean	127.0	130.1	123.6	124.2	133.0	130.5
	SD	79.5	57.4	58.3	63.1	76.4	87.4
	Min	18	14	27	16	23	57
	Median	103.0	123.0	123.9	120.0	119.0	94.5
	Max	374	226	277	317	333	279

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.3 Fasting LDL (mg/dl)

6.2.3.1 Fasting LDL (mg/dl) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	191	134	116	88	55	25
	Missing	69	126	144	172	205	235
	Mean	134.9	130.6	137.7	135.1	134.5	146.2
	SD	49.9	46.8	45.5	38.1	44.6	58.9
	Min	3	3	27	40	5	78
	Median	132.0	131.0	129.6	134.5	143.0	136.0
	Max	271	277	302	276	273	374

Absolute values - as documented

		M00	M03	M06	M12	M24	M36
Total	N	191	134	116	88	55	25
	Missing	69	126	144	172	205	235
	Mean	138.8	135.9	137.7	135.1	138.0	146.2
	SD	44.4	40.6	45.5	38.1	41.8	58.9
	Min	41	31	27	40	32	78
	Median	133.0	132.2	129.6	134.5	143.0	136.0
	Max	271	277	302	276	273	374

Absolute values - values < 16 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.3 Fasting LDL (mg/dl)

6.2.3.2 Fasting LDL (mg/dl) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	103	93	69	46	18
	Missing	157	167	191	214	242
	Mean	-3.5	-1.4	0.7	5.1	0.9
	SD	39.2	36.4	34.1	40.4	24.5
	Min	-148	-122	-118	-95	-51
	Median	0.0	0.4	0.0	6.2	-0.5
	Max	172	100	94	118	56

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.3 Fasting LDL (mg/dl)

6.2.3.3 Fasting LDL (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	36	29	31	32	25	10
	Missing	13	20	18	17	24	39
	Mean	133.1	128.3	143.0	134.0	133.6	137.8
	SD	47.6	30.6	38.5	35.9	32.5	46.5
	Min	41	51	74	58	78	78
	Median	139.0	131.0	132.0	132.5	139.0	136.5
	Max	234	202	234	214	199	253
Moderate response	N	19	14	11	16	10	6
	Missing	7	12	15	10	16	20
	Mean	132.4	149.1	134.5	151.2	165.4	175.7
	SD	34.8	43.7	38.2	47.1	57.6	100.6
	Min	78	100	61	100	82	96
	Median	123.0	142.0	126.6	143.6	149.1	140.0
	Max	234	261	210	276	273	374

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.3 Fasting LDL (mg/dl)

6.2.3.3 Fasting LDL (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	23	20	21	18	9	3
	Missing	9	12	11	14	23	29
	Mean	137.2	135.0	122.9	126.2	124.8	143.0
	SD	49.0	42.6	37.8	35.2	35.9	31.1
	Min	45	31	27	40	68	109
	Median	135.0	134.7	129.0	137.5	147.0	150.0
	Max	252	234	171	169	159	170

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.3 Fasting LDL (mg/dl)

6.2.3.4 Fasting LDL (mg/dl) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement ≥ 1.8 at M12							
Yes	N	39	30	32	35	27	13
	Missing	14	23	21	18	26	40
	Mean	132.9	132.2	143.0	136.0	138.9	155.2
	SD	44.2	32.1	39.4	36.1	36.3	78.8
	Min	41	51	61	58	78	78
	Median	124.0	137.0	131.5	131.0	143.0	139.0
	Max	234	218	234	226	245	374
No	N	39	33	31	31	17	6
	Missing	15	21	23	23	37	48
	Mean	135.4	137.6	126.3	136.1	139.2	140.5
	SD	45.8	43.0	36.6	43.0	50.5	21.2
	Min	45	31	27	40	68	109
	Median	135.0	137.0	130.0	144.1	147.0	142.0
	Max	252	261	201	276	273	170

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.4 Fasting HDL (mg/dl)

6.2.4.1 Fasting HDL (mg/dl) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	194	139	121	89	56	24
	Missing	66	121	139	171	204	236
	Mean	61.2	63.4	69.3	72.2	64.5	71.5
	SD	29.3	25.1	35.4	61.9	19.5	25.3
	Min	1	1	25	18	32	36
	Median	58.9	62.0	67.0	66.0	62.0	75.0
	Max	262	175	361	519	133	127

Absolute values - as documented

		M00	M03	M06	M12	M24	M36
Total	N	194	139	121	89	56	24
	Missing	66	121	139	171	204	236
	Mean	63.6	65.1	69.3	72.2	64.5	71.5
	SD	27.3	22.8	35.4	61.9	19.5	25.3
	Min	23	25	25	18	32	36
	Median	60.0	63.0	67.0	66.0	62.0	75.0
	Max	262	175	361	519	133	127

Absolute values - values < 18 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.4 Fasting HDL (mg/dl)

6.2.4.2 Fasting HDL (mg/dl) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	109	99	72	48	19
	Missing	151	161	188	212	241
	Mean	2.4	1.9	5.0	-1.9	-7.5
	SD	27.1	27.4	60.8	33.9	46.6
	Min	-213	-194	-174	-191	-191
	Median	2.0	2.0	0.5	0.5	-3.0
	Max	117	132	465	68	32

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.4 Fasting HDL (mg/dl)

6.2.4.3 Fasting HDL (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	36	32	33	32	25	10
	Missing	13	17	16	17	24	39
	Mean	63.0	64.4	67.4	62.8	63.3	75.5
	SD	39.1	26.7	27.8	19.1	16.7	27.6
	Min	23	36	30	18	32	40
	Median	56.2	60.1	66.2	66.0	62.0	76.0
	Max	262	175	186	97	97	127
Moderate response	N	20	14	12	16	10	5
	Missing	6	12	14	10	16	21
	Mean	64.7	71.4	77.5	63.2	70.2	67.2
	SD	18.6	22.3	25.7	18.4	25.9	17.2
	Min	33	32	40	38	45	48
	Median	64.2	69.0	76.5	63.0	60.3	62.3
	Max	104	124	132	100	133	92

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.4 Fasting HDL (mg/dl)

6.2.4.3 Fasting HDL (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	24	21	21	19	9	3
	Missing	8	11	11	13	23	29
	Mean	60.4	65.2	59.0	59.2	64.9	96.3
	SD	19.0	22.8	19.3	17.3	14.6	20.6
	Min	31	25	25	29	33	82
	Median	58.0	63.0	57.0	64.0	63.9	87.0
	Max	114	113	88	89	87	120

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.4 Fasting HDL (mg/dl)

6.2.4.4 Fasting HDL (mg/dl) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement ≥ 1.8 at M12							
Yes	N	40	33	36	35	27	12
	Missing	13	20	17	18	26	41
	Mean	66.0	69.2	72.7	65.0	65.8	75.9
	SD	37.7	28.3	28.7	19.5	16.3	25.6
	Min	23	32	30	18	38	40
	Median	61.6	66.0	70.0	66.0	64.0	76.0
	Max	262	175	186	100	97	127
No	N	40	34	30	32	17	6
	Missing	14	20	24	22	37	48
	Mean	59.3	63.1	59.1	58.5	64.4	78.2
	SD	17.8	20.1	18.8	16.4	22.1	25.6
	Min	31	25	25	29	32	46
	Median	58.0	64.0	58.0	61.5	61.0	79.0
	Max	114	113	91	89	133	120

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.5 Fasting total cholesterol (mg/dl)

6.2.5.1 Fasting total cholesterol (mg/dl) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	203	150	128	92	56	26
	Missing	57	110	132	168	204	234
	Mean	213.4	218.0	220.0	218.2	218.3	229.8
	SD	63.1	63.1	50.6	42.2	49.1	61.7
	Min	4	4	50	76	78	146
	Median	214.0	216.0	215.6	219.0	219.0	222.5
	Max	370	537	387	344	362	446

Absolute values - values < 20 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

		M00	M03	M06	M12	M24	M36
Total	N	203	150	128	92	56	26
	Missing	57	110	132	168	204	234
	Mean	223.0	223.3	220.0	218.2	218.3	229.8
	SD	60.4	52.7	50.6	42.2	49.1	61.7
	Min	60	85	50	76	78	146
	Median	215.0	216.3	215.6	219.0	219.0	222.5
	Max	701	537	387	344	362	446

Absolute values - values < 20 were multiplied with 38.941 (supposing mmol/l -> mg/dl)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.5 Fasting total cholesterol (mg/dl)

6.2.5.2 Fasting total cholesterol (mg/dl) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	122	109	78	50	22
	Missing	138	151	182	210	238
	Mean	4.5	-0.2	7.3	13.0	19.2
	SD	35.6	64.1	37.1	47.7	68.0
	Min	-97	-495	-125	-72	-66
	Median	4.0	7.0	4.0	8.5	13.5
	Max	143	124	124	136	239

Differences

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.5 Fasting total cholesterol (mg/dl)

6.2.5.3 Fasting total cholesterol (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	38	34	35	33	25	11
	Missing	11	15	14	16	24	38
	Mean	207.8	210.8	217.1	209.9	210.6	227.9
	SD	53.8	33.9	50.2	40.5	31.0	80.2
	Min	60	133	50	103	131	146
	Median	206.5	206.0	214.2	212.0	217.0	204.0
	Max	312	300	328	308	260	446
Moderate response	N	21	14	12	17	10	6
	Missing	5	12	14	9	16	20
	Mean	221.7	242.4	226.4	242.7	239.0	239.7
	SD	32.8	51.1	49.7	48.1	80.2	56.5
	Min	175	147	130	176	78	169
	Median	213.0	230.0	222.5	245.0	235.9	237.0
	Max	295	327	312	344	362	317

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.5 Fasting total cholesterol (mg/dl)

6.2.5.3 Fasting total cholesterol (mg/dl) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	23	23	22	17	9	3
	Missing	9	9	10	15	23	29
	Mean	216.0	209.3	205.4	203.4	216.0	256.7
	SD	60.4	44.0	47.2	44.8	50.7	27.5
	Min	85	85	65	76	155	225
	Median	216.0	217.0	208.5	207.0	215.0	270.0
	Max	370	268	271	269	302	275

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.5 Fasting total cholesterol (mg/dl)

6.2.5.4 Fasting total cholesterol (mg/dl) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement ≥ 1.8 at M12							
Yes	N	42	35	37	36	27	14
	Missing	11	18	16	17	26	39
	Mean	214.5	221.1	223.4	219.8	214.8	237.5
	SD	46.0	38.3	51.8	43.2	47.8	74.8
	Min	83	154	50	103	78	156
	Median	209.5	212.0	218.0	219.5	219.0	212.0
	Max	312	324	328	320	362	446
No	N	40	36	32	31	17	6
	Missing	14	18	22	23	37	48
	Mean	212.8	212.1	205.3	212.8	223.4	231.7
	SD	56.6	46.2	44.4	48.8	54.3	46.9
	Min	60	85	65	76	131	146
	Median	214.0	217.5	215.0	216.0	228.0	237.0
	Max	370	327	271	344	335	275

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.6 CRP (mg/l)

6.2.6.1 CRP (mg/l) - absolute values

		M00	M03	M06	M12	M24	M36
Total	N	231	189	156	115	69	36
	Missing	29	71	104	145	191	224
	Mean	14.0	10.4	7.6	6.6	5.1	4.6
	SD	34.7	20.3	16.4	14.4	9.9	3.5
	Min	0	0	0	0	0	1
	Median	6.0	4.0	3.0	3.0	3.0	3.6
	Max	430	156	130	111	80	16

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.6 CRP (mg/l)

6.2.6.2 CRP (mg/l) - differences

		M03 - M00	M06 - M00	M12 - M00	M24 - M00	M36 - M00
Total	N	169	141	107	63	33
	Missing	91	119	153	197	227
	Mean	-5.9	-8.3	-11.1	-7.5	-10.6
	SD	38.8	41.9	47.9	16.0	24.9
	Min	-430	-430	-430	-75	-134
	Median	-1.0	-1.0	-2.0	-2.0	-4.0
	Max	54	85	108	13	10

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.6 CRP (mg/l)

6.2.6.3 CRP (mg/l) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
Good response	N	47	41	40	41	29	17
	Missing	2	8	9	8	20	32
	Mean	11.2	5.3	3.9	3.6	3.0	3.9
	SD	17.1	10.1	4.3	8.3	2.1	3.4
	Min	0	0	0	0	0	1
	Median	6.0	2.0	2.0	2.0	2.2	3.0
	Max	75	56	19	52	7	16
Moderate response	N	24	18	19	20	15	7
	Missing	2	8	7	6	11	19
	Mean	27.8	12.6	12.9	7.3	10.7	6.2
	SD	35.3	29.2	26.6	10.0	19.9	4.3
	Min	1	0	0	1	1	1
	Median	13.9	3.3	3.0	3.5	5.0	6.0
	Max	141	121	115	43	80	13

(Continued)

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.6 CRP (mg/l)

6.2.6.3 CRP (mg/l) - absolute values - by EULAR response

		M00	M03	M06	M12	M24	M36
DAS28 EULAR improvement (M12)							
No response	N	29	30	25	26	8	4
	Missing	3	2	7	6	24	28
	Mean	13.9	13.9	10.9	12.1	3.7	5.4
	SD	34.2	32.5	25.9	26.0	3.2	2.1
	Min	0	0	0	0	0	4
	Median	5.0	3.5	3.7	3.0	2.5	4.6
	Max	173	156	130	111	9	9

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.2 Laboratory

6.2.6 CRP (mg/l)

6.2.6.4 CRP (mg/l) - absolute values - by DAS28 dcrit response

		M00	M03	M06	M12	M24	M36
DAS28 improvement ≥ 1.8 at M12							
Yes	N	50	42	42	43	32	19
	Missing	3	11	11	10	21	34
	Mean	15.8	5.5	4.2	4.7	6.5	4.9
	SD	26.8	9.9	4.5	8.7	14.0	4.1
	Min	0	0	0	0	0	1
	Median	8.0	2.5	2.4	2.0	3.0	3.2
	Max	141	56	19	52	80	16
No	N	50	47	42	44	20	9
	Missing	4	7	12	10	34	45
	Mean	16.2	13.4	11.8	9.2	3.4	4.2
	SD	30.0	31.4	26.6	21.0	2.5	2.4
	Min	0	0	0	0	0	1
	Median	5.5	3.0	3.0	3.0	3.0	4.2
	Max	173	156	130	111	9	9

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.1 Clinical diagnosed pericarditis

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Pericarditis												
Total	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.2 Pleurisy

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Pericarditis												
Total	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.3 Adult still disease

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Adult still disease												
Total	Yes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.4 Polyneuropathy

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Polyneuropathy												
Total	Yes	1	0.4	1	0.4	0	0.0	1	0.7	1	1.1	0	0.0
	No	254	99.6	234	99.6	191	100.0	146	99.3	91	98.9	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.5 Mononeuropathy

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Mononeuropathy												
Total	Yes	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
	No	255	100.0	235	100.0	191	100.0	146	99.3	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.6 Scleritis

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Scleritis												
Total	Yes	1	0.4	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
	No	254	99.6	234	99.6	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.7 Episcleritis

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Episcleritis												
Total	Yes	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
	No	255	100.0	234	99.6	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.8 Glomerulonephritis

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Glomerulonephritis												
Total	Yes	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	No	254	99.6	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.9 Pronounced cutane vasculitis

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Pronounced cutane vasculitis												
Total	Yes	1	0.4	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
	No	254	99.6	234	99.6	191	100.0	147	100.0	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

AGIL-CV patient data set

6. AGIL-CV data in the course of the study

6.3 Concomitant symptoms to rheumatoid arthritis

6.3.10 Vasculitis other organs

		Visit											
		M0		M3		M6		M12		M24		M36	
		n	%	n	%	n	%	n	%	n	%	n	%
	Vasculitis other organs												
Total	Yes	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
	No	255	100.0	235	100.0	191	100.0	146	99.3	92	100.0	46	100.0
	Total	255	100.0	235	100.0	191	100.0	147	100.0	92	100.0	46	100.0

Appendix 9 Statistical Tables for Safety Set

**Long-term Documentation of the
Safety, Effectiveness, and Effects on
Quality of Life and Work Productivity in
Patients with Rheumatoid Arthritis
during HUMIRA® (Adalimumab)
Therapy in Routine Clinical Practice
(AGIL) and Supplementary
Documentation to Record
Cardiovascular and Metabolic Risk
Factors (AGIL-CV)**

**Final analysis
Appendix: Statistical Tables for
Safety Set**

March, 05 2018

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Safety patient data set

1. General parameters

1.1 Exclusion criteria for safety evaluation

For safety evaluation no patients were excluded

Safety patient data set
 1. General parameters
 1.2 Gender

	Gender				Total	
	Male		Female			
	n	%	n	%	n	%
Total	1909	26.6	5267	73.4	7176	100.0

Safety patient data set
1. General parameters
1.3 Age (years)
1.3.1 Age - total

	Total
N	7165
Missing	64
Mean	54.9
SD	13.2
Min	15
Median	55.0
Max	90

Safety patient data set

1. General parameters

1.3 Age (years)

1.3.2 Age by gender

	Missing	Male	Female
N	4	1907	5254
Missing	49	2	13
Mean	44.8	54.9	54.9
SD	14.0	12.4	13.5
Min	27	15	16
Median	45.5	55.0	55.0
Max	61	85	90

Safety patient data set
1. General parameters
1.4 Height (cm)
1.4.1 Height - total

	Total
N	7072
Missing	157
Mean	168.4
SD	8.9
Min	130
Median	168.0
Max	214

Safety patient data set

1. General parameters

1.4 Height (cm)

1.4.2 Height by gender

	Missing	Male	Female
N	4	1880	5188
Missing	49	29	79
Mean	171.8	177.8	165.1
SD	9.1	7.4	6.8
Min	163	150	130
Median	171.5	178.0	165.0
Max	181	214	190

Safety patient data set
1. General parameters
1.5 Weight (kg)
1.5.1 Weight - total

	Total
N	7074
Missing	155
Mean	76.4
SD	17.0
Min	36
Median	74.0
Max	194

Safety patient data set
 1. General parameters
 1.5 Weight (kg)
 1.5.2 Weight by gender

	Missing	Male	Female
N	4	1880	5190
Missing	49	29	77
Mean	71.5	86.0	72.9
SD	15.8	15.9	16.0
Min	55	50	36
Median	73.0	84.0	70.0
Max	85	194	177

Safety patient data set
1. General parameters
1.6 BMI (kg/m²)
1.6.1 BMI - total

	Total
N	7068
Missing	161
Mean	26.9
SD	5.5
Min	14
Median	26.0
Max	72

Safety patient data set

1. General parameters

1.6 BMI (kg/m²)

1.6.2 BMI by gender

	Missing	Male	Female
N	4	1878	5186
Missing	49	31	81
Mean	24.0	27.2	26.8
SD	3.0	4.7	5.7
Min	20	17	14
Median	24.5	26.3	25.8
Max	27	72	65

Safety patient data set
 1. General parameters
 1.7 Smoking habits

	Smoking habits				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1559	22.2	5475	77.8	7034	100.0

Safety patient data set

1. General parameters

1.8 Duration of disease (years)

1.8.1 Duration - total

	Total
N	7039
Missing	190
Mean	9.6
SD	8.8
Min	0
Median	7.1
Max	63

	Duration of disease (grouped)																		Total	
	< 2 years		2 - 4 years		4 - 6 years		6 - 8 years		8 - 10 years		10 - 15 years		15 - 20 years		20 - 30 years		> 30 years			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	1215	17.3	1068	15.2	835	11.9	661	9.4	641	9.1	1134	16.1	620	8.8	595	8.5	270	3.8	7039	100.0

Safety patient data set
 1. General parameters
 1.9 Erosive changes

	Erosive changes				Total	
	Yes		No			
	n	%	n	%	n	%
Total	3501	63.6	2007	36.4	5508	100.0

Safety patient data set

1. General parameters

1.10 Indications for receiving adalimumab therapy

	n	%
Indications for current adalimumab therapy		
Patient base	7229	100.0
High disease activity	5781	80.0
Lack of effectiveness of previous therapy	4901	67.8
Intolerance of previous therapy	2027	28.0
Rapid radiologic progression	1162	16.1
Other	227	3.1

Safety patient data set
 1. General parameters
 1.11 Humira therapy
 1.11.1 Dose (mg) at baseline

	Dose				Total	
	40mg each 14 days		Other			
	n	%	n	%	n	%
Total	6977	97.8	160	2.2	7137	100.0

Safety patient data set
1. General parameters
1.11 Humira therapy
1.11.2 Exposure (years) of study drug

	Total
N	7131
Missing	98
Mean	2.06
SD	1.77
Min	0.0
Median	1.39
Max	7.2

Safety patient data set

1. General parameters

1.12 Physician global assessment of disease activity

	Total
N	7111
Missing	118
Mean	5.5
SD	2.2
Min	0
Median	6.0
Max	10

Safety patient data set
 1. General parameters
 1.13 Morning stiffness
 1.13.1 Patients with morning stiffness(%)

	Morning stiffness				Total	
	Yes		No			
	n	%	n	%	n	%
Total	5390	76.5	1660	23.5	7050	100.0

Safety patient data set
1. General parameters
1.13 Morning stiffness
1.13.2 Morning stiffness (minutes)

	Total
N	6975
Missing	254
Mean	56.9
SD	71.0
Min	0
Median	30.0
Max	800

Safety patient data set
 1. General parameters
 1.14 Rheumatic nodules

	Rheumatic nodules				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1025	14.5	6024	85.5	7049	100.0

Safety patient data set

1. General parameters

1.15 Prior joint surgery

	Prior joint surgery				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1638	23.2	5428	76.8	7066	100.0

Safety patient data set
 1. General parameters
 1.16 Joint involvement

		TJC (M0)	SJC (M0)
Total	N	7111	7111
	Missing	118	118
	Mean	7.4	5.0
	SD	6.8	5.3
	Min	0	0
	Median	6.0	4.0
	Max	28	28

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.1 Rheumatic factor

	Rheumatic Factor				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	4340	65.0	2338	35.0	6678	100.0

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.2 Anti-CCP

	Anti-ccp				Total	
	Positive		Negative			
	n	%	n	%	n	%
Total	4032	65.6	2118	34.4	6150	100.0

Safety patient data set
1. General parameters
1.17 Laboratory
1.17.3 CRP (mg/l)

	Total
N	6764
Missing	465
Mean	17.3
SD	48.7
Min	0
Median	6.0
Max	978

Safety patient data set
1. General parameters
1.17 Laboratory
1.17.4 ESR (mm/h)
1.17.4.1 ESR - total

	Total
N	6348
Missing	881
Mean	26.5
SD	21.7
Min	1
Median	20.0
Max	138

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.4 ESR (mm/h)
 1.17.4.2 ESR by gender

	Missing	Male	Female
N	3	1685	4660
Missing	50	224	607
Mean	8.3	27.0	26.3
SD	6.7	23.6	20.9
Min	4	1	1
Median	5.0	20.0	20.0
Max	16	138	131

Safety patient data set
1. General parameters
1.17 Laboratory
1.17.5 Hemoglobin (g/dl)

	Total
N	6596
Missing	633
Mean	18.6
SD	28.5
Min	0
Median	13.0
Max	980

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.6 Hepatitis B

	Hepatitis B				Total	
	Yes		No			
	n	%	n	%	n	%
Total	33	0.6	5663	99.4	5696	100.0

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.7 Hepatitis C

	Hepatitis C				Total	
	Yes		No			
	n	%	n	%	n	%
Total	17	0.3	5646	99.7	5663	100.0

Safety patient data set
 1. General parameters
 1.17 Laboratory
 1.17.8 Latent tuberculosis

	Latent tuberculosis				Total	
	Yes		No			
	n	%	n	%	n	%
Total	264	3.8	6635	96.2	6899	100.0

Safety patient data set
 1. General parameters
 1.18 School leaving certificate

	School leaving certificate								Total	
	Without graduation		Secondary school certificate (Hauptschule)		Secondary school level I certificate (Realschulabschluss - mittlere Reife)		Diploma from German secondary school qualifying for university admission or matriculation (Abitur)			
	n	%	n	%	n	%	n	%	n	%
Total	145	2.1	2403	34.6	2838	40.8	1564	22.5	6950	100.0

Safety patient data set

1. General parameters

1.19 Professional education

	n	%
Professional education		
Patient base	7229	100.0
Alternance training (School and on-the-job training)	3056	42.3
Off-the-job training	1384	19.1
Technical college / Master craftsman training	984	13.6
University of applied science	539	7.5
University	513	7.1
Semiskilled	495	6.8
None	476	6.6

Safety patient data set
 1. General parameters
 1.20 Employment

	Employment												Total	
	Full time job (35h and more)		Part-time work		School, education, studying		Home making, child-rearing		Unemployed		Retirement			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Total	2156	31.2	1129	16.3	151	2.2	324	4.7	451	6.5	2703	39.1	6914	100.0

Safety patient data set

1. General parameters

1.21 Early retirement due to rheumatic disease (only patients in retirement)

	Retirement due to rheumatic disease				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1070	40.6	1564	59.4	2634	100.0

Safety patient data set

1. General parameters

1.22 Occupational status (only patients with occupation)

	Occupational status								Total	
	Salaried		Civil servant		Leading function		Freelancer			
	n	%	n	%	n	%	n	%	n	%
Total	2633	82.0	131	4.1	158	4.9	290	9.0	3212	100.0

Safety patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.1 Household

	Household								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	4773	66.0	1497	20.7	309	4.3	650	9.0	7229	100.0

	Household				Total	
	Yes		No			
	n	%	n	%	n	%
Total	4773	76.1	1497	23.9	6270	100.0

Without not applicable and missings

	Total
N	5283
Missing	1946
Mean	51.2
SD	63.8
Min	0
Median	20.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Safety patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.2 Parenting

	Parenting								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	462	6.4	1694	23.4	2758	38.2	2315	32.0	7229	100.0

	Parenting				Total	
	Yes		No			
	n	%	n	%	n	%
Total	462	21.4	1694	78.6	2156	100.0

Without not applicable and missings

	Total
N	2052
Missing	5177
Mean	12.0
SD	37.7
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Safety patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.3 Education

	Education								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	225	3.1	1495	20.7	3038	42.0	2471	34.2	7229	100.0

	Education				Total	
	Yes		No			
	n	%	n	%	n	%
Total	225	13.1	1495	86.9	1720	100.0

Without not applicable and missings

	Total
N	1679
Missing	5550
Mean	6.5
SD	28.0
Min	0
Median	0.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Safety patient data set

1. General parameters

1.23 Impairment of non-occupational activities

1.23.4 Recreational (free-time)

	Recreational(free-time)								Total	
	Yes		No		Not applicable		Missing			
	n	%	n	%	n	%	n	%	n	%
Total	4384	60.6	1355	18.7	333	4.6	1157	16.0	7229	100.0

	Recreational(free-time)				Total	
	Yes		No			
	n	%	n	%	n	%
Total	4384	76.4	1355	23.6	5739	100.0

Without not applicable and missings

	Total
N	4863
Missing	2366
Mean	53.4
SD	65.2
Min	0
Median	20.0
Max	183

Days with impairment, patients with no impairment were counted as 0, patients with impairment but missing were not taken into account

Safety patient data set

1. General parameters

1.24 Missed work days in the last 6 month

	M00				Total	
	Yes		No			
	n	%	n	%	n	%
Total	1951	49.2	2013	50.8	3964	100.0

Missed work days in the last 6 month (% of patients)

	Total
N	3887
Missing	3342
Mean	19.9
SD	41.7
Min	0
Median	0.0
Max	183

Number of missed work days in the last 6 month

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.1 Number of visits at the rheumatologist

	Total
N	6781
Missing	448
Mean	3.2
SD	3.0
Min	0
Median	2.0
Max	70

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.2 Number of visits at the general practitioner

	Total
N	6780
Missing	449
Mean	3.8
SD	4.7
Min	0
Median	3.0
Max	68

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.3 Number of visits at the orthopaedic specialist

	Total
N	6780
Missing	449
Mean	0.9
SD	2.1
Min	0
Median	0.0
Max	40

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.4 Number of visits at other medical specialists

	Total
N	6780
Missing	449
Mean	1.2
SD	2.8
Min	0
Median	0.0
Max	78

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.5 Number of hospitalizations

	Total
N	6780
Missing	449
Mean	0.4
SD	1.5
Min	0
Median	0.0
Max	40

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.6 Total duration of hospitalizations (days)

	Total
N	6780
Missing	449
Mean	2.1
SD	6.8
Min	0
Median	0.0
Max	183

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.7 Number of convalescent cares, stationary rehabilitations

	Total
N	6780
Missing	449
Mean	0.2
SD	1.6
Min	0
Median	0.0
Max	42

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.8 Total duration of convalescent cares, stationary rehabilitations (days)

	Total
N	6780
Missing	449
Mean	1.5
SD	6.9
Min	0
Median	0.0
Max	183

Safety patient data set

1. General parameters

1.25 Number of physician visits and number and duration of hospitalizations in the last 6 month

1.25.9 Number of physical therapies, for example physiotherapy

	Total
N	6780
Missing	449
Mean	3.9
SD	10.0
Min	0
Median	0.0
Max	98

Safety patient data set
1. General parameters
1.26 Modified WAI

	Total
N	2183
Missing	5046
Mean	32.1
SD	7.8
Min	7
Median	32.5
Max	49

Safety patient data set
1. General parameters
1.27 WPAI
1.27.1 Presenteeism (%)

	Total
N	3046
Missing	4183
Mean	47.2
SD	27.3
Min	0
Median	50.0
Max	100

Safety patient data set
1. General parameters
1.27 WPAI
1.27.2 Absenteeism (%)

	Total
N	2362
Missing	4867
Mean	21.4
SD	36.9
Min	0
Median	0.0
Max	100

Safety patient data set

1. General parameters

1.27 WPAI

1.27.3 Total work productivity impairment (%)

	Total
N	2124
Missing	5105
Mean	50.9
SD	29.2
Min	0
Median	50.0
Max	100

Safety patient data set
1. General parameters
1.27 WPAI
1.27.4 Total activity impairment (%)

	Total
N	6862
Missing	367
Mean	54.9
SD	25.0
Min	0
Median	60.0
Max	100

Safety patient data set

1. General parameters

1.28 Patient global assessment of disease activity

	Total
N	6914
Missing	315
Mean	5.6
SD	2.5
Min	0
Median	6.0
Max	10

Safety patient data set
1. General parameters
1.29 Fatigue

	Total
N	6937
Missing	292
Mean	5.4
SD	2.8
Min	0
Median	6.0
Max	10

Safety patient data set
 1. General parameters
 1.30 Pain

	Total
N	6946
Missing	283
Mean	5.6
SD	2.5
Min	0
Median	6.0
Max	10

Safety patient data set
1. General parameters
1.31 HAQ-DI

	Total
N	6977
Missing	252
Mean	1.19
SD	0.74
Min	0.0
Median	1.13
Max	3.0

Safety patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.1 Mobility

	Mobility						Total	
	No problems		Some problems		Confined to bed			
	n	%	n	%	n	%	n	%
Total	3032	44.1	3837	55.7	14	0.2	6883	100.0

Safety patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.2 Self-care

	Self-care						Total	
	No problems		Some problems		Unable to wash or dress myself			
	n	%	n	%	n	%	n	%
Total	4446	64.6	2248	32.7	186	2.7	6880	100.0

Safety patient data set

1. General parameters

1.32 EQ-5D

1.32.3 Usual activities (e.g., work, study, housework, family or leisure activities)

	Usual activities						Total	
	No problems		Some problems		Unable to perform			
	n	%	n	%	n	%	n	%
Total	1968	28.6	4608	66.9	310	4.5	6886	100.0

Safety patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.4 Pain/discomfort

	Pain/discomfort						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	475	6.9	4661	67.6	1761	25.5	6897	100.0

Safety patient data set
 1. General parameters
 1.32 EQ-5D
 1.32.5 Anxiety/depression

	Anxiety/depression						Total	
	None		Moderate		Extreme			
	n	%	n	%	n	%	n	%
Total	3598	52.3	2894	42.1	388	5.6	6880	100.0

Safety patient data set
1. General parameters
1.32 EQ-5D
1.32.6 Mean EQ VAS

	Total
N	6912
Missing	317
Mean	52.2
SD	22.0
Min	0
Median	50.0
Max	100

Safety patient data set
1. General parameters
1.33 DAS28

	Total
N	6132
Missing	1097
Mean	4.63
SD	1.51
Min	0.0
Median	4.70
Max	8.9

Safety patient data set
 1. General parameters
 1.34 Participation in Abbott Care

	Participation in Abbott Care service program				Total	
	Yes		No			
	n	%	n	%	n	%
Total	2188	35.4	3994	64.6	6182	100.0

Safety patient data set
2. Concomitant diseases

	n	%
Previous concomitant diseases		
Patient base	7229	100.0
Total	4829	66.8
Arterial hypertension	2447	33.8
Other disease	2236	30.9
Degenerative joint disease	1265	17.5
Osteoporosis	1042	14.4
Degenerative spinal disease	1023	14.2
Diabetes Type II	596	8.2
Hyperlipidemia	559	7.7
Mental illness (e.g. depression)	457	6.3
Coronary heart disease	395	5.5
Chronic obstructive pulmonary disease	329	4.6
Chronic inflammatory disease	145	2.0
Diabetes Type I	101	1.4

Safety patient data set
 3.Previous and concomitant medication
 3.1 Previous documented DMARDs

	n	%
Previous documented DMARDs		
Patient base	7229	100.0
MTX	4490	62.1
Leflunomide	4003	55.4
Glucocorticoides	3172	43.9
NSAID, Coxibe	2530	35.0
SASP	2256	31.2
Analgesics	1612	22.3
Other	1143	15.8

Safety patient data set
 3.Previous and concomitant medication
 3.2 Documented DMARDs at baseline

	n	%
Documented DMARDs at baseline		
Patient base	7229	100.0
Glucocorticoides	4620	63.9
MTX	3745	51.8
NSAID, Coxibe	1474	20.4
Leflunomide	784	10.8
Analgesics	741	10.3
Other	281	3.9
SASP	244	3.4

Safety patient data set

3.Previous and concomitant medication

3.3 Documented DMARDs during study, baseline included

	n	%
Concomitant DMARDs		
Total	6566	90.8
Glucocorticoids	5006	69.2
MTX	4083	56.5
NSAIDs, Coxibe	1614	22.3
Leflunomide	854	11.8
Analgesics	839	11.6
Other	685	9.5
SASP	274	3.8

Safety patient data set

3.Previous and concomitant medication

3.4 Glucocorticoid dosage at baseline and maximum dosage during study

		Glucocorticode dosage at baseline mg/d	Maximum Glucocorticode dosage during study mg/d
Total	N	4558	4955
	Missing	2671	2274
	Mean	7.5	8.9
	SD	5.7	7.8
	Min	1	1
	Median	5.0	5.0
	Max	103	103

Safety patient data set

3.Previous and concomitant medication

3.5 MTX dosage at baseline and maximum dosage during study

		MTX dosage at baseline mg/w	Maximum MTX dosage during study mg/w
Total	N	3666	4020
	Missing	3563	3209
	Mean	14.5	14.5
	SD	6.4	6.3
	Min	1	1
	Median	15.0	15.0
	Max	215	215

Safety patient data set
 3.Previous and concomitant medication
 3.6 Previous biologic therapies
 3.6.1 Percentage previous biologics

	n	%
Documented previous biologics at baseline		
Patient base	7229	100.0
Etanercept	1314	18.2
Other	437	6.0
Infliximab	237	3.3
Tocilizumab	217	3.0
Certolizumab	157	2.2
Golimumab	127	1.8
Abatacept	96	1.3
Rituximab	85	1.2

Safety patient data set

3.Previous and concomitant medication

3.6 Previous biologic therapies

3.6.2 Mean duration of previous biologics (month)

		Infliximab	Etanercept	Golimumab	Certolizumab	Abatacept	Rituximab	Tocilizumab
Total	N	233	1293	127	154	94	78	216
	Missing	6996	5936	7102	7075	7135	7151	7013
	Mean	29.5	28.0	14.9	10.6	10.9	19.6	14.0
	SD	33.3	32.5	20.5	11.7	11.1	23.1	18.6
	Min	1	1	1	1	1	1	1
	Median	15.0	14.0	7.0	6.0	7.0	8.5	8.0
	Max	177	196	169	66	62	96	183

Safety patient data set
 3.Previous and concomitant medication
 3.7 Number of previous biologics

	Number of previous biologics						Total	
	0		1		>=2			
	n	%	n	%	n	%	n	%
Total	5037	69.7	1836	25.4	356	4.9	7229	100.0

Safety patient data set

3.Previous and concomitant medication

3.8 Main reasons for discontinuing the previous biologic therapy

	Reason for discontinuing the previous biologic therapy						Total	
	Lack of effectiveness		Lack of tolerance		Other reason			
	n	%	n	%	n	%	n	%
Total	1381	64.9	407	19.1	340	16.0	2128	100.0

Safety patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.1 Withdrawal reasons by visit

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Patients in safety data set	Adverse drug reaction	132	2.0	61	1.1	50	1.1	33	1.0	9	0.4	12	0.7	2	0.2
	Lack of effectiveness	354	5.3	337	6.0	308	6.6	251	7.4	110	4.6	39	2.2	24	1.8
	Other reason	253	3.8	142	2.5	196	4.2	192	5.6	124	5.2	88	5.0	80	6.1
	Unknown Reason	7	0.1	14	0.2	17	0.4	15	0.4	12	0.5	6	0.3	0	0.0
	Ongoing patients at the end of visit	5886	88.8	5048	90.1	4107	87.8	2919	85.6	2137	89.3	1608	91.7	1210	91.9
	Total	6632	100.0	5602	100.0	4678	100.0	3410	100.0	2392	100.0	1753	100.0	1316	100.0

Safety patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.2 Disposition of patients (cumulated withdrawal rates)

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Patients in safety data set	Adverse drug reaction	132	1.8	193	2.7	243	3.4	276	3.8	285	3.9	297	4.1	299	4.1
	Lack of effectiveness	354	4.9	691	9.6	999	13.8	1250	17.3	1360	18.8	1399	19.4	1423	19.7
	Other reason	253	3.5	395	5.5	591	8.2	783	10.8	907	12.5	995	13.8	1075	14.9
	Unknown Reason	7	0.1	21	0.3	38	0.5	53	0.7	65	0.9	71	1.0	71	1.0
	Lost to follow up (cummulated)	318	4.4	670	9.3	1128	15.6	1810	25.0	2363	32.7	2765	38.2	3151	43.6
	Ongoing patients at the end of visit	5886	81.4	5048	69.8	4107	56.8	2919	40.4	2137	29.6	1608	22.2	1210	16.7
	Single visit missing (a later visit is following)	279	3.9	211	2.9	123	1.7	138	1.9	112	1.5	94	1.3	0	0.0
	Total	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0

Safety patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

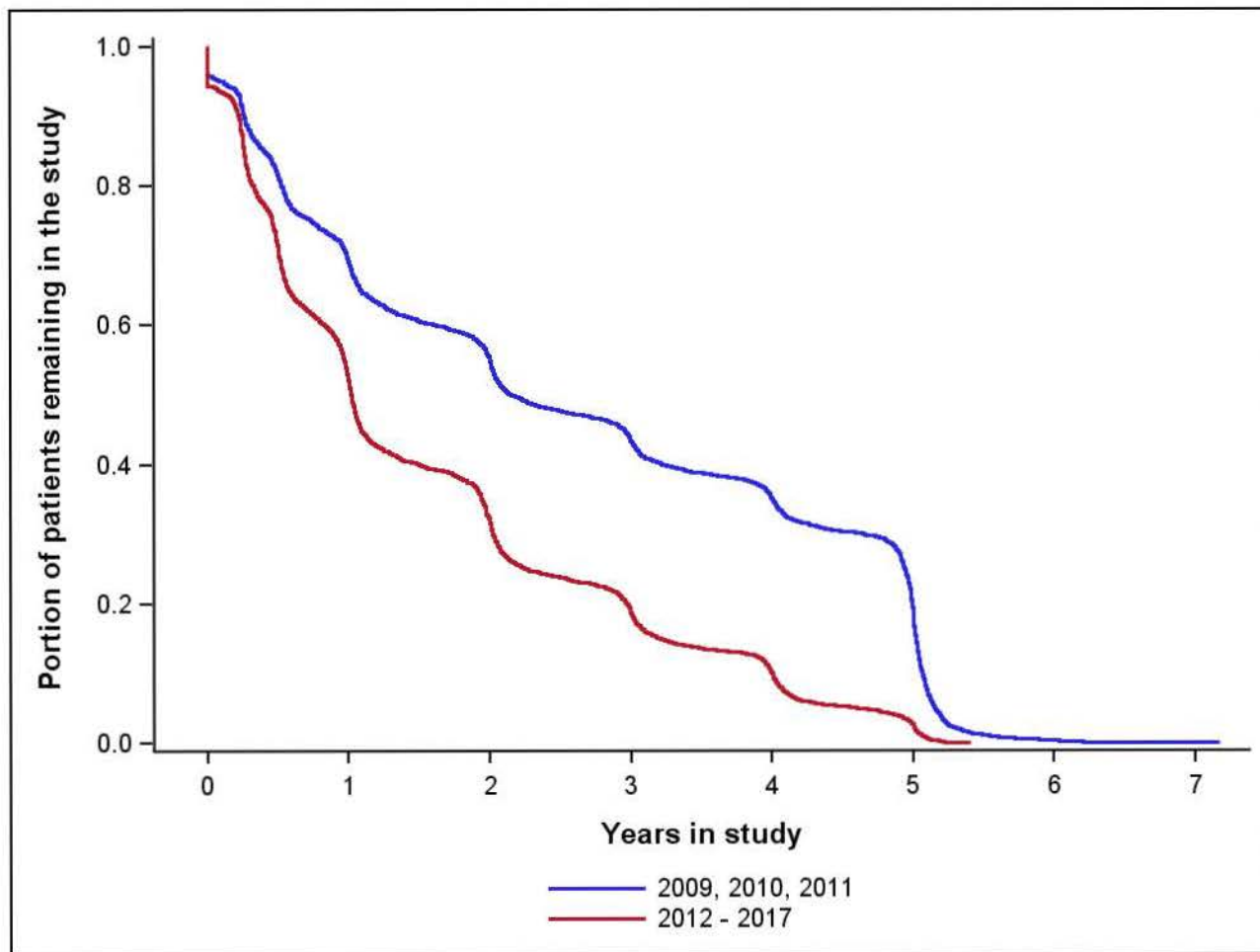
4.3 Disposition of patients (shortened)

		Visit													
		M03		M06		M12		M24		M36		M48		M60	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Withdrawal														
Patients in safety data set	Cummulative documented withdrawals	746	10.3	1300	18.0	1871	25.9	2362	32.7	2617	36.2	2762	38.2	2868	39.7
	Ongoing patients at the end of visit	5886	81.4	5048	69.8	4107	56.8	2919	40.4	2137	29.6	1608	22.2	1210	16.7
	Single visit missing (a later visit is following)	279	3.9	211	2.9	123	1.7	138	1.9	112	1.5	94	1.3	0	0.0
	Lost to follow up (cummulated)	318	4.4	670	9.3	1128	15.6	1810	25.0	2363	32.7	2765	38.2	3151	43.6
	Total	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0	7229	100.0

Safety patient data set

4. Disposition of patients, documented withdrawal and Kaplan-Meier

4.4 Total duration of study (Kaplan-Meier, computed by visit dates) by year of baseline



5. Documented adverse events by patient

5.1 All documented adverse events by system organ class

	n	%
System Organ Class		
Total	2764	38.2
Infections and infestations	1252	17.3
Surgical and medical procedures	698	9.7
General disorders and administration site conditions	620	8.6
Musculoskeletal and connective tissue disorders	459	6.3
Skin and subcutaneous tissue disorders	426	5.9
Gastrointestinal disorders	297	4.1
Nervous system disorders	272	3.8
Respiratory, thoracic and mediastinal disorders	255	3.5
Investigations	250	3.5
Injury, poisoning and procedural complications	208	2.9
Cardiac disorders	139	1.9
Vascular disorders	134	1.9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	116	1.6
Psychiatric disorders	80	1.1
Renal and urinary disorders	75	1.0
Eye disorders	71	1.0

(Continued)

5. Documented adverse events by patient

5.1 All documented adverse events by system organ class

	n	%
System Organ Class		
Blood and lymphatic system disorders	64	0.9
Metabolism and nutrition disorders	60	0.8
Ear and labyrinth disorders	42	0.6
Hepatobiliary disorders	36	0.5
Reproductive system and breast disorders	33	0.5
Immune system disorders	30	0.4
Endocrine disorders	23	0.3
Pregnancy, puerperium and perinatal conditions	18	0.2
Product issues	7	0.1
Congenital, familial and genetic disorders	3	0.0
Social circumstances	3	0.0

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Total	2764	38.2
Influenza like illness	215	3.0
Bronchitis	186	2.6
Nasopharyngitis	138	1.9
Upper respiratory tract infection	131	1.8
Hospitalisation	115	1.6
Respiratory tract infection	110	1.5
Rheumatoid arthritis	104	1.4
Infection	100	1.4
Pneumonia	98	1.4
Therapy cessation	87	1.2
Herpes zoster	85	1.2
Pyrexia	82	1.1
Urinary tract infection	77	1.1
Cough	73	1.0
Elective surgery	73	1.0
Nausea	73	1.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Diarrhoea	71	1.0
Rash	67	0.9
Sinusitis	65	0.9
Headache	59	0.8
Pruritus	55	0.8
Dizziness	53	0.7
Drug ineffective	52	0.7
Fall	47	0.7
Oral herpes	47	0.7
Fatigue	45	0.6
Hypertension	45	0.6
Antibiotic therapy	43	0.6
Injection site erythema	40	0.6
Knee arthroplasty	40	0.6
Osteoarthritis	36	0.5
Psoriasis	36	0.5
Arthralgia	35	0.5

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Arthrodesis	35	0.5
Cystitis	34	0.5
Depression	34	0.5
Erythema	33	0.5
Liver function test increased	33	0.5
Rash pruritic	29	0.4
Synovectomy	29	0.4
Unevaluable event	29	0.4
Alopecia	28	0.4
Back pain	28	0.4
Gastroenteritis	28	0.4
Hip arthroplasty	28	0.4
Vomiting	28	0.4
Bursitis	27	0.4
Pain in extremity	27	0.4
Foot operation	26	0.4
Intervertebral disc protrusion	26	0.4

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Laboratory test abnormal	26	0.4
Antibiotic prophylaxis	25	0.3
Pulpitis dental	25	0.3
Joint arthroplasty	24	0.3
Paraesthesia	23	0.3
Tonsillitis	23	0.3
Dyspnoea	22	0.3
Eczema	22	0.3
Erysipelas	22	0.3
Urticaria	22	0.3
Arthritis	21	0.3
Blood pressure increased	21	0.3
Gastrointestinal infection	21	0.3
Injection site reaction	20	0.3
Oropharyngeal pain	20	0.3
Palpitations	20	0.3
Skin ulcer	20	0.3

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Conjunctivitis	19	0.3
Foot deformity	19	0.3
Hypersensitivity	19	0.3
Pharyngitis	19	0.3
Respiratory distress	19	0.3
Rhinitis	19	0.3
Coronary artery disease	18	0.2
Cystitis noninfective	18	0.2
Dermatitis allergic	18	0.2
Injection site pruritus	18	0.2
Joint surgery	18	0.2
Joint swelling	18	0.2
Synovial cyst	18	0.2
Abdominal discomfort	17	0.2
Arthroscopy	17	0.2
Bunion operation	17	0.2
Hyperhidrosis	17	0.2

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Impaired healing	17	0.2
Leukopenia	17	0.2
Breast cancer female	16	0.2
Cataract operation	16	0.2
Cerebrovascular accident	16	0.2
Death	16	0.2
Myocardial infarction	16	0.2
Pain	16	0.2
Sciatica	16	0.2
Therapy change	16	0.2
Tooth extraction	16	0.2
Angina pectoris	15	0.2
Atrial fibrillation	15	0.2
Cholelithiasis	15	0.2
Diverticulitis	15	0.2
Knee operation	15	0.2
Sleep disorder	15	0.2

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Viral infection	15	0.2
Foot fracture	14	0.2
Otitis media	14	0.2
Pregnancy	14	0.2
Rotator cuff syndrome	14	0.2
Spinal pain	14	0.2
Surgery	14	0.2
Abdominal pain upper	13	0.2
Aphthous ulcer	13	0.2
Asthenia	13	0.2
Dry mouth	13	0.2
Epistaxis	13	0.2
Gastritis	13	0.2
Lumbar spinal stenosis	13	0.2
Peripheral swelling	13	0.2
Rash generalised	13	0.2
Subcutaneous abscess	13	0.2

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Tendon rupture	13	0.2
Acute myocardial infarction	12	0.2
Cholecystectomy	12	0.2
Gamma-glutamyltransferase increased	12	0.2
Haematoma	12	0.2
Humerus fracture	12	0.2
Oedema peripheral	12	0.2
Rash pustular	12	0.2
Rheumatoid nodule removal	12	0.2
Abscess limb	11	0.2
Complication associated with device	11	0.2
Dyspnoea exertional	11	0.2
Influenza	11	0.2
Osteoporosis	11	0.2
Productive cough	11	0.2
Pyelonephritis	11	0.2
Rhinorrhoea	11	0.2

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Spinal operation	11	0.2
Urosepsis	11	0.2
Burning sensation	10	0.1
Cardiac failure	10	0.1
Chest pain	10	0.1
Diabetes mellitus	10	0.1
General physical health deterioration	10	0.1
Hypoaesthesia	10	0.1
Intervertebral disc operation	10	0.1
Joint dislocation	10	0.1
Joint effusion	10	0.1
Laryngitis	10	0.1
Lymphadenopathy	10	0.1
Night sweats	10	0.1
Pulmonary embolism	10	0.1
Radius fracture	10	0.1
Thrombosis	10	0.1

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Alanine aminotransferase increased	9	0.1
Anaemia	9	0.1
Basal cell carcinoma	9	0.1
Bursa removal	9	0.1
Cataract	9	0.1
Chronic obstructive pulmonary disease	9	0.1
Dental operation	9	0.1
Dermatitis psoriasiform	9	0.1
Goitre	9	0.1
Haematuria	9	0.1
Infection susceptibility increased	9	0.1
Limb injury	9	0.1
Osteopenia	9	0.1
Osteotomy	9	0.1
Pleural effusion	9	0.1
Post procedural infection	9	0.1
Postoperative wound infection	9	0.1

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Pruritus generalised	9	0.1
Rehabilitation therapy	9	0.1
Renal failure	9	0.1
Rheumatoid nodule	9	0.1
Skin neoplasm excision	9	0.1
Spinal osteoarthritis	9	0.1
Stomatitis	9	0.1
Synovitis	9	0.1
Tenosynovitis	9	0.1
Tinnitus	9	0.1
Transaminases increased	9	0.1
Arrhythmia	8	0.1
Arthropod bite	8	0.1
Arthroscopic surgery	8	0.1
Borrelia infection	8	0.1
Carpal tunnel decompression	8	0.1
Coronary artery bypass	8	0.1

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Fracture treatment	8	0.1
Herpes virus infection	8	0.1
Inflammation	8	0.1
Injection site pain	8	0.1
Laparoscopic surgery	8	0.1
Ligament sprain	8	0.1
Local reaction	8	0.1
Lumbar vertebral fracture	8	0.1
Meniscus operation	8	0.1
Myalgia	8	0.1
Osteosynthesis	8	0.1
Pleurisy	8	0.1
Polyneuropathy	8	0.1
Pustular psoriasis	8	0.1
Skin disorder	8	0.1
Swelling	8	0.1
Thrombocytopenia	8	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Weight decreased	8	0.1
Abscess drainage	7	0.1
Antinuclear antibody increased	7	0.1
Anxiety	7	0.1
Bacterial infection	7	0.1
Bronchitis bacterial	7	0.1
Carpal tunnel syndrome	7	0.1
Chest discomfort	7	0.1
Chills	7	0.1
Coronary arterial stent insertion	7	0.1
Coronary artery stenosis	7	0.1
Dermatitis	7	0.1
Drug intolerance	7	0.1
Dysphagia	7	0.1
Eye inflammation	7	0.1
Femoral neck fracture	7	0.1
Flushing	7	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Fungal infection	7	0.1
Gingivitis	7	0.1
Hyperuricaemia	7	0.1
Inguinal hernia repair	7	0.1
Middle ear inflammation	7	0.1
Multiple fractures	7	0.1
Musculoskeletal discomfort	7	0.1
Osteoporotic fracture	7	0.1
Rash macular	7	0.1
Sepsis	7	0.1
Skin reaction	7	0.1
Sudden hearing loss	7	0.1
Tachycardia	7	0.1
Vasculitis	7	0.1
Vision blurred	7	0.1
Visual impairment	7	0.1
Vitamin D deficiency	7	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Accident at work	6	0.1
Acute kidney injury	6	0.1
Asthma	6	0.1
Cellulitis	6	0.1
Cholecystitis	6	0.1
Chronic sinusitis	6	0.1
Deep vein thrombosis	6	0.1
Drug eruption	6	0.1
Dry skin	6	0.1
Ear pain	6	0.1
Fungal skin infection	6	0.1
Gastroenteritis norovirus	6	0.1
Hip surgery	6	0.1
Hypothyroidism	6	0.1
Injection site swelling	6	0.1
Iritis	6	0.1
Migraine	6	0.1

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Movement disorder	6	0.1
Musculoskeletal pain	6	0.1
Nail bed inflammation	6	0.1
Onychomycosis	6	0.1
Ovarian cyst	6	0.1
Paronychia	6	0.1
Peripheral arterial occlusive disease	6	0.1
Prostate cancer	6	0.1
Pulmonary fibrosis	6	0.1
Renal colic	6	0.1
Rheumatoid factor increased	6	0.1
Road traffic accident	6	0.1
Shoulder operation	6	0.1
Somnolence	6	0.1
Spinal fusion surgery	6	0.1
Tendon operation	6	0.1
Ulna fracture	6	0.1

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Vertigo	6	0.1
Vulvovaginal mycotic infection	6	0.1
Abdominal distension	5	0.1
Acquired claw toe	5	0.1
Aortic valve replacement	5	0.1
Baker's cyst excision	5	0.1
Benign prostatic hyperplasia	5	0.1
Blood creatinine increased	5	0.1
Body temperature increased	5	0.1
Breast abscess	5	0.1
Cardiac pacemaker insertion	5	0.1
Cerebral infarction	5	0.1
Cholecystitis acute	5	0.1
Colitis	5	0.1
Colitis microscopic	5	0.1
Dental care	5	0.1
Dermatosis	5	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Device related infection	5	0.1
Exostosis	5	0.1
Femur fracture	5	0.1
Folliculitis	5	0.1
Fracture	5	0.1
Gastroenteritis viral	5	0.1
Gastrointestinal pain	5	0.1
Gastroesophageal reflux disease	5	0.1
Haematochezia	5	0.1
Hyperlipidaemia	5	0.1
Leukocytosis	5	0.1
Lupus-like syndrome	5	0.1
Meniscus removal	5	0.1
Oral candidiasis	5	0.1
Osteochondrosis	5	0.1
Osteomyelitis	5	0.1
Rosacea	5	0.1

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(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Sinus operation	5	0.1
Sjogren's syndrome	5	0.1
Spinal column stenosis	5	0.1
Syncope	5	0.1
Thoracic vertebral fracture	5	0.1
Thyroidectomy	5	0.1
Toe operation	5	0.1
Tooth abscess	5	0.1
Transient ischaemic attack	5	0.1
Tuberculosis	5	0.1
Type 2 diabetes mellitus	5	0.1
Abdominal pain	4	0.1
Abscess	4	0.1
Ankle arthroplasty	4	0.1
Ankle fracture	4	0.1
Anxiety disorder	4	0.1
Bladder cancer	4	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
C-reactive protein increased	4	0.1
Cerebellar infarction	4	0.1
Chronic kidney disease	4	0.1
Computerised tomogram thorax abnormal	4	0.1
Condition aggravated	4	0.1
Decreased appetite	4	0.1
Depressed mood	4	0.1
Device dislocation	4	0.1
Dry eye	4	0.1
Ear discomfort	4	0.1
Endocarditis	4	0.1
Endodontic procedure	4	0.1
Enteritis	4	0.1
Enthesopathy	4	0.1
Epilepsy	4	0.1
Erythema migrans	4	0.1
Essential hypertension	4	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Fracture displacement	4	0.1
Gastric ulcer	4	0.1
Genital herpes	4	0.1
Glaucoma	4	0.1
Gout	4	0.1
Haemoptysis	4	0.1
Hemiparesis	4	0.1
Histology normal	4	0.1
Hypercholesterolaemia	4	0.1
Hypertensive crisis	4	0.1
Hypoaesthesia oral	4	0.1
Hysterectomy	4	0.1
Inflammatory marker increased	4	0.1
Inguinal hernia	4	0.1
Injection site hypersensitivity	4	0.1
Injection site urticaria	4	0.1
Joint range of motion decreased	4	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Laryngeal inflammation	4	0.1
Localised infection	4	0.1
Lower limb fracture	4	0.1
Lung infection	4	0.1
Lymphoedema	4	0.1
Malaise	4	0.1
Meningitis	4	0.1
Meniscus injury	4	0.1
Muscle spasms	4	0.1
Nephrolithiasis	4	0.1
No adverse event	4	0.1
Osteitis	4	0.1
Pain management	4	0.1
Pelvic fracture	4	0.1
Perforated ulcer	4	0.1
Peripheral venous disease	4	0.1
Post procedural complication	4	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Rash erythematous	4	0.1
Rash papular	4	0.1
Renal stone removal	4	0.1
Rheumatoid lung	4	0.1
Rib fracture	4	0.1
Rotator cuff repair	4	0.1
Seasonal allergy	4	0.1
Skin abrasion	4	0.1
Skin infection	4	0.1
Skin lesion	4	0.1
Skin papilloma	4	0.1
Sleep apnoea syndrome	4	0.1
Soft tissue infection	4	0.1
Spinal decompression	4	0.1
Squamous cell carcinoma	4	0.1
Stent placement	4	0.1
Swelling face	4	0.1

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Tendon sheath incision	4	0.1
Tibia fracture	4	0.1
Tooth infection	4	0.1
Toothache	4	0.1
Vertebral foraminal stenosis	4	0.1
Weight increased	4	0.1
Wisdom teeth removal	4	0.1
Wound	4	0.1
Wrist fracture	4	0.1
Wrist surgery	4	0.1
Abdominal operation	3	0.0
Accident	3	0.0
Accident at home	3	0.0
Adrenocortical steroid therapy	3	0.0
Alveolitis	3	0.0
Angina unstable	3	0.0
Ankle operation	3	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Aortic aneurysm	3	0.0
Aortic valve stenosis	3	0.0
Arthropathy	3	0.0
Autoimmune thyroiditis	3	0.0
Bile duct stone	3	0.0
Blepharitis	3	0.0
Blood cholesterol increased	3	0.0
Blood creatine phosphokinase increased	3	0.0
Blood pressure measurement	3	0.0
Bradycardia	3	0.0
Breast conserving surgery	3	0.0
Bronchitis chronic	3	0.0
Bronchitis viral	3	0.0
Bronchoscopy	3	0.0
Campylobacter infection	3	0.0
Cancer surgery	3	0.0
Cardiac failure chronic	3	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Cardiac operation	3	0.0
Cardiovascular disorder	3	0.0
Cerebrovascular disorder	3	0.0
Contusion	3	0.0
Coronary angioplasty	3	0.0
Cyst	3	0.0
Cyst removal	3	0.0
Delivery	3	0.0
Dental implantation	3	0.0
Diabetic foot	3	0.0
Disturbance in attention	3	0.0
Dizziness postural	3	0.0
Double stranded DNA antibody positive	3	0.0
Drug hypersensitivity	3	0.0
Dysaesthesia	3	0.0
Emergency care	3	0.0
Epicondylitis	3	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Epigastric discomfort	3	0.0
Epstein-Barr virus infection	3	0.0
Eye operation	3	0.0
Eyelid oedema	3	0.0
Feeling cold	3	0.0
Fibromyalgia	3	0.0
Furuncle	3	0.0
Gallbladder operation	3	0.0
Gingival recession	3	0.0
Groin abscess	3	0.0
Haemarthrosis	3	0.0
Haematoma evacuation	3	0.0
Haemorrhage	3	0.0
Hand dermatitis	3	0.0
Hand fracture	3	0.0
Hepatic cirrhosis	3	0.0
Hepatic enzyme increased	3	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Hepatic steatosis	3	0.0
Herpes simplex	3	0.0
Hot flush	3	0.0
Hypertonia	3	0.0
Injection site inflammation	3	0.0
Injection site rash	3	0.0
Intervertebral discitis	3	0.0
Invasive ductal breast carcinoma	3	0.0
Iridocyclitis	3	0.0
Liver disorder	3	0.0
Menorrhagia	3	0.0
Metastases to bone	3	0.0
Mouth ulceration	3	0.0
Musculoskeletal stiffness	3	0.0
Myelodysplastic syndrome	3	0.0
Nasal herpes	3	0.0
Nasal inflammation	3	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Nasal operation	3	0.0
Noninfective gingivitis	3	0.0
Obesity	3	0.0
Oedema	3	0.0
Pancreatic carcinoma	3	0.0
Patella fracture	3	0.0
Performance status decreased	3	0.0
Pertussis	3	0.0
Photosensitivity reaction	3	0.0
Pulmonary tuberculosis	3	0.0
Removal of internal fixation	3	0.0
Renal impairment	3	0.0
Restlessness	3	0.0
Retching	3	0.0
Root canal infection	3	0.0
Salmonellosis	3	0.0
Seizure	3	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Septic shock	3	0.0
Shoulder arthroplasty	3	0.0
Sigmoidectomy	3	0.0
Skin burning sensation	3	0.0
Skin cancer	3	0.0
Skin graft	3	0.0
Spinal fracture	3	0.0
Spondylolisthesis	3	0.0
Sputum discoloured	3	0.0
Thrombophlebitis	3	0.0
Thyroid mass	3	0.0
Transurethral prostatectomy	3	0.0
Venous thrombosis limb	3	0.0
Wound infection	3	0.0
Abdominal pain lower	2	0.0
Abscess neck	2	0.0
Abscess oral	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Acne	2	0.0
Adverse reaction	2	0.0
Agoraphobia	2	0.0
Alcohol detoxification	2	0.0
Allergic sinusitis	2	0.0
Alveolitis allergic	2	0.0
Animal bite	2	0.0
Antiallergic therapy	2	0.0
Antinuclear antibody	2	0.0
Antinuclear antibody positive	2	0.0
Aortic dilatation	2	0.0
Aortic valve incompetence	2	0.0
Apathy	2	0.0
Aphasia	2	0.0
Appendectomy	2	0.0
Appendicitis perforated	2	0.0
Arterial stent insertion	2	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Aspartate aminotransferase increased	2	0.0
B-cell lymphoma	2	0.0
Balance disorder	2	0.0
Biliary colic	2	0.0
Biopsy bone marrow	2	0.0
Biopsy liver	2	0.0
Blood pressure decreased	2	0.0
Blood triglycerides increased	2	0.0
Bone contusion	2	0.0
Bowen's disease	2	0.0
Breast neoplasm	2	0.0
Breast reconstruction	2	0.0
Bronchial carcinoma	2	0.0
Cardiac ablation	2	0.0
Cartilage operation	2	0.0
Cerebral ischaemia	2	0.0
Cervical conisation	2	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Cervix carcinoma	2	0.0
Chemotherapy	2	0.0
Cholangitis	2	0.0
Cholestasis	2	0.0
Colitis ulcerative	2	0.0
Computerised tomogram thorax	2	0.0
Constipation	2	0.0
Craniocerebral injury	2	0.0
Crohn's disease	2	0.0
Decubitus ulcer	2	0.0
Dehydration	2	0.0
Dental discomfort	2	0.0
Device breakage	2	0.0
Diabetic neuropathy	2	0.0
Diplopia	2	0.0
Diverticular perforation	2	0.0
Drug effect decreased	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Dyspepsia	2	0.0
Dysphonia	2	0.0
Ear infection	2	0.0
Emphysema	2	0.0
Eosinophilia	2	0.0
Erectile dysfunction	2	0.0
Escherichia sepsis	2	0.0
Eye haemorrhage	2	0.0
Eye infection	2	0.0
Eye pain	2	0.0
Eye swelling	2	0.0
Facet joint syndrome	2	0.0
Fibula fracture	2	0.0
Fractured ischium	2	0.0
Gait disturbance	2	0.0
Gastrectomy	2	0.0
Gastritis erosive	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Genital infection fungal	2	0.0
Genitourinary tract infection	2	0.0
Guttate psoriasis	2	0.0
Gynaecomastia	2	0.0
Haemoglobin decreased	2	0.0
Haemorrhoids	2	0.0
Hernia repair	2	0.0
Herpes dermatitis	2	0.0
Herpes ophthalmic	2	0.0
Hiatus hernia	2	0.0
Hypercalcaemia	2	0.0
Hyperchromic anaemia	2	0.0
Hyperglycaemia	2	0.0
Hypertensive heart disease	2	0.0
Hyperthyroidism	2	0.0
Hyperventilation	2	0.0
Hypotension	2	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Immunosuppression	2	0.0
Infectious colitis	2	0.0
Infectious pleural effusion	2	0.0
Infiltration anaesthesia	2	0.0
Injection	2	0.0
Injection site abscess	2	0.0
Injection site dermatitis	2	0.0
Injection site induration	2	0.0
Injection site warmth	2	0.0
Injury	2	0.0
Interstitial lung disease	2	0.0
Intervertebral disc disorder	2	0.0
Iron deficiency anaemia	2	0.0
Jaundice	2	0.0
Jaw operation	2	0.0
Joint dislocation reduction	2	0.0
Joint injection	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Joint stabilisation	2	0.0
Joint warmth	2	0.0
Keratitis	2	0.0
Latent tuberculosis	2	0.0
Left ventricular failure	2	0.0
Leg amputation	2	0.0
Leukocyturia	2	0.0
Ligament operation	2	0.0
Ligament rupture	2	0.0
Limb discomfort	2	0.0
Limb operation	2	0.0
Lip swelling	2	0.0
Lipoma	2	0.0
Lung infiltration	2	0.0
Lymph node tuberculosis	2	0.0
Macular degeneration	2	0.0
Massage	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Mastectomy	2	0.0
Mediastinoscopy	2	0.0
Medical device removal	2	0.0
Metatarsalgia	2	0.0
Metrorrhagia	2	0.0
Middle insomnia	2	0.0
Mitral valve incompetence	2	0.0
Monoparesis	2	0.0
Mood swings	2	0.0
Mucosal dryness	2	0.0
Myocarditis	2	0.0
Nasal congestion	2	0.0
Nasal polypectomy	2	0.0
Neck pain	2	0.0
Neoplasm skin	2	0.0
Neuralgia	2	0.0
Neurodermatitis	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Neuroma	2	0.0
Neutropenia	2	0.0
Nodal osteoarthritis	2	0.0
Ocular discomfort	2	0.0
Open reduction of fracture	2	0.0
Ostectomy	2	0.0
Osteonecrosis	2	0.0
Ovarian cancer	2	0.0
Ovarian cystectomy	2	0.0
Painful respiration	2	0.0
Pancreatitis acute	2	0.0
Papule	2	0.0
Paranasal sinus discomfort	2	0.0
Parkinson's disease	2	0.0
Parotitis	2	0.0
Pericarditis	2	0.0
Periodontitis	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Peripheral artery occlusion	2	0.0
Peritoneal abscess	2	0.0
Peritonitis	2	0.0
Pharyngeal inflammation	2	0.0
Plasma cell myeloma	2	0.0
Pneumonitis	2	0.0
Polypectomy	2	0.0
Poor quality sleep	2	0.0
Post procedural fistula	2	0.0
Postoperative care	2	0.0
Precancerous mucosal lesion	2	0.0
Prostatic operation	2	0.0
Pseudarthrosis	2	0.0
Pulmonary oedema	2	0.0
Pulmonary resection	2	0.0
Purpura	2	0.0
Purulence	2	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Radiotherapy	2	0.0
Rash maculo-papular	2	0.0
Rash vesicular	2	0.0
Rectal cancer	2	0.0
Red blood cell sedimentation rate increased	2	0.0
Renal pain	2	0.0
Restless legs syndrome	2	0.0
Scoliosis	2	0.0
Sensory disturbance	2	0.0
Sinobronchitis	2	0.0
Sinus node dysfunction	2	0.0
Sinus tachycardia	2	0.0
Skin exfoliation	2	0.0
Skin fissures	2	0.0
Skin lesion removal	2	0.0
Skin wound	2	0.0
Somatic symptom disorder	2	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Spinal instability	2	0.0
Staphylococcal infection	2	0.0
Staphylococcus test positive	2	0.0
Stress	2	0.0
Subarachnoid haemorrhage	2	0.0
Subileus	2	0.0
Suture related complication	2	0.0
Synovial rupture	2	0.0
Tendonitis	2	0.0
Tenoplasty	2	0.0
Thyroid operation	2	0.0
Tinea versicolour	2	0.0
Tongue discomfort	2	0.0
Tonsillectomy	2	0.0
Transitional cell carcinoma	2	0.0
Tremor	2	0.0
Ulcerative keratitis	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Ureteral stent insertion	2	0.0
Ureterolithiasis	2	0.0
Urinary tract obstruction	2	0.0
Urticarial vasculitis	2	0.0
Vaginal infection	2	0.0
Varicose vein operation	2	0.0
Vascular graft	2	0.0
Ventricular extrasystoles	2	0.0
Vertigo positional	2	0.0
Vestibular neuritis	2	0.0
Visual acuity reduced	2	0.0
Vitamin B12 deficiency	2	0.0
Vocal cord inflammation	2	0.0
Vulvovaginal candidiasis	2	0.0
Vulvovaginal inflammation	2	0.0
White blood cell count increased	2	0.0
Wound treatment	2	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Abdominal abscess	1	0.0
Abdominal hernia	1	0.0
Abdominal hernia repair	1	0.0
Abdominal tenderness	1	0.0
Abdominal wall abscess	1	0.0
Abortion spontaneous	1	0.0
Abscess jaw	1	0.0
Abscess of eyelid	1	0.0
Abscess soft tissue	1	0.0
Accidental death	1	0.0
Acetabulum fracture	1	0.0
Acinetobacter infection	1	0.0
Acne pustular	1	0.0
Activated partial thromboplastin time normal	1	0.0
Acute coronary syndrome	1	0.0
Acute myeloid leukaemia	1	0.0
Acute respiratory failure	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Acute sinusitis	1	0.0
Acute stress disorder	1	0.0
Adams-Stokes syndrome	1	0.0
Adhesiolysis	1	0.0
Adjustment disorder with depressed mood	1	0.0
Adrenocortical insufficiency acute	1	0.0
Adverse drug reaction	1	0.0
Agitation	1	0.0
Agranulocytosis	1	0.0
Alcohol use	1	0.0
Alcoholism	1	0.0
Allergic cough	1	0.0
Amenorrhoea	1	0.0
Anaemia vitamin B12 deficiency	1	0.0
Anal abscess	1	0.0
Anal erosion	1	0.0
Analgesic therapy	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Anaphylactic reaction	1	0.0
Aneurysm repair	1	0.0
Angioedema	1	0.0
Angiogram peripheral	1	0.0
Angioplasty	1	0.0
Ankle impingement	1	0.0
Anogenital warts	1	0.0
Anti-cyclic citrullinated peptide antibody positive	1	0.0
Antibody test abnormal	1	0.0
Anticoagulant therapy	1	0.0
Aortic aneurysm repair	1	0.0
Apicectomy	1	0.0
Apnoea	1	0.0
Application site reaction	1	0.0
Arterial aneurysm repair	1	0.0
Arterial bypass operation	1	0.0
Arterial catheterisation	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Arterial occlusive disease	1	0.0
Arteriogram coronary	1	0.0
Arteriosclerosis	1	0.0
Arteritis	1	0.0
Arthritis bacterial	1	0.0
Arthritis infective	1	0.0
Arthritis reactive	1	0.0
Arthrotomy	1	0.0
Aspartate aminotransferase normal	1	0.0
Atelectasis	1	0.0
Atrial flutter	1	0.0
Atypical fibroxanthoma	1	0.0
Atypical pneumonia	1	0.0
Auditory disorder	1	0.0
Auricular swelling	1	0.0
Autoantibody test	1	0.0
Autoimmune pancreatitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Autonomic ganglionectomy	1	0.0
Autonomic nervous system imbalance	1	0.0
Axonal neuropathy	1	0.0
Azotaemia	1	0.0
Bacterial vaginosis	1	0.0
Bacteriuria	1	0.0
Bartholin's cyst	1	0.0
Basedow's disease	1	0.0
Benign cardiac neoplasm	1	0.0
Bicytopenia	1	0.0
Biliary cirrhosis primary	1	0.0
Biopsy	1	0.0
Biopsy lymph gland	1	0.0
Bladder diverticulum	1	0.0
Bladder irritation	1	0.0
Bladder neoplasm	1	0.0
Bladder stenosis	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Blister infected	1	0.0
Blood bactericidal activity	1	0.0
Blood bilirubin increased	1	0.0
Blood calcium	1	0.0
Blood count abnormal	1	0.0
Blood glucose fluctuation	1	0.0
Blood immunoglobulin M increased	1	0.0
Blood lactate dehydrogenase	1	0.0
Blood pressure abnormal	1	0.0
Blood urea increased	1	0.0
Blood uric acid	1	0.0
Bone densitometry	1	0.0
Bone disorder	1	0.0
Bone fissure	1	0.0
Bone graft	1	0.0
Bone operation	1	0.0
Bone pain	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Bordetella infection	1	0.0
Borrelia test positive	1	0.0
Bradyarrhythmia	1	0.0
Brain neoplasm	1	0.0
Brain neoplasm malignant	1	0.0
Brain stem infarction	1	0.0
Breast mass	1	0.0
Breast pain	1	0.0
Bronchial lesion excision	1	0.0
Bronchial neoplasm	1	0.0
Bronchiectasis	1	0.0
Bronchiolitis	1	0.0
Bronchoscopy abnormal	1	0.0
Burns second degree	1	0.0
Bursal haematoma	1	0.0
Bursal operation	1	0.0
Bursitis infective	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Calcific deposits removal	1	0.0
Calculus urinary	1	0.0
Candida infection	1	0.0
Candida pneumonia	1	0.0
Candida test positive	1	0.0
Carbuncle	1	0.0
Cardiac flutter	1	0.0
Cardiac pacemaker replacement	1	0.0
Carotid arteriosclerosis	1	0.0
Carotid artery stenosis	1	0.0
Cartilage injury	1	0.0
Cast application	1	0.0
Catheterisation cardiac	1	0.0
Central obesity	1	0.0
Cerebral haemorrhage	1	0.0
Cerebral microangiopathy	1	0.0
Cerebrovascular operation	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Cervical dysplasia	1	0.0
Cervical laser therapy	1	0.0
Cervical spinal stenosis	1	0.0
Cervicobrachial syndrome	1	0.0
Cervix carcinoma stage 0	1	0.0
Chest X-ray abnormal	1	0.0
Chest wall operation	1	0.0
Chillblains	1	0.0
Chlamydia test positive	1	0.0
Chlamydial infection	1	0.0
Cholangiocarcinoma	1	0.0
Cholangitis infective	1	0.0
Cholecystitis chronic	1	0.0
Chondromalacia	1	0.0
Chronic gastritis	1	0.0
Chronic hepatitis C	1	0.0
Chronic lymphocytic leukaemia	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Chronic tonsillitis	1	0.0
Circulatory collapse	1	0.0
Clavicle fracture	1	0.0
Clostridial infection	1	0.0
Clostridial sepsis	1	0.0
Cognitive disorder	1	0.0
Colon cancer	1	0.0
Colon neoplasm	1	0.0
Colonoscopy	1	0.0
Colonoscopy normal	1	0.0
Compartment syndrome	1	0.0
Complex regional pain syndrome	1	0.0
Computerised tomogram abdomen abnormal	1	0.0
Computerised tomogram kidney abnormal	1	0.0
Congenital tongue anomaly	1	0.0
Coronary revascularisation	1	0.0
Cryotherapy	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Cutaneous leishmaniasis	1	0.0
Cutaneous lupus erythematosus	1	0.0
Cytopenia	1	0.0
DNA antibody positive	1	0.0
Debridement	1	0.0
Demyelinating polyneuropathy	1	0.0
Dermatophytosis	1	0.0
Developmental hip dysplasia	1	0.0
Device expulsion	1	0.0
Diabetes mellitus management	1	0.0
Diabetic gangrene	1	0.0
Diarrhoea haemorrhagic	1	0.0
Diffuse alopecia	1	0.0
Disseminated tuberculosis	1	0.0
Diverticulum intestinal	1	0.0
Drug interaction	1	0.0
Drug reaction with eosinophilia and systemic symptoms	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Drug specific antibody present	1	0.0
Duodenal ulcer	1	0.0
Duodenitis haemorrhagic	1	0.0
Dysgeusia	1	0.0
Dyskinesia	1	0.0
Dyspareunia	1	0.0
Dysphonia psychogenic	1	0.0
Dysplasia	1	0.0
Dysuria	1	0.0
Ear neoplasm malignant	1	0.0
Ear operation	1	0.0
Echocardiogram	1	0.0
Ectopic pregnancy	1	0.0
Eczema asteatotic	1	0.0
Eczema weeping	1	0.0
Ejection fraction decreased	1	0.0
Electrolyte imbalance	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Emergency care examination	1	0.0
Emphysematous cholecystitis	1	0.0
Encephalitis viral	1	0.0
Endocarditis staphylococcal	1	0.0
Endometriosis	1	0.0
Endoscopic retrograde cholangiopancreatography	1	0.0
Endoscopy	1	0.0
Endoscopy normal	1	0.0
Endoscopy upper gastrointestinal tract	1	0.0
Enterocolitis bacterial	1	0.0
Enterovirus infection	1	0.0
Epiglottic carcinoma	1	0.0
Epiglottic cyst	1	0.0
Epstein-Barr virus antibody positive	1	0.0
Erosive duodenitis	1	0.0
Erythema multiforme	1	0.0
Erythema of eyelid	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Erythropenia	1	0.0
Eschar	1	0.0
Escherichia urinary tract infection	1	0.0
Exercise tolerance decreased	1	0.0
Exfoliative rash	1	0.0
External ear pain	1	0.0
Extrasystoles	1	0.0
Extravasation	1	0.0
Eye disorder	1	0.0
Eye infection bacterial	1	0.0
Eye infection viral	1	0.0
Facial paresis	1	0.0
Faecaloma	1	0.0
Feeling abnormal	1	0.0
Feeling hot	1	0.0
Felty's syndrome	1	0.0
Femoral hernia	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Femoral hernia repair	1	0.0
Fibrin D dimer increased	1	0.0
Fibrosis	1	0.0
Fine motor skill dysfunction	1	0.0
Finger deformity	1	0.0
Fistula	1	0.0
Fistula repair	1	0.0
Flatulence	1	0.0
Fluid replacement	1	0.0
Food poisoning	1	0.0
Forced expiratory volume	1	0.0
Forearm fracture	1	0.0
Foreign travel	1	0.0
Fracture debridement	1	0.0
Frontal sinus operation	1	0.0
Gait inability	1	0.0
Gallbladder empyema	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Gallbladder perforation	1	0.0
Gamma-glutamyltransferase abnormal	1	0.0
Gastric antral vascular ectasia	1	0.0
Gastric cancer stage I	1	0.0
Gastric cancer stage III	1	0.0
Gastric operation	1	0.0
Gastric ulcer haemorrhage	1	0.0
Gastrointestinal haemorrhage	1	0.0
Gastrointestinal mucosal disorder	1	0.0
Gastrointestinal viral infection	1	0.0
Generalised tonic-clonic seizure	1	0.0
Genital candidiasis	1	0.0
Genital herpes zoster	1	0.0
Giardiasis	1	0.0
Gingival bleeding	1	0.0
Gingival discomfort	1	0.0
Gingival graft	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Gingival operation	1	0.0
Glaucoma surgery	1	0.0
Gliosis	1	0.0
Glossodynia	1	0.0
Granuloma	1	0.0
Groin pain	1	0.0
Gynaecological examination	1	0.0
Gynaecological examination normal	1	0.0
Haematocrit decreased	1	0.0
Haemochromatosis	1	0.0
Haemorrhagic diathesis	1	0.0
Haemostasis	1	0.0
Hallucination	1	0.0
Hallucination, auditory	1	0.0
Hand-foot-and-mouth disease	1	0.0
Head discomfort	1	0.0
Head injury	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Heart rate increased	1	0.0
Heart rate irregular	1	0.0
Heart valve replacement	1	0.0
Heat stroke	1	0.0
Helicobacter gastritis	1	0.0
Helicobacter infection	1	0.0
Henoch-Schonlein purpura	1	0.0
Hepatic enzyme abnormal	1	0.0
Hepatic fibrosis	1	0.0
Hepatitis cholestatic	1	0.0
Hereditary neuropathic amyloidosis	1	0.0
Herpes simplex encephalitis	1	0.0
Hidradenitis	1	0.0
Hip deformity	1	0.0
Hodgkin's disease	1	0.0
Hodgkin's disease mixed cellularity stage unspecified	1	0.0
Hordeolum	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Hyperaesthesia	1	0.0
Hyperferritinaemia	1	0.0
Hyperkalaemia	1	0.0
Hypertriglyceridaemia	1	0.0
Hypochloraemia	1	0.0
Hypochromic anaemia	1	0.0
Hypokalaemia	1	0.0
Hypophosphataemia	1	0.0
Hyposmia	1	0.0
Hypoventilation	1	0.0
Ileus	1	0.0
Ilium fracture	1	0.0
Illusion	1	0.0
Impetigo	1	0.0
Implantable defibrillator insertion	1	0.0
Increased bronchial secretion	1	0.0
Increased tendency to bruise	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Induration	1	0.0
Infected bite	1	0.0
Infected dermal cyst	1	0.0
Infected seroma	1	0.0
Infected skin ulcer	1	0.0
Infectious mononucleosis	1	0.0
Inflammation of lacrimal passage	1	0.0
Inflammation of wound	1	0.0
Infusion	1	0.0
Ingrowing nail	1	0.0
Injection related reaction	1	0.0
Injection site bruising	1	0.0
Injection site infection	1	0.0
Injection site oedema	1	0.0
Insomnia	1	0.0
Intercostal neuralgia	1	0.0
Intertrigo	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Intervertebral disc degeneration	1	0.0
Intestinal operation	1	0.0
Intestinal resection	1	0.0
Intestinal stenosis	1	0.0
Intracranial aneurysm	1	0.0
Intracranial venous sinus thrombosis	1	0.0
Intraductal papilloma of breast	1	0.0
Intraductal proliferative breast lesion	1	0.0
Intraocular lens implant	1	0.0
Invasive breast carcinoma	1	0.0
Iron deficiency	1	0.0
Irritable bowel syndrome	1	0.0
Jaw cyst	1	0.0
Joint debridement	1	0.0
Joint destruction	1	0.0
Joint fluid drainage	1	0.0
Joint injury	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Joint stiffness	1	0.0
Keratoplasty	1	0.0
Keratouveitis	1	0.0
Kidney infection	1	0.0
Kidney rupture	1	0.0
Laboratory test	1	0.0
Lactose intolerance	1	0.0
Lacunar infarction	1	0.0
Laparoscopy	1	0.0
Laparotomy	1	0.0
Laryngeal oedema	1	0.0
Left ventricular dysfunction	1	0.0
Leukoplakia oral	1	0.0
Lichenoid keratosis	1	0.0
Ligament pain	1	0.0
Limb crushing injury	1	0.0
Limb mass	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Limb traumatic amputation	1	0.0
Lip injury	1	0.0
Lip oedema	1	0.0
Lip repair	1	0.0
Lipoatrophy	1	0.0
Lithotripsy	1	0.0
Liver abscess	1	0.0
Liver function test	1	0.0
Lividity	1	0.0
Loss of consciousness	1	0.0
Low density lipoprotein increased	1	0.0
Lower respiratory tract infection	1	0.0
Lung abscess	1	0.0
Lung disorder	1	0.0
Lung neoplasm malignant	1	0.0
Lung squamous cell carcinoma stage III	1	0.0
Lung transplant	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Lymphadenitis	1	0.0
Lymphangitis	1	0.0
Lymphatic fistula	1	0.0
Lymphocyte count decreased	1	0.0
Lymphocytosis	1	0.0
Lymphoma	1	0.0
Lymphoma operation	1	0.0
Lymphopenia	1	0.0
Macular cyst	1	0.0
Madarosis	1	0.0
Malignant melanoma	1	0.0
Malignant melanoma in situ	1	0.0
Mammoplasty	1	0.0
Mania	1	0.0
Mastoiditis	1	0.0
Mean cell volume abnormal	1	0.0
Melaena	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Memory impairment	1	0.0
Meniere's disease	1	0.0
Meningoencephalitis herpetic	1	0.0
Meniscal degeneration	1	0.0
Menstrual disorder	1	0.0
Menstruation irregular	1	0.0
Metastases to liver	1	0.0
Metastases to lung	1	0.0
Metastases to lymph nodes	1	0.0
Metastases to thorax	1	0.0
Metastatic neoplasm	1	0.0
Microembolism	1	0.0
Mole excision	1	0.0
Mouth cyst	1	0.0
Mucocutaneous ulceration	1	0.0
Mucosal inflammation	1	0.0
Mucous membrane disorder	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Multiple injuries	1	0.0
Multiple organ dysfunction syndrome	1	0.0
Muscle contractions involuntary	1	0.0
Muscle fatigue	1	0.0
Muscle spasticity	1	0.0
Muscle strain	1	0.0
Muscular weakness	1	0.0
Mycobacterium marinum infection	1	0.0
Mycobacterium tuberculosis complex test positive	1	0.0
Myoclonus	1	0.0
Myofascial pain syndrome	1	0.0
Nail disorder	1	0.0
Nail operation	1	0.0
Nasal dryness	1	0.0
Nasal mucosal disorder	1	0.0
Nasal septal operation	1	0.0
Nasal septum deviation	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Nasal ulcer	1	0.0
Necrotising fasciitis	1	0.0
Nephrectomy	1	0.0
Nephroplasty	1	0.0
Nephrostomy	1	0.0
Nerve compression	1	0.0
Nerve injury	1	0.0
Nerve root compression	1	0.0
Neurectomy	1	0.0
Neuritis cranial	1	0.0
Neuroendocrine carcinoma	1	0.0
Neurological examination	1	0.0
Neurological symptom	1	0.0
Neurolysis	1	0.0
Neuropathy peripheral	1	0.0
Neurostimulator removal	1	0.0
Neutrophil count decreased	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Neutrophil count increased	1	0.0
Nightmare	1	0.0
Nocturnal dyspnoea	1	0.0
Non-Hodgkin's lymphoma	1	0.0
Noninfective sialoadenitis	1	0.0
Nystagmus	1	0.0
Ocular hyperaemia	1	0.0
Ocular hypertension	1	0.0
Odynophagia	1	0.0
Oedema mucosal	1	0.0
Oesophageal candidiasis	1	0.0
Oesophagitis	1	0.0
Off label use	1	0.0
Onychoclasia	1	0.0
Oophorectomy	1	0.0
Ophthalmic vein thrombosis	1	0.0
Optic neuritis	1	0.0

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(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Oral discomfort	1	0.0
Oral fungal infection	1	0.0
Oral mucosa erosion	1	0.0
Oral mucosal blistering	1	0.0
Orchitis	1	0.0
Orchitis noninfective	1	0.0
Organising pneumonia	1	0.0
Oropharyngitis fungal	1	0.0
Orthostatic intolerance	1	0.0
Ossiculoplasty	1	0.0
Otitis externa bacterial	1	0.0
Otitis externa fungal	1	0.0
Otitis media acute	1	0.0
Otosclerosis	1	0.0
Ovarian adhesion	1	0.0
Overdose	1	0.0
Pain in jaw	1	0.0

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(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Pancreatic duct rupture	1	0.0
Pancreatic duct stenosis	1	0.0
Pancreatic mass	1	0.0
Pancreatic operation	1	0.0
Pancreatitis	1	0.0
Pancreatitis chronic	1	0.0
Pancytopenia	1	0.0
Panic attack	1	0.0
Panic disorder	1	0.0
Panic reaction	1	0.0
Papilloedema	1	0.0
Papilloma excision	1	0.0
Papilloma viral infection	1	0.0
Paradoxical drug reaction	1	0.0
Paranasal cyst	1	0.0
Paraplegia	1	0.0
Parkinsonism	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Parotidectomy	1	0.0
Partial seizures	1	0.0
Pathological fracture	1	0.0
Pelvic venous thrombosis	1	0.0
Percutaneous coronary intervention	1	0.0
Pericardial effusion	1	0.0
Periodontal disease	1	0.0
Periodontal inflammation	1	0.0
Periostitis	1	0.0
Peripheral artery aneurysm	1	0.0
Peripheral artery stenosis	1	0.0
Peripheral artery thrombosis	1	0.0
Peripheral ischaemia	1	0.0
Peripheral sensorimotor neuropathy	1	0.0
Peritoneal lavage	1	0.0
Peritonsillitis	1	0.0
Perivascular dermatitis	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Petechiae	1	0.0
Pharyngeal operation	1	0.0
Pharyngitis streptococcal	1	0.0
Phlebectomy	1	0.0
Photophobia	1	0.0
Physiotherapy	1	0.0
Pigmentation disorder	1	0.0
Plantar erythema	1	0.0
Plasmacytoma	1	0.0
Platelet count normal	1	0.0
Platelet disorder	1	0.0
Pleural decortication	1	0.0
Pleural fibrosis	1	0.0
Pleurodesis	1	0.0
Pneumococcal sepsis	1	0.0
Pneumonia bacterial	1	0.0
Pneumonia escherichia	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Pneumonia fungal	1	0.0
Pneumonia legionella	1	0.0
Pneumonia necrotising	1	0.0
Pneumonia pseudomonal	1	0.0
Pneumonia viral	1	0.0
Poliomyelitis	1	0.0
Polyarthritis	1	0.0
Post herpetic neuralgia	1	0.0
Post polio syndrome	1	0.0
Post procedural haemorrhage	1	0.0
Postmenopause	1	0.0
Presyncope	1	0.0
Proctitis	1	0.0
Product intolerance	1	0.0
Prostatic dysplasia	1	0.0
Prostatic haemorrhage	1	0.0
Prostatitis	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Proteus test positive	1	0.0
Prothrombin time normal	1	0.0
Prurigo	1	0.0
Pseudomonas infection	1	0.0
Psoriatic arthropathy	1	0.0
Psychomotor retardation	1	0.0
Pulmonary congestion	1	0.0
Pulmonary hilum mass	1	0.0
Pulmonary mass	1	0.0
Pulmonary mycosis	1	0.0
Pulmonary sepsis	1	0.0
Pulmonary tuberculoma	1	0.0
Pyelocystitis	1	0.0
Pyeloplasty	1	0.0
Pyoderma	1	0.0
Pyonephrosis	1	0.0
Radical prostatectomy	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Radioactive iodine therapy	1	0.0
Raynaud's phenomenon	1	0.0
Rectal haemorrhage	1	0.0
Rectal polyp	1	0.0
Rectal polypectomy	1	0.0
Refractory cytopenia with unilineage dysplasia	1	0.0
Renal artery arteriosclerosis	1	0.0
Renal artery stenosis	1	0.0
Renal artery stent placement	1	0.0
Renal cell carcinoma recurrent	1	0.0
Renal function test abnormal	1	0.0
Renal infarct	1	0.0
Resuscitation	1	0.0
Retinal detachment	1	0.0
Rheumatic disorder	1	0.0
Rhinitis allergic	1	0.0
Rhonchi	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Right ventricular failure	1	0.0
Rubber sensitivity	1	0.0
SAPHO syndrome	1	0.0
Sacroiliitis	1	0.0
Salivary gland neoplasm	1	0.0
Salivary gland pain	1	0.0
Salpingo-oophorectomy	1	0.0
Sarcoidosis	1	0.0
Scar	1	0.0
Secretion discharge	1	0.0
Septic encephalopathy	1	0.0
Serum ferritin decreased	1	0.0
Serum ferritin increased	1	0.0
Shock haemorrhagic	1	0.0
Shock hypoglycaemic	1	0.0
Single functional kidney	1	0.0
Skin atrophy	1	0.0

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(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Skin cyst excision	1	0.0
Skin discomfort	1	0.0
Skin hypertrophy	1	0.0
Skin induration	1	0.0
Skin irritation	1	0.0
Skin necrosis	1	0.0
Skin tightness	1	0.0
Soft tissue injury	1	0.0
Soft tissue swelling	1	0.0
Spermatocele	1	0.0
Spinal cord ischaemia	1	0.0
Spinal cord operation	1	0.0
Spinal nerve stimulator implantation	1	0.0
Spondyloarthropathy	1	0.0
Spontaneous haematoma	1	0.0
Sputum purulent	1	0.0
Stab wound	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Staphylococcal sepsis	1	0.0
Stasis dermatitis	1	0.0
Sternotomy	1	0.0
Steroid therapy	1	0.0
Stress cardiomyopathy	1	0.0
Stress fracture	1	0.0
Stress urinary incontinence	1	0.0
Subcutaneous emphysema	1	0.0
Superinfection	1	0.0
Superinfection bacterial	1	0.0
Supraventricular tachycardia	1	0.0
Swollen tongue	1	0.0
Synovial cyst removal	1	0.0
Synovial disorder	1	0.0
Synoviorthesis	1	0.0
Systemic lupus erythematosus	1	0.0
Systemic lupus erythematosus rash	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Tachyarrhythmia	1	0.0
Tachycardia induced cardiomyopathy	1	0.0
Temporomandibular joint surgery	1	0.0
Tendon disorder	1	0.0
Tendon injury	1	0.0
Tenosynovitis stenans	1	0.0
Testicular abscess	1	0.0
Thalamic infarction	1	0.0
Therapeutic embolisation	1	0.0
Thirst	1	0.0
Thoracic cavity drainage	1	0.0
Throat clearing	1	0.0
Throat irritation	1	0.0
Throat tightness	1	0.0
Thrombolysis	1	0.0
Thrombophlebitis septic	1	0.0
Thyroid adenoma	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Thyroid cancer	1	0.0
Thyroid cancer recurrent	1	0.0
Thyroiditis	1	0.0
Thyroiditis subacute	1	0.0
Tinea pedis	1	0.0
Tobacco abuse	1	0.0
Toe amputation	1	0.0
Tongue blistering	1	0.0
Tongue operation	1	0.0
Tonsillar inflammation	1	0.0
Tonsillitis bacterial	1	0.0
Tonsillitis streptococcal	1	0.0
Tooth fracture	1	0.0
Tooth loss	1	0.0
Toxic encephalopathy	1	0.0
Tracheitis	1	0.0
Tracheobronchitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Transaminases abnormal	1	0.0
Transfusion	1	0.0
Traumatic fracture	1	0.0
Trigeminal neuralgia	1	0.0
Tuberculin test positive	1	0.0
Tuberculosis gastrointestinal	1	0.0
Tuberculosis of genitourinary system	1	0.0
Tuberculosis of intrathoracic lymph nodes	1	0.0
Tuberculous pleurisy	1	0.0
Tumour excision	1	0.0
Twin pregnancy	1	0.0
Tympanomastoidectomy	1	0.0
Ulcerative gastritis	1	0.0
Ultrasound abdomen abnormal	1	0.0
Ultrasound abdomen normal	1	0.0
Ultrasound scan	1	0.0
Ultrasound scan normal	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Umbilical hernia	1	0.0
Umbilical hernia repair	1	0.0
Unevaluable therapy	1	0.0
Upper limb fracture	1	0.0
Ureterectomy	1	0.0
Ureteric operation	1	0.0
Ureteric stenosis	1	0.0
Urinary hesitation	1	0.0
Urinary incontinence	1	0.0
Urinary incontinence surgery	1	0.0
Urinary sediment present	1	0.0
Urinary tract inflammation	1	0.0
Urinary tract neoplasm	1	0.0
Urogenital haemorrhage	1	0.0
Urogenital infection bacterial	1	0.0
Uterine cancer	1	0.0
Uterine dilation and curettage	1	0.0

(Continued)

5. Documented adverse events by patient

5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Uterine leiomyoma	1	0.0
Uterine polyp	1	0.0
Uterine polypectomy	1	0.0
Uveitis	1	0.0
Varicella	1	0.0
Varicella zoster virus infection	1	0.0
Varicose vein	1	0.0
Vascular stenosis	1	0.0
Vascular stent insertion	1	0.0
Venous operation	1	0.0
Venous thrombosis	1	0.0
Ventricular fibrillation	1	0.0
Vertebral artery dissection	1	0.0
Vertebral body replacement	1	0.0
Vertebral column mass	1	0.0
Vertebroplasty	1	0.0
Vestibular migraine	1	0.0

(Continued)

5. Documented adverse events by patient
 5.2 All documented adverse events by preferred term

	n	%
Preferred Term		
Vocal cord polyp	1	0.0
Vocal cord thickening	1	0.0
Vulval abscess	1	0.0
Weight bearing difficulty	1	0.0
White blood cell analysis abnormal	1	0.0
White blood cell count	1	0.0
White blood cell count decreased	1	0.0
Wolff-Parkinson-White syndrome	1	0.0
Wound closure	1	0.0
Wound drainage	1	0.0
Wound healing normal	1	0.0
Wound infection bacterial	1	0.0
Wrist deformity	1	0.0

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Total	1252	17.3
	Bronchitis	186	2.6
	Nasopharyngitis	138	1.9
	Upper respiratory tract infection	131	1.8
	Respiratory tract infection	110	1.5
	Infection	100	1.4
	Pneumonia	98	1.4
	Herpes zoster	85	1.2
	Urinary tract infection	77	1.1
	Sinusitis	65	0.9
	Oral herpes	47	0.7
	Cystitis	34	0.5
	Gastroenteritis	28	0.4
	Pulpitis dental	25	0.3
	Tonsillitis	23	0.3
	Erysipelas	22	0.3
Gastrointestinal infection	21	0.3	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Conjunctivitis	19	0.3
	Pharyngitis	19	0.3
	Rhinitis	19	0.3
	Diverticulitis	15	0.2
	Viral infection	15	0.2
	Otitis media	14	0.2
	Subcutaneous abscess	13	0.2
	Rash pustular	12	0.2
	Abscess limb	11	0.2
	Influenza	11	0.2
	Pyelonephritis	11	0.2
	Urosepsis	11	0.2
	Laryngitis	10	0.1
	Infection susceptibility increased	9	0.1
	Post procedural infection	9	0.1
	Postoperative wound infection	9	0.1
Borrelia infection	8	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Herpes virus infection	8	0.1
	Bacterial infection	7	0.1
	Bronchitis bacterial	7	0.1
	Fungal infection	7	0.1
	Gingivitis	7	0.1
	Sepsis	7	0.1
	Cellulitis	6	0.1
	Chronic sinusitis	6	0.1
	Fungal skin infection	6	0.1
	Gastroenteritis norovirus	6	0.1
	Onychomycosis	6	0.1
	Paronychia	6	0.1
	Vulvovaginal mycotic infection	6	0.1
	Breast abscess	5	0.1
	Device related infection	5	0.1
	Folliculitis	5	0.1
Gastroenteritis viral	5	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Oral candidiasis	5	0.1
	Osteomyelitis	5	0.1
	Tooth abscess	5	0.1
	Tuberculosis	5	0.1
	Abscess	4	0.1
	Endocarditis	4	0.1
	Erythema migrans	4	0.1
	Genital herpes	4	0.1
	Localised infection	4	0.1
	Lung infection	4	0.1
	Meningitis	4	0.1
	Skin infection	4	0.1
	Soft tissue infection	4	0.1
	Tooth infection	4	0.1
	Bronchitis viral	3	0.0
	Campylobacter infection	3	0.0
Epstein-Barr virus infection	3	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Furuncle	3	0.0
	Groin abscess	3	0.0
	Herpes simplex	3	0.0
	Intervertebral discitis	3	0.0
	Nasal herpes	3	0.0
	Pertussis	3	0.0
	Pulmonary tuberculosis	3	0.0
	Root canal infection	3	0.0
	Salmonellosis	3	0.0
	Septic shock	3	0.0
	Wound infection	3	0.0
	Abscess neck	2	0.0
	Abscess oral	2	0.0
	Appendicitis perforated	2	0.0
	Ear infection	2	0.0
	Escherichia sepsis	2	0.0
	Eye infection	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Genital infection fungal	2	0.0
	Genitourinary tract infection	2	0.0
	Herpes dermatitis	2	0.0
	Herpes ophthalmic	2	0.0
	Infectious colitis	2	0.0
	Infectious pleural effusion	2	0.0
	Injection site abscess	2	0.0
	Latent tuberculosis	2	0.0
	Lymph node tuberculosis	2	0.0
	Parotitis	2	0.0
	Periodontitis	2	0.0
	Peritoneal abscess	2	0.0
	Peritonitis	2	0.0
	Purulence	2	0.0
	Sinobronchitis	2	0.0
	Staphylococcal infection	2	0.0
Tinea versicolour	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Vaginal infection	2	0.0
	Vestibular neuronitis	2	0.0
	Vulvovaginal candidiasis	2	0.0
	Abdominal abscess	1	0.0
	Abdominal wall abscess	1	0.0
	Abscess jaw	1	0.0
	Abscess of eyelid	1	0.0
	Abscess soft tissue	1	0.0
	Acinetobacter infection	1	0.0
	Acne pustular	1	0.0
	Acute sinusitis	1	0.0
	Anal abscess	1	0.0
	Arthritis bacterial	1	0.0
	Arthritis infective	1	0.0
	Atypical pneumonia	1	0.0
	Bacterial vaginosis	1	0.0
	Bacteriuria	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Blister infected	1	0.0
	Bordetella infection	1	0.0
	Bronchiolitis	1	0.0
	Bursitis infective	1	0.0
	Candida infection	1	0.0
	Candida pneumonia	1	0.0
	Carbuncle	1	0.0
	Chlamydial infection	1	0.0
	Cholangitis infective	1	0.0
	Chronic hepatitis C	1	0.0
	Chronic tonsillitis	1	0.0
	Clostridial infection	1	0.0
	Clostridial sepsis	1	0.0
	Cutaneous leishmaniasis	1	0.0
	Dermatophytosis	1	0.0
	Diabetic gangrene	1	0.0
Disseminated tuberculosis	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Emphysematous cholecystitis	1	0.0
	Encephalitis viral	1	0.0
	Endocarditis staphylococcal	1	0.0
	Enterocolitis bacterial	1	0.0
	Enterovirus infection	1	0.0
	Escherichia urinary tract infection	1	0.0
	Eye infection bacterial	1	0.0
	Eye infection viral	1	0.0
	Gallbladder empyema	1	0.0
	Gastrointestinal viral infection	1	0.0
	Genital candidiasis	1	0.0
	Genital herpes zoster	1	0.0
	Giardiasis	1	0.0
	Hand-foot-and-mouth disease	1	0.0
	Helicobacter gastritis	1	0.0
	Helicobacter infection	1	0.0
Herpes simplex encephalitis	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Hordeolum	1	0.0
	Impetigo	1	0.0
	Infected bite	1	0.0
	Infected dermal cyst	1	0.0
	Infected seroma	1	0.0
	Infected skin ulcer	1	0.0
	Infectious mononucleosis	1	0.0
	Injection site infection	1	0.0
	Keratouveitis	1	0.0
	Kidney infection	1	0.0
	Liver abscess	1	0.0
	Lower respiratory tract infection	1	0.0
	Lung abscess	1	0.0
	Lymphangitis	1	0.0
	Mastoiditis	1	0.0
	Meningoencephalitis herpetic	1	0.0
Mycobacterium marinum infection	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Necrotising fasciitis	1	0.0
	Oesophageal candidiasis	1	0.0
	Oral fungal infection	1	0.0
	Orchitis	1	0.0
	Oropharyngitis fungal	1	0.0
	Otitis externa bacterial	1	0.0
	Otitis externa fungal	1	0.0
	Otitis media acute	1	0.0
	Papilloma viral infection	1	0.0
	Peritonsillitis	1	0.0
	Pharyngitis streptococcal	1	0.0
	Pneumococcal sepsis	1	0.0
	Pneumonia bacterial	1	0.0
	Pneumonia escherichia	1	0.0
	Pneumonia fungal	1	0.0
	Pneumonia legionella	1	0.0
Pneumonia necrotising	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Pneumonia pseudomonal	1	0.0
	Pneumonia viral	1	0.0
	Poliomyelitis	1	0.0
	Pseudomonas infection	1	0.0
	Pulmonary mycosis	1	0.0
	Pulmonary sepsis	1	0.0
	Pulmonary tuberculoma	1	0.0
	Pyelocystitis	1	0.0
	Pyoderma	1	0.0
	Pyonephrosis	1	0.0
	Septic encephalopathy	1	0.0
	Sputum purulent	1	0.0
	Staphylococcal sepsis	1	0.0
	Superinfection	1	0.0
	Superinfection bacterial	1	0.0
	Testicular abscess	1	0.0
Thrombophlebitis septic	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Tinea pedis	1	0.0
	Tonsillitis bacterial	1	0.0
	Tonsillitis streptococcal	1	0.0
	Tracheitis	1	0.0
	Tracheobronchitis	1	0.0
	Tuberculosis gastrointestinal	1	0.0
	Tuberculosis of genitourinary system	1	0.0
	Tuberculosis of intrathoracic lymph nodes	1	0.0
	Tuberculous pleurisy	1	0.0
	Urogenital infection bacterial	1	0.0
	Varicella	1	0.0
	Varicella zoster virus infection	1	0.0
	Vulval abscess	1	0.0
	Wound infection bacterial	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Total	698	9.7
	Hospitalisation	115	1.6
	Therapy cessation	87	1.2
	Elective surgery	73	1.0
	Antibiotic therapy	43	0.6
	Knee arthroplasty	40	0.6
	Arthrodesis	35	0.5
	Synovectomy	29	0.4
	Hip arthroplasty	28	0.4
	Foot operation	26	0.4
	Antibiotic prophylaxis	25	0.3
	Joint arthroplasty	24	0.3
	Joint surgery	18	0.2
	Bunion operation	17	0.2
	Cataract operation	16	0.2
	Therapy change	16	0.2
Tooth extraction	16	0.2	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Knee operation	15	0.2
	Surgery	14	0.2
	Cholecystectomy	12	0.2
	Rheumatoid nodule removal	12	0.2
	Spinal operation	11	0.2
	Intervertebral disc operation	10	0.1
	Bursa removal	9	0.1
	Dental operation	9	0.1
	Osteotomy	9	0.1
	Rehabilitation therapy	9	0.1
	Skin neoplasm excision	9	0.1
	Arthroscopic surgery	8	0.1
	Carpal tunnel decompression	8	0.1
	Coronary artery bypass	8	0.1
	Fracture treatment	8	0.1
	Laparoscopic surgery	8	0.1
	Meniscus operation	8	0.1

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Osteosynthesis	8	0.1
	Abscess drainage	7	0.1
	Coronary arterial stent insertion	7	0.1
	Inguinal hernia repair	7	0.1
	Hip surgery	6	0.1
	Shoulder operation	6	0.1
	Spinal fusion surgery	6	0.1
	Tendon operation	6	0.1
	Aortic valve replacement	5	0.1
	Baker's cyst excision	5	0.1
	Cardiac pacemaker insertion	5	0.1
	Dental care	5	0.1
	Meniscus removal	5	0.1
	Sinus operation	5	0.1
	Thyroidectomy	5	0.1
	Toe operation	5	0.1
	Ankle arthroplasty	4	0.1

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Endodontic procedure	4	0.1
	Hysterectomy	4	0.1
	Pain management	4	0.1
	Renal stone removal	4	0.1
	Rotator cuff repair	4	0.1
	Spinal decompression	4	0.1
	Stent placement	4	0.1
	Tendon sheath incision	4	0.1
	Wisdom teeth removal	4	0.1
	Wrist surgery	4	0.1
	Abdominal operation	3	0.0
	Adrenocortical steroid therapy	3	0.0
	Ankle operation	3	0.0
	Breast conserving surgery	3	0.0
	Cancer surgery	3	0.0
	Cardiac operation	3	0.0
Coronary angioplasty	3	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Cyst removal	3	0.0
	Dental implantation	3	0.0
	Emergency care	3	0.0
	Eye operation	3	0.0
	Gallbladder operation	3	0.0
	Haematoma evacuation	3	0.0
	Nasal operation	3	0.0
	Removal of internal fixation	3	0.0
	Shoulder arthroplasty	3	0.0
	Sigmoidectomy	3	0.0
	Skin graft	3	0.0
	Transurethral prostatectomy	3	0.0
	Alcohol detoxification	2	0.0
	Antiallergic therapy	2	0.0
	Appendectomy	2	0.0
	Arterial stent insertion	2	0.0
	Breast reconstruction	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Cardiac ablation	2	0.0
	Cartilage operation	2	0.0
	Cervical conisation	2	0.0
	Chemotherapy	2	0.0
	Gastrectomy	2	0.0
	Hernia repair	2	0.0
	Infiltration anaesthesia	2	0.0
	Injection	2	0.0
	Jaw operation	2	0.0
	Joint dislocation reduction	2	0.0
	Joint injection	2	0.0
	Joint stabilisation	2	0.0
	Leg amputation	2	0.0
	Ligament operation	2	0.0
	Limb operation	2	0.0
	Massage	2	0.0
Mastectomy	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Medical device removal	2	0.0
	Nasal polypectomy	2	0.0
	Open reduction of fracture	2	0.0
	Ostectomy	2	0.0
	Ovarian cystectomy	2	0.0
	Polypectomy	2	0.0
	Postoperative care	2	0.0
	Prostatic operation	2	0.0
	Pulmonary resection	2	0.0
	Radiotherapy	2	0.0
	Skin lesion removal	2	0.0
	Tenoplasty	2	0.0
	Thyroid operation	2	0.0
	Tonsillectomy	2	0.0
	Ureteral stent insertion	2	0.0
Varicose vein operation	2	0.0	
Vascular graft	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Wound treatment	2	0.0
	Abdominal hernia repair	1	0.0
	Adhesiolysis	1	0.0
	Analgesic therapy	1	0.0
	Aneurysm repair	1	0.0
	Angioplasty	1	0.0
	Anticoagulant therapy	1	0.0
	Aortic aneurysm repair	1	0.0
	Apicectomy	1	0.0
	Arterial aneurysm repair	1	0.0
	Arterial bypass operation	1	0.0
	Arterial catheterisation	1	0.0
	Arthrotomy	1	0.0
	Autonomic ganglionectomy	1	0.0
	Bone graft	1	0.0
	Bone operation	1	0.0
Bronchial lesion excision	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Bursal operation	1	0.0
	Calcific deposits removal	1	0.0
	Cardiac pacemaker replacement	1	0.0
	Cast application	1	0.0
	Cerebrovascular operation	1	0.0
	Cervical laser therapy	1	0.0
	Chest wall operation	1	0.0
	Coronary revascularisation	1	0.0
	Cryotherapy	1	0.0
	Debridement	1	0.0
	Diabetes mellitus management	1	0.0
	Ear operation	1	0.0
	Femoral hernia repair	1	0.0
	Fistula repair	1	0.0
	Fluid replacement	1	0.0
	Fracture debridement	1	0.0
Frontal sinus operation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Gastric operation	1	0.0
	Gingival graft	1	0.0
	Gingival operation	1	0.0
	Glaucoma surgery	1	0.0
	Haemostasis	1	0.0
	Heart valve replacement	1	0.0
	Implantable defibrillator insertion	1	0.0
	Infusion	1	0.0
	Intestinal operation	1	0.0
	Intestinal resection	1	0.0
	Intraocular lens implant	1	0.0
	Joint debridement	1	0.0
	Joint fluid drainage	1	0.0
	Keratoplasty	1	0.0
	Laparotomy	1	0.0
	Lip repair	1	0.0
Lithotripsy	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Lung transplant	1	0.0
	Lymphoma operation	1	0.0
	Mammoplasty	1	0.0
	Mole excision	1	0.0
	Nail operation	1	0.0
	Nasal septal operation	1	0.0
	Nephrectomy	1	0.0
	Nephroplasty	1	0.0
	Nephrostomy	1	0.0
	Neurectomy	1	0.0
	Neurolysis	1	0.0
	Neurostimulator removal	1	0.0
	Oophorectomy	1	0.0
	Ossiculoplasty	1	0.0
	Pancreatic operation	1	0.0
	Papilloma excision	1	0.0
Parotidectomy	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Percutaneous coronary intervention	1	0.0
	Peritoneal lavage	1	0.0
	Pharyngeal operation	1	0.0
	Phlebectomy	1	0.0
	Physiotherapy	1	0.0
	Pleural decortication	1	0.0
	Pleurodesis	1	0.0
	Pyeloplasty	1	0.0
	Radical prostatectomy	1	0.0
	Radioactive iodine therapy	1	0.0
	Rectal polypectomy	1	0.0
	Renal artery stent placement	1	0.0
	Resuscitation	1	0.0
	Salpingo-oophorectomy	1	0.0
	Skin cyst excision	1	0.0
Spinal cord operation	1	0.0	
Spinal nerve stimulator implantation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Sternotomy	1	0.0
	Steroid therapy	1	0.0
	Synovial cyst removal	1	0.0
	Synoviorthesis	1	0.0
	Temporomandibular joint surgery	1	0.0
	Therapeutic embolisation	1	0.0
	Thoracic cavity drainage	1	0.0
	Thrombolysis	1	0.0
	Toe amputation	1	0.0
	Tongue operation	1	0.0
	Transfusion	1	0.0
	Tumour excision	1	0.0
	Tympanomastoidectomy	1	0.0
	Umbilical hernia repair	1	0.0
	Unevaluable therapy	1	0.0
Ureterectomy	1	0.0	
Ureteric operation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Urinary incontinence surgery	1	0.0
	Uterine dilation and curettage	1	0.0
	Uterine polypectomy	1	0.0
	Vascular stent insertion	1	0.0
	Venous operation	1	0.0
	Vertebral body replacement	1	0.0
	Vertebroplasty	1	0.0
	Wound closure	1	0.0
	Wound drainage	1	0.0
General disorders and administration site conditions	Total	620	8.6
	Influenza like illness	215	3.0
	Pyrexia	82	1.1
	Drug ineffective	52	0.7
	Fatigue	45	0.6
	Injection site erythema	40	0.6
	Unevaluable event	29	0.4
	Injection site reaction	20	0.3

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Injection site pruritus	18	0.2
	Impaired healing	17	0.2
	Death	16	0.2
	Pain	16	0.2
	Asthenia	13	0.2
	Peripheral swelling	13	0.2
	Oedema peripheral	12	0.2
	Complication associated with device	11	0.2
	Chest pain	10	0.1
	General physical health deterioration	10	0.1
	Inflammation	8	0.1
	Injection site pain	8	0.1
	Local reaction	8	0.1
	Swelling	8	0.1
	Chest discomfort	7	0.1
	Chills	7	0.1
Drug intolerance	7	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Injection site swelling	6	0.1
	Condition aggravated	4	0.1
	Injection site hypersensitivity	4	0.1
	Injection site urticaria	4	0.1
	Malaise	4	0.1
	No adverse event	4	0.1
	Perforated ulcer	4	0.1
	Cyst	3	0.0
	Feeling cold	3	0.0
	Injection site inflammation	3	0.0
	Injection site rash	3	0.0
	Oedema	3	0.0
	Performance status decreased	3	0.0
	Adverse reaction	2	0.0
	Drug effect decreased	2	0.0
	Gait disturbance	2	0.0
	Injection site dermatitis	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Injection site induration	2	0.0
	Injection site warmth	2	0.0
	Mucosal dryness	2	0.0
	Precancerous mucosal lesion	2	0.0
	Accidental death	1	0.0
	Adverse drug reaction	1	0.0
	Application site reaction	1	0.0
	Drug interaction	1	0.0
	Dysplasia	1	0.0
	Exercise tolerance decreased	1	0.0
	Extravasation	1	0.0
	Feeling abnormal	1	0.0
	Feeling hot	1	0.0
	Fibrosis	1	0.0
	Gait inability	1	0.0
	Granuloma	1	0.0
Induration	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Injection site bruising	1	0.0
	Injection site oedema	1	0.0
	Mucosal inflammation	1	0.0
	Mucous membrane disorder	1	0.0
	Multiple organ dysfunction syndrome	1	0.0
	Oedema mucosal	1	0.0
	Paradoxical drug reaction	1	0.0
	Product intolerance	1	0.0
	Secretion discharge	1	0.0
	Thirst	1	0.0
Musculoskeletal and connective tissue disorders	Total	459	6.3
	Rheumatoid arthritis	104	1.4
	Osteoarthritis	36	0.5
	Arthralgia	35	0.5
	Back pain	28	0.4
	Bursitis	27	0.4
	Pain in extremity	27	0.4

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Intervertebral disc protrusion	26	0.4
	Arthritis	21	0.3
	Foot deformity	19	0.3
	Joint swelling	18	0.2
	Synovial cyst	18	0.2
	Rotator cuff syndrome	14	0.2
	Spinal pain	14	0.2
	Lumbar spinal stenosis	13	0.2
	Osteoporosis	11	0.2
	Joint effusion	10	0.1
	Osteopenia	9	0.1
	Rheumatoid nodule	9	0.1
	Spinal osteoarthritis	9	0.1
	Synovitis	9	0.1
	Tenosynovitis	9	0.1
	Myalgia	8	0.1
Musculoskeletal discomfort	7	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Osteoporotic fracture	7	0.1
	Musculoskeletal pain	6	0.1
	Acquired claw toe	5	0.1
	Exostosis	5	0.1
	Lupus-like syndrome	5	0.1
	Osteochondrosis	5	0.1
	Sjogren's syndrome	5	0.1
	Spinal column stenosis	5	0.1
	Enthesopathy	4	0.1
	Joint range of motion decreased	4	0.1
	Muscle spasms	4	0.1
	Osteitis	4	0.1
	Vertebral foraminal stenosis	4	0.1
	Arthropathy	3	0.0
	Fibromyalgia	3	0.0
	Haemarthrosis	3	0.0
Musculoskeletal stiffness	3	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Spondylolisthesis	3	0.0
	Facet joint syndrome	2	0.0
	Intervertebral disc disorder	2	0.0
	Joint warmth	2	0.0
	Limb discomfort	2	0.0
	Metatarsalgia	2	0.0
	Neck pain	2	0.0
	Nodal osteoarthritis	2	0.0
	Osteonecrosis	2	0.0
	Pseudarthrosis	2	0.0
	Scoliosis	2	0.0
	Spinal instability	2	0.0
	Tendonitis	2	0.0
	Ankle impingement	1	0.0
	Arthritis reactive	1	0.0
	Bone disorder	1	0.0
Bone pain	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Bursal haematoma	1	0.0
	Cervical spinal stenosis	1	0.0
	Chondromalacia	1	0.0
	Compartment syndrome	1	0.0
	Felty's syndrome	1	0.0
	Finger deformity	1	0.0
	Fistula	1	0.0
	Groin pain	1	0.0
	Hip deformity	1	0.0
	Intervertebral disc degeneration	1	0.0
	Jaw cyst	1	0.0
	Joint destruction	1	0.0
	Joint stiffness	1	0.0
	Ligament pain	1	0.0
	Limb mass	1	0.0
	Meniscal degeneration	1	0.0
Muscle fatigue	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Muscular weakness	1	0.0
	Myofascial pain syndrome	1	0.0
	Pain in jaw	1	0.0
	Pathological fracture	1	0.0
	Periostitis	1	0.0
	Polyarthritis	1	0.0
	Psoriatic arthropathy	1	0.0
	Rheumatic disorder	1	0.0
	SAPHO syndrome	1	0.0
	Sacroiliitis	1	0.0
	Soft tissue swelling	1	0.0
	Spondyloarthropathy	1	0.0
	Synovial disorder	1	0.0
	Systemic lupus erythematosus	1	0.0
	Tendon disorder	1	0.0
	Tenosynovitis stenosans	1	0.0
Vertebral column mass	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Weight bearing difficulty	1	0.0
	Wrist deformity	1	0.0
Skin and subcutaneous tissue disorders	Total	426	5.9
	Rash	67	0.9
	Pruritus	55	0.8
	Psoriasis	36	0.5
	Erythema	33	0.5
	Rash pruritic	29	0.4
	Alopecia	28	0.4
	Eczema	22	0.3
	Urticaria	22	0.3
	Skin ulcer	20	0.3
	Dermatitis allergic	18	0.2
	Hyperhidrosis	17	0.2
	Rash generalised	13	0.2
	Night sweats	10	0.1
Dermatitis psoriasiform	9	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Pruritus generalised	9	0.1
	Pustular psoriasis	8	0.1
	Skin disorder	8	0.1
	Dermatitis	7	0.1
	Rash macular	7	0.1
	Skin reaction	7	0.1
	Drug eruption	6	0.1
	Dry skin	6	0.1
	Nail bed inflammation	6	0.1
	Dermatosis	5	0.1
	Rosacea	5	0.1
	Rash erythematous	4	0.1
	Rash papular	4	0.1
	Skin lesion	4	0.1
	Swelling face	4	0.1
	Diabetic foot	3	0.0
Hand dermatitis	3	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Photosensitivity reaction	3	0.0
	Skin burning sensation	3	0.0
	Acne	2	0.0
	Decubitus ulcer	2	0.0
	Guttate psoriasis	2	0.0
	Neurodermatitis	2	0.0
	Papule	2	0.0
	Purpura	2	0.0
	Rash maculo-papular	2	0.0
	Rash vesicular	2	0.0
	Skin exfoliation	2	0.0
	Skin fissures	2	0.0
	Urticarial vasculitis	2	0.0
	Angioedema	1	0.0
	Cutaneous lupus erythematosus	1	0.0
	Diffuse alopecia	1	0.0
Drug reaction with eosinophilia and systemic symptoms	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Eczema asteatotic	1	0.0
	Eczema weeping	1	0.0
	Erythema multiforme	1	0.0
	Exfoliative rash	1	0.0
	Henoch-Schonlein purpura	1	0.0
	Hidradenitis	1	0.0
	Ingrowing nail	1	0.0
	Intertrigo	1	0.0
	Lichenoid keratosis	1	0.0
	Lipoatrophy	1	0.0
	Lividity	1	0.0
	Madarosis	1	0.0
	Mucocutaneous ulceration	1	0.0
	Nail disorder	1	0.0
	Onychoclasia	1	0.0
Perivascular dermatitis	1	0.0	
Petechiae	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Pigmentation disorder	1	0.0
	Plantar erythema	1	0.0
	Prurigo	1	0.0
	Skin atrophy	1	0.0
	Skin discomfort	1	0.0
	Skin hypertrophy	1	0.0
	Skin induration	1	0.0
	Skin irritation	1	0.0
	Skin necrosis	1	0.0
	Skin tightness	1	0.0
	Stasis dermatitis	1	0.0
	Subcutaneous emphysema	1	0.0
	Systemic lupus erythematosus rash	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Total	297	4.1
	Nausea	73	1.0
	Diarrhoea	71	1.0
	Vomiting	28	0.4
	Abdominal discomfort	17	0.2
	Abdominal pain upper	13	0.2
	Aphthous ulcer	13	0.2
	Dry mouth	13	0.2
	Gastritis	13	0.2
	Stomatitis	9	0.1
	Dysphagia	7	0.1
	Abdominal distension	5	0.1
	Colitis	5	0.1
	Colitis microscopic	5	0.1
	Gastrointestinal pain	5	0.1
	Gastroesophageal reflux disease	5	0.1
Haematochezia	5	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Abdominal pain	4	0.1
	Enteritis	4	0.1
	Gastric ulcer	4	0.1
	Hypoaesthesia oral	4	0.1
	Inguinal hernia	4	0.1
	Toothache	4	0.1
	Epigastric discomfort	3	0.0
	Gingival recession	3	0.0
	Mouth ulceration	3	0.0
	Noninfective gingivitis	3	0.0
	Retching	3	0.0
	Abdominal pain lower	2	0.0
	Colitis ulcerative	2	0.0
	Constipation	2	0.0
	Crohn's disease	2	0.0
	Dental discomfort	2	0.0
	Diverticular perforation	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Dyspepsia	2	0.0
	Gastritis erosive	2	0.0
	Haemorrhoids	2	0.0
	Hiatus hernia	2	0.0
	Lip swelling	2	0.0
	Pancreatitis acute	2	0.0
	Subileus	2	0.0
	Tongue discomfort	2	0.0
	Abdominal hernia	1	0.0
	Abdominal tenderness	1	0.0
	Anal erosion	1	0.0
	Autoimmune pancreatitis	1	0.0
	Chronic gastritis	1	0.0
	Diarrhoea haemorrhagic	1	0.0
	Diverticulum intestinal	1	0.0
	Duodenal ulcer	1	0.0
	Duodenitis haemorrhagic	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Erosive duodenitis	1	0.0
	Faecaloma	1	0.0
	Femoral hernia	1	0.0
	Flatulence	1	0.0
	Food poisoning	1	0.0
	Gastric antral vascular ectasia	1	0.0
	Gastric ulcer haemorrhage	1	0.0
	Gastrointestinal haemorrhage	1	0.0
	Gastrointestinal mucosal disorder	1	0.0
	Gingival bleeding	1	0.0
	Gingival discomfort	1	0.0
	Glossodynia	1	0.0
	Ileus	1	0.0
	Intestinal stenosis	1	0.0
	Irritable bowel syndrome	1	0.0
	Leukoplakia oral	1	0.0
	Lip oedema	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Melaena	1	0.0
	Mouth cyst	1	0.0
	Noninfective sialoadenitis	1	0.0
	Odynophagia	1	0.0
	Oesophagitis	1	0.0
	Oral discomfort	1	0.0
	Oral mucosa erosion	1	0.0
	Oral mucosal blistering	1	0.0
	Pancreatic duct stenosis	1	0.0
	Pancreatic mass	1	0.0
	Pancreatitis	1	0.0
	Pancreatitis chronic	1	0.0
	Periodontal disease	1	0.0
	Periodontal inflammation	1	0.0
	Proctitis	1	0.0
	Rectal haemorrhage	1	0.0
	Rectal polyp	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Salivary gland pain	1	0.0
	Swollen tongue	1	0.0
	Tongue blistering	1	0.0
	Tooth loss	1	0.0
	Ulcerative gastritis	1	0.0
	Umbilical hernia	1	0.0
Nervous system disorders	Total	272	3.8
	Headache	59	0.8
	Dizziness	53	0.7
	Paraesthesia	23	0.3
	Cerebrovascular accident	16	0.2
	Sciatica	16	0.2
	Burning sensation	10	0.1
	Hypoaesthesia	10	0.1
	Polyneuropathy	8	0.1
	Carpal tunnel syndrome	7	0.1
	Migraine	6	0.1

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Movement disorder	6	0.1
	Somnolence	6	0.1
	Cerebral infarction	5	0.1
	Syncope	5	0.1
	Transient ischaemic attack	5	0.1
	Cerebellar infarction	4	0.1
	Epilepsy	4	0.1
	Hemiparesis	4	0.1
	Cerebrovascular disorder	3	0.0
	Disturbance in attention	3	0.0
	Dizziness postural	3	0.0
	Dysaesthesia	3	0.0
	Hypertonia	3	0.0
	Seizure	3	0.0
	Aphasia	2	0.0
	Balance disorder	2	0.0
Cerebral ischaemia	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Diabetic neuropathy	2	0.0
	Monoparesis	2	0.0
	Neuralgia	2	0.0
	Parkinson's disease	2	0.0
	Poor quality sleep	2	0.0
	Restless legs syndrome	2	0.0
	Sensory disturbance	2	0.0
	Tremor	2	0.0
	Autonomic nervous system imbalance	1	0.0
	Axonal neuropathy	1	0.0
	Brain stem infarction	1	0.0
	Carotid arteriosclerosis	1	0.0
	Carotid artery stenosis	1	0.0
	Cerebral haemorrhage	1	0.0
	Cerebral microangiopathy	1	0.0
	Cervicobrachial syndrome	1	0.0
Cognitive disorder	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Complex regional pain syndrome	1	0.0
	Demyelinating polyneuropathy	1	0.0
	Dysgeusia	1	0.0
	Dyskinesia	1	0.0
	Dysphonia psychogenic	1	0.0
	Facial paresis	1	0.0
	Fine motor skill dysfunction	1	0.0
	Generalised tonic-clonic seizure	1	0.0
	Gliositis	1	0.0
	Head discomfort	1	0.0
	Hyperaesthesia	1	0.0
	Hyposmia	1	0.0
	Intercostal neuralgia	1	0.0
	Intracranial aneurysm	1	0.0
	Intracranial venous sinus thrombosis	1	0.0
	Lacunar infarction	1	0.0
Loss of consciousness	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Memory impairment	1	0.0
	Muscle contractions involuntary	1	0.0
	Muscle spasticity	1	0.0
	Myoclonus	1	0.0
	Nerve compression	1	0.0
	Nerve root compression	1	0.0
	Neuritis cranial	1	0.0
	Neurological symptom	1	0.0
	Neuropathy peripheral	1	0.0
	Nystagmus	1	0.0
	Optic neuritis	1	0.0
	Orthostatic intolerance	1	0.0
	Paraplegia	1	0.0
	Parkinsonism	1	0.0
	Partial seizures	1	0.0
Peripheral sensorimotor neuropathy	1	0.0	
Post herpetic neuralgia	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Post polio syndrome	1	0.0
	Presyncope	1	0.0
	Spinal cord ischaemia	1	0.0
	Thalamic infarction	1	0.0
	Toxic encephalopathy	1	0.0
	Trigeminal neuralgia	1	0.0
	Vertebral artery dissection	1	0.0
	Vestibular migraine	1	0.0
Respiratory, thoracic and mediastinal disorders	Total	255	3.5
	Cough	73	1.0
	Dyspnoea	22	0.3
	Oropharyngeal pain	20	0.3
	Respiratory distress	19	0.3
	Epistaxis	13	0.2
	Dyspnoea exertional	11	0.2
	Productive cough	11	0.2
	Rhinorrhoea	11	0.2

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism	10	0.1
	Chronic obstructive pulmonary disease	9	0.1
	Pleural effusion	9	0.1
	Pleurisy	8	0.1
	Asthma	6	0.1
	Pulmonary fibrosis	6	0.1
	Haemoptysis	4	0.1
	Laryngeal inflammation	4	0.1
	Rheumatoid lung	4	0.1
	Sleep apnoea syndrome	4	0.1
	Alveolitis	3	0.0
	Bronchitis chronic	3	0.0
	Nasal inflammation	3	0.0
	Sputum discoloured	3	0.0
	Allergic sinusitis	2	0.0
	Alveolitis allergic	2	0.0
Dysphonia	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Emphysema	2	0.0
	Hyperventilation	2	0.0
	Interstitial lung disease	2	0.0
	Lung infiltration	2	0.0
	Nasal congestion	2	0.0
	Painful respiration	2	0.0
	Paranasal sinus discomfort	2	0.0
	Pharyngeal inflammation	2	0.0
	Pneumonitis	2	0.0
	Pulmonary oedema	2	0.0
	Vocal cord inflammation	2	0.0
	Acute respiratory failure	1	0.0
	Allergic cough	1	0.0
	Apnoea	1	0.0
	Atelectasis	1	0.0
Bronchiectasis	1	0.0	
Epiglottic cyst	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Hypoventilation	1	0.0
	Increased bronchial secretion	1	0.0
	Laryngeal oedema	1	0.0
	Lung disorder	1	0.0
	Nasal dryness	1	0.0
	Nasal mucosal disorder	1	0.0
	Nasal septum deviation	1	0.0
	Nasal ulcer	1	0.0
	Nocturnal dyspnoea	1	0.0
	Organising pneumonia	1	0.0
	Paranasal cyst	1	0.0
	Pleural fibrosis	1	0.0
	Pulmonary congestion	1	0.0
	Pulmonary hilum mass	1	0.0
	Pulmonary mass	1	0.0
	Rhinitis allergic	1	0.0
Rhonchi	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Throat clearing	1	0.0
	Throat irritation	1	0.0
	Throat tightness	1	0.0
	Tonsillar inflammation	1	0.0
	Vocal cord polyp	1	0.0
	Vocal cord thickening	1	0.0
Investigations	Total	250	3.5
	Liver function test increased	33	0.5
	Laboratory test abnormal	26	0.4
	Blood pressure increased	21	0.3
	Arthroscopy	17	0.2
	Gamma-glutamyltransferase increased	12	0.2
	Alanine aminotransferase increased	9	0.1
	Transaminases increased	9	0.1
	Weight decreased	8	0.1
	Antinuclear antibody increased	7	0.1
	Rheumatoid factor increased	6	0.1

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Blood creatinine increased	5	0.1
	Body temperature increased	5	0.1
	C-reactive protein increased	4	0.1
	Computerised tomogram thorax abnormal	4	0.1
	Histology normal	4	0.1
	Inflammatory marker increased	4	0.1
	Weight increased	4	0.1
	Blood cholesterol increased	3	0.0
	Blood creatine phosphokinase increased	3	0.0
	Blood pressure measurement	3	0.0
	Bronchoscopy	3	0.0
	Double stranded DNA antibody positive	3	0.0
	Hepatic enzyme increased	3	0.0
	Antinuclear antibody	2	0.0
	Antinuclear antibody positive	2	0.0
	Aspartate aminotransferase increased	2	0.0
	Biopsy bone marrow	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Biopsy liver	2	0.0
	Blood pressure decreased	2	0.0
	Blood triglycerides increased	2	0.0
	Computerised tomogram thorax	2	0.0
	Haemoglobin decreased	2	0.0
	Mediastinoscopy	2	0.0
	Red blood cell sedimentation rate increased	2	0.0
	Staphylococcus test positive	2	0.0
	White blood cell count increased	2	0.0
	Activated partial thromboplastin time normal	1	0.0
	Angiogram peripheral	1	0.0
	Anti-cyclic citrullinated peptide antibody positive	1	0.0
	Antibody test abnormal	1	0.0
	Arteriogram coronary	1	0.0
	Aspartate aminotransferase normal	1	0.0
	Autoantibody test	1	0.0
	Biopsy	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Biopsy lymph gland	1	0.0
	Blood bactericidal activity	1	0.0
	Blood bilirubin increased	1	0.0
	Blood calcium	1	0.0
	Blood count abnormal	1	0.0
	Blood glucose fluctuation	1	0.0
	Blood immunoglobulin M increased	1	0.0
	Blood lactate dehydrogenase	1	0.0
	Blood pressure abnormal	1	0.0
	Blood urea increased	1	0.0
	Blood uric acid	1	0.0
	Bone densitometry	1	0.0
	Borrelia test positive	1	0.0
	Bronchoscopy abnormal	1	0.0
	Candida test positive	1	0.0
Catheterisation cardiac	1	0.0	
Chest X-ray abnormal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Chlamydia test positive	1	0.0
	Colonoscopy	1	0.0
	Colonoscopy normal	1	0.0
	Computerised tomogram abdomen abnormal	1	0.0
	Computerised tomogram kidney abnormal	1	0.0
	DNA antibody positive	1	0.0
	Drug specific antibody present	1	0.0
	Echocardiogram	1	0.0
	Ejection fraction decreased	1	0.0
	Emergency care examination	1	0.0
	Endoscopic retrograde cholangiopancreatography	1	0.0
	Endoscopy	1	0.0
	Endoscopy normal	1	0.0
	Endoscopy upper gastrointestinal tract	1	0.0
	Epstein-Barr virus antibody positive	1	0.0
	Fibrin D dimer increased	1	0.0
Forced expiratory volume	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Gamma-glutamyltransferase abnormal	1	0.0
	Gynaecological examination	1	0.0
	Gynaecological examination normal	1	0.0
	Haematocrit decreased	1	0.0
	Heart rate increased	1	0.0
	Heart rate irregular	1	0.0
	Hepatic enzyme abnormal	1	0.0
	Laboratory test	1	0.0
	Laparoscopy	1	0.0
	Liver function test	1	0.0
	Low density lipoprotein increased	1	0.0
	Lymphocyte count decreased	1	0.0
	Mean cell volume abnormal	1	0.0
	Mycobacterium tuberculosis complex test positive	1	0.0
	Neurological examination	1	0.0
	Neutrophil count decreased	1	0.0
Neutrophil count increased	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Platelet count normal	1	0.0
	Proteus test positive	1	0.0
	Prothrombin time normal	1	0.0
	Renal function test abnormal	1	0.0
	Serum ferritin decreased	1	0.0
	Serum ferritin increased	1	0.0
	Transaminases abnormal	1	0.0
	Tuberculin test positive	1	0.0
	Ultrasound abdomen abnormal	1	0.0
	Ultrasound abdomen normal	1	0.0
	Ultrasound scan	1	0.0
	Ultrasound scan normal	1	0.0
	Urinary sediment present	1	0.0
	White blood cell analysis abnormal	1	0.0
	White blood cell count	1	0.0
	White blood cell count decreased	1	0.0
Wound healing normal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Total	208	2.9
	Fall	47	0.7
	Foot fracture	14	0.2
	Tendon rupture	13	0.2
	Humerus fracture	12	0.2
	Joint dislocation	10	0.1
	Radius fracture	10	0.1
	Limb injury	9	0.1
	Arthropod bite	8	0.1
	Ligament sprain	8	0.1
	Lumbar vertebral fracture	8	0.1
	Femoral neck fracture	7	0.1
	Multiple fractures	7	0.1
	Accident at work	6	0.1
	Road traffic accident	6	0.1
Ulna fracture	6	0.1	
Femur fracture	5	0.1	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Fracture	5	0.1
	Thoracic vertebral fracture	5	0.1
	Ankle fracture	4	0.1
	Fracture displacement	4	0.1
	Lower limb fracture	4	0.1
	Meniscus injury	4	0.1
	Pelvic fracture	4	0.1
	Post procedural complication	4	0.1
	Rib fracture	4	0.1
	Skin abrasion	4	0.1
	Tibia fracture	4	0.1
	Wound	4	0.1
	Wrist fracture	4	0.1
	Accident	3	0.0
	Accident at home	3	0.0
	Contusion	3	0.0
Epicondylitis	3	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Hand fracture	3	0.0
	Patella fracture	3	0.0
	Spinal fracture	3	0.0
	Animal bite	2	0.0
	Bone contusion	2	0.0
	Craniocerebral injury	2	0.0
	Fibula fracture	2	0.0
	Fractured ischium	2	0.0
	Injury	2	0.0
	Ligament rupture	2	0.0
	Post procedural fistula	2	0.0
	Skin wound	2	0.0
	Subarachnoid haemorrhage	2	0.0
	Suture related complication	2	0.0
	Synovial rupture	2	0.0
	Acetabulum fracture	1	0.0
Bone fissure	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Burns second degree	1	0.0
	Cartilage injury	1	0.0
	Chillblains	1	0.0
	Clavicle fracture	1	0.0
	Eschar	1	0.0
	Forearm fracture	1	0.0
	Head injury	1	0.0
	Heat stroke	1	0.0
	Ilium fracture	1	0.0
	Inflammation of wound	1	0.0
	Injection related reaction	1	0.0
	Joint injury	1	0.0
	Kidney rupture	1	0.0
	Limb crushing injury	1	0.0
	Limb traumatic amputation	1	0.0
Lip injury	1	0.0	
Multiple injuries	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Muscle strain	1	0.0
	Nerve injury	1	0.0
	Off label use	1	0.0
	Overdose	1	0.0
	Pancreatic duct rupture	1	0.0
	Post procedural haemorrhage	1	0.0
	Scar	1	0.0
	Soft tissue injury	1	0.0
	Stab wound	1	0.0
	Stress fracture	1	0.0
	Tendon injury	1	0.0
	Tooth fracture	1	0.0
	Traumatic fracture	1	0.0
Upper limb fracture	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Total	139	1.9
	Palpitations	20	0.3
	Coronary artery disease	18	0.2
	Myocardial infarction	16	0.2
	Angina pectoris	15	0.2
	Atrial fibrillation	15	0.2
	Acute myocardial infarction	12	0.2
	Cardiac failure	10	0.1
	Arrhythmia	8	0.1
	Coronary artery stenosis	7	0.1
	Tachycardia	7	0.1
	Angina unstable	3	0.0
	Aortic valve stenosis	3	0.0
	Bradycardia	3	0.0
	Cardiac failure chronic	3	0.0
Cardiovascular disorder	3	0.0	
Aortic valve incompetence	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Hypertensive heart disease	2	0.0
	Left ventricular failure	2	0.0
	Mitral valve incompetence	2	0.0
	Myocarditis	2	0.0
	Pericarditis	2	0.0
	Sinus node dysfunction	2	0.0
	Sinus tachycardia	2	0.0
	Ventricular extrasystoles	2	0.0
	Acute coronary syndrome	1	0.0
	Adams-Stokes syndrome	1	0.0
	Atrial flutter	1	0.0
	Bradyarrhythmia	1	0.0
	Cardiac flutter	1	0.0
	Extrasystoles	1	0.0
	Left ventricular dysfunction	1	0.0
	Pericardial effusion	1	0.0
Right ventricular failure	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Stress cardiomyopathy	1	0.0
	Supraventricular tachycardia	1	0.0
	Tachyarrhythmia	1	0.0
	Tachycardia induced cardiomyopathy	1	0.0
	Ventricular fibrillation	1	0.0
	Wolff-Parkinson-White syndrome	1	0.0
Vascular disorders	Total	134	1.9
	Hypertension	45	0.6
	Haematoma	12	0.2
	Thrombosis	10	0.1
	Flushing	7	0.1
	Vasculitis	7	0.1
	Deep vein thrombosis	6	0.1
	Peripheral arterial occlusive disease	6	0.1
	Essential hypertension	4	0.1
	Hypertensive crisis	4	0.1
	Lymphoedema	4	0.1

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Vascular disorders	Peripheral venous disease	4	0.1
	Aortic aneurysm	3	0.0
	Haemorrhage	3	0.0
	Hot flush	3	0.0
	Thrombophlebitis	3	0.0
	Venous thrombosis limb	3	0.0
	Aortic dilatation	2	0.0
	Hypotension	2	0.0
	Peripheral artery occlusion	2	0.0
	Arterial occlusive disease	1	0.0
	Arteriosclerosis	1	0.0
	Arteritis	1	0.0
	Circulatory collapse	1	0.0
	Lymphatic fistula	1	0.0
	Microembolism	1	0.0
	Pelvic venous thrombosis	1	0.0
Peripheral artery aneurysm	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Vascular disorders	Peripheral artery stenosis	1	0.0
	Peripheral artery thrombosis	1	0.0
	Peripheral ischaemia	1	0.0
	Raynaud's phenomenon	1	0.0
	Shock haemorrhagic	1	0.0
	Varicose vein	1	0.0
	Vascular stenosis	1	0.0
	Venous thrombosis	1	0.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Total	116	1.6
	Breast cancer female	16	0.2
	Basal cell carcinoma	9	0.1
	Prostate cancer	6	0.1
	Bladder cancer	4	0.1
	Skin papilloma	4	0.1
	Squamous cell carcinoma	4	0.1
	Invasive ductal breast carcinoma	3	0.0
	Metastases to bone	3	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Myelodysplastic syndrome	3	0.0
	Pancreatic carcinoma	3	0.0
	Skin cancer	3	0.0
	B-cell lymphoma	2	0.0
	Bowen's disease	2	0.0
	Breast neoplasm	2	0.0
	Bronchial carcinoma	2	0.0
	Cervix carcinoma	2	0.0
	Lipoma	2	0.0
	Neoplasm skin	2	0.0
	Neuroma	2	0.0
	Ovarian cancer	2	0.0
	Plasma cell myeloma	2	0.0
	Rectal cancer	2	0.0
	Transitional cell carcinoma	2	0.0
	Acute myeloid leukaemia	1	0.0
Anogenital warts	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Atypical fibroxanthoma	1	0.0
	Benign cardiac neoplasm	1	0.0
	Bladder neoplasm	1	0.0
	Brain neoplasm	1	0.0
	Brain neoplasm malignant	1	0.0
	Bronchial neoplasm	1	0.0
	Cervix carcinoma stage 0	1	0.0
	Cholangiocarcinoma	1	0.0
	Chronic lymphocytic leukaemia	1	0.0
	Colon cancer	1	0.0
	Colon neoplasm	1	0.0
	Ear neoplasm malignant	1	0.0
	Epiglottic carcinoma	1	0.0
	Gastric cancer stage I	1	0.0
	Gastric cancer stage III	1	0.0
	Hodgkin's disease	1	0.0
	Hodgkin's disease mixed cellularity stage unspecified	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Intraductal papilloma of breast	1	0.0
	Intraductal proliferative breast lesion	1	0.0
	Invasive breast carcinoma	1	0.0
	Lung neoplasm malignant	1	0.0
	Lung squamous cell carcinoma stage III	1	0.0
	Lymphoma	1	0.0
	Malignant melanoma	1	0.0
	Malignant melanoma in situ	1	0.0
	Metastases to liver	1	0.0
	Metastases to lung	1	0.0
	Metastases to lymph nodes	1	0.0
	Metastases to thorax	1	0.0
	Metastatic neoplasm	1	0.0
	Neuroendocrine carcinoma	1	0.0
	Non-Hodgkin's lymphoma	1	0.0
	Plasmacytoma	1	0.0
Refractory cytopenia with unilineage dysplasia	1	0.0	

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(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Renal cell carcinoma recurrent	1	0.0
	Salivary gland neoplasm	1	0.0
	Thyroid adenoma	1	0.0
	Thyroid cancer	1	0.0
	Thyroid cancer recurrent	1	0.0
	Urinary tract neoplasm	1	0.0
	Uterine cancer	1	0.0
	Uterine leiomyoma	1	0.0
Psychiatric disorders	Total	80	1.1
	Depression	34	0.5
	Sleep disorder	15	0.2
	Anxiety	7	0.1
	Anxiety disorder	4	0.1
	Depressed mood	4	0.1
	Restlessness	3	0.0
	Agoraphobia	2	0.0
	Apathy	2	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Psychiatric disorders	Middle insomnia	2	0.0
	Mood swings	2	0.0
	Somatic symptom disorder	2	0.0
	Stress	2	0.0
	Acute stress disorder	1	0.0
	Adjustment disorder with depressed mood	1	0.0
	Agitation	1	0.0
	Alcoholism	1	0.0
	Hallucination	1	0.0
	Hallucination, auditory	1	0.0
	Illusion	1	0.0
	Insomnia	1	0.0
	Mania	1	0.0
	Nightmare	1	0.0
	Panic attack	1	0.0
Panic disorder	1	0.0	
Panic reaction	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Psychiatric disorders	Psychomotor retardation	1	0.0
	Tobacco abuse	1	0.0
Renal and urinary disorders	Total	75	1.0
	Cystitis noninfective	18	0.2
	Haematuria	9	0.1
	Renal failure	9	0.1
	Acute kidney injury	6	0.1
	Renal colic	6	0.1
	Chronic kidney disease	4	0.1
	Nephrolithiasis	4	0.1
	Renal impairment	3	0.0
	Leukocyturia	2	0.0
	Renal pain	2	0.0
	Ureterolithiasis	2	0.0
	Urinary tract obstruction	2	0.0
	Azotaemia	1	0.0
Bladder diverticulum	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Renal and urinary disorders	Bladder irritation	1	0.0
	Bladder stenosis	1	0.0
	Calculus urinary	1	0.0
	Dysuria	1	0.0
	Renal artery arteriosclerosis	1	0.0
	Renal artery stenosis	1	0.0
	Renal infarct	1	0.0
	Single functional kidney	1	0.0
	Stress urinary incontinence	1	0.0
	Ureteric stenosis	1	0.0
	Urinary hesitation	1	0.0
	Urinary incontinence	1	0.0
	Urinary tract inflammation	1	0.0
	Urogenital haemorrhage	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Eye disorders	Total	71	1.0
	Cataract	9	0.1
	Eye inflammation	7	0.1
	Vision blurred	7	0.1
	Visual impairment	7	0.1
	Iritis	6	0.1
	Dry eye	4	0.1
	Glaucoma	4	0.1
	Blepharitis	3	0.0
	Eyelid oedema	3	0.0
	Iridocyclitis	3	0.0
	Diplopia	2	0.0
	Eye haemorrhage	2	0.0
	Eye pain	2	0.0
	Eye swelling	2	0.0
	Keratitis	2	0.0
Macular degeneration	2	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Eye disorders	Ocular discomfort	2	0.0
	Ulcerative keratitis	2	0.0
	Visual acuity reduced	2	0.0
	Erythema of eyelid	1	0.0
	Eye disorder	1	0.0
	Inflammation of lacrimal passage	1	0.0
	Macular cyst	1	0.0
	Ocular hyperaemia	1	0.0
	Ocular hypertension	1	0.0
	Ophthalmic vein thrombosis	1	0.0
	Papilloedema	1	0.0
	Photophobia	1	0.0
	Retinal detachment	1	0.0
	Uveitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Blood and lymphatic system disorders	Total	64	0.9
	Leukopenia	17	0.2
	Lymphadenopathy	10	0.1
	Anaemia	9	0.1
	Thrombocytopenia	8	0.1
	Leukocytosis	5	0.1
	Eosinophilia	2	0.0
	Hyperchromic anaemia	2	0.0
	Iron deficiency anaemia	2	0.0
	Neutropenia	2	0.0
	Agranulocytosis	1	0.0
	Anaemia vitamin B12 deficiency	1	0.0
	Bicytopenia	1	0.0
	Cytopenia	1	0.0
	Erythropenia	1	0.0
Haemorrhagic diathesis	1	0.0	
Hypochromic anaemia	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Blood and lymphatic system disorders	Increased tendency to bruise	1	0.0
	Lymphadenitis	1	0.0
	Lymphocytosis	1	0.0
	Lymphopenia	1	0.0
	Pancytopenia	1	0.0
	Platelet disorder	1	0.0
	Spontaneous haematoma	1	0.0
Metabolism and nutrition disorders	Total	60	0.8
	Diabetes mellitus	10	0.1
	Hyperuricaemia	7	0.1
	Vitamin D deficiency	7	0.1
	Hyperlipidaemia	5	0.1
	Type 2 diabetes mellitus	5	0.1
	Decreased appetite	4	0.1
	Gout	4	0.1
	Hypercholesterolaemia	4	0.1
	Obesity	3	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Metabolism and nutrition disorders	Dehydration	2	0.0
	Hypercalcaemia	2	0.0
	Hyperglycaemia	2	0.0
	Vitamin B12 deficiency	2	0.0
	Central obesity	1	0.0
	Electrolyte imbalance	1	0.0
	Haemochromatosis	1	0.0
	Hyperferritinaemia	1	0.0
	Hyperkalaemia	1	0.0
	Hypertriglyceridaemia	1	0.0
	Hypochloraemia	1	0.0
	Hypokalaemia	1	0.0
	Hypophosphataemia	1	0.0
	Iron deficiency	1	0.0
	Lactose intolerance	1	0.0
Shock hypoglycaemic	1	0.0	

(Continued)

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5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Ear and labyrinth disorders	Total	42	0.6
	Tinnitus	9	0.1
	Middle ear inflammation	7	0.1
	Sudden hearing loss	7	0.1
	Ear pain	6	0.1
	Vertigo	6	0.1
	Ear discomfort	4	0.1
	Vertigo positional	2	0.0
	Auditory disorder	1	0.0
	Auricular swelling	1	0.0
	External ear pain	1	0.0
	Meniere's disease	1	0.0
	Otosclerosis	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Hepatobiliary disorders	Total	36	0.5
	Cholelithiasis	15	0.2
	Cholecystitis	6	0.1
	Cholecystitis acute	5	0.1
	Bile duct stone	3	0.0
	Hepatic cirrhosis	3	0.0
	Hepatic steatosis	3	0.0
	Liver disorder	3	0.0
	Biliary colic	2	0.0
	Cholangitis	2	0.0
	Cholestasis	2	0.0
	Jaundice	2	0.0
	Biliary cirrhosis primary	1	0.0
	Cholecystitis chronic	1	0.0
	Gallbladder perforation	1	0.0
	Hepatic fibrosis	1	0.0
Hepatitis cholestatic	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Reproductive system and breast disorders	Total	33	0.5
	Ovarian cyst	6	0.1
	Benign prostatic hyperplasia	5	0.1
	Menorrhagia	3	0.0
	Erectile dysfunction	2	0.0
	Gynaecomastia	2	0.0
	Metrorrhagia	2	0.0
	Vulvovaginal inflammation	2	0.0
	Amenorrhoea	1	0.0
	Bartholin's cyst	1	0.0
	Breast mass	1	0.0
	Breast pain	1	0.0
	Cervical dysplasia	1	0.0
	Dyspareunia	1	0.0
	Endometriosis	1	0.0
	Menstrual disorder	1	0.0
Menstruation irregular	1	0.0	

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Reproductive system and breast disorders	Orchitis noninfective	1	0.0
	Ovarian adhesion	1	0.0
	Prostatic dysplasia	1	0.0
	Prostatic haemorrhage	1	0.0
	Prostatitis	1	0.0
	Spermatocoele	1	0.0
	Uterine polyp	1	0.0
Immune system disorders	Total	30	0.4
	Hypersensitivity	19	0.3
	Seasonal allergy	4	0.1
	Drug hypersensitivity	3	0.0
	Immunosuppression	2	0.0
	Anaphylactic reaction	1	0.0
	Rubber sensitivity	1	0.0
	Sarcoidosis	1	0.0

(Continued)

5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Endocrine disorders	Total	23	0.3
	Goitre	9	0.1
	Hypothyroidism	6	0.1
	Autoimmune thyroiditis	3	0.0
	Thyroid mass	3	0.0
	Hyperthyroidism	2	0.0
	Adrenocortical insufficiency acute	1	0.0
	Basedow's disease	1	0.0
	Thyroiditis	1	0.0
	Thyroiditis subacute	1	0.0
Pregnancy, puerperium and perinatal conditions	Total	18	0.2
	Pregnancy	14	0.2
	Delivery	3	0.0
	Abortion spontaneous	1	0.0
	Ectopic pregnancy	1	0.0
	Twin pregnancy	1	0.0

(Continued)

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5. Documented adverse events by patient

5.3 All documented adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Product issues	Total	7	0.1
	Device dislocation	4	0.1
	Device breakage	2	0.0
	Device expulsion	1	0.0
Congenital, familial and genetic disorders	Total	3	0.0
	Congenital tongue anomaly	1	0.0
	Developmental hip dysplasia	1	0.0
	Hereditary neuropathic amyloidosis	1	0.0
Social circumstances	Total	3	0.0
	Alcohol use	1	0.0
	Foreign travel	1	0.0
	Postmenopause	1	0.0

5. Documented adverse events by patient

5.4 All documented serious adverse events by system organ class

	n	%
System Organ Class		
Total	932	12.9
Surgical and medical procedures	405	5.6
Infections and infestations	267	3.7
Musculoskeletal and connective tissue disorders	163	2.3
General disorders and administration site conditions	110	1.5
Injury, poisoning and procedural complications	96	1.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	90	1.2
Cardiac disorders	80	1.1
Nervous system disorders	70	1.0
Gastrointestinal disorders	60	0.8
Respiratory, thoracic and mediastinal disorders	59	0.8
Investigations	57	0.8
Skin and subcutaneous tissue disorders	49	0.7
Vascular disorders	45	0.6
Renal and urinary disorders	29	0.4
Hepatobiliary disorders	23	0.3
Blood and lymphatic system disorders	21	0.3

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(Continued)

5. Documented adverse events by patient

5.4 All documented serious adverse events by system organ class

	n	%
System Organ Class		
Psychiatric disorders	17	0.2
Metabolism and nutrition disorders	12	0.2
Reproductive system and breast disorders	11	0.2
Ear and labyrinth disorders	8	0.1
Endocrine disorders	8	0.1
Eye disorders	7	0.1
Immune system disorders	4	0.1
Product issues	4	0.1
Pregnancy, puerperium and perinatal conditions	3	0.0
Social circumstances	3	0.0
Congenital, familial and genetic disorders	2	0.0

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Total	932	12.9
Hospitalisation	110	1.5
Pneumonia	59	0.8
Rheumatoid arthritis	35	0.5
Knee arthroplasty	30	0.4
Elective surgery	27	0.4
Arthrodesis	25	0.3
Hip arthroplasty	24	0.3
Fall	19	0.3
Synovectomy	19	0.3
Foot operation	18	0.2
Joint arthroplasty	18	0.2
Death	16	0.2
Breast cancer female	15	0.2
Cerebrovascular accident	15	0.2
Myocardial infarction	15	0.2
Osteoarthritis	15	0.2

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Bunion operation	14	0.2
Coronary artery disease	14	0.2
Foot deformity	14	0.2
Infection	14	0.2
Pyrexia	14	0.2
Atrial fibrillation	13	0.2
Bronchitis	13	0.2
Intervertebral disc protrusion	13	0.2
Acute myocardial infarction	12	0.2
Cholecystectomy	12	0.2
Therapy cessation	12	0.2
Unevaluable event	12	0.2
Urosepsis	11	0.2
Bursitis	10	0.1
Cholelithiasis	10	0.1
Diverticulitis	10	0.1
Lumbar spinal stenosis	10	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Surgery	10	0.1
Therapy change	10	0.1
Urinary tract infection	10	0.1
Arthralgia	9	0.1
Complication associated with device	9	0.1
Hypertension	9	0.1
Impaired healing	9	0.1
Rehabilitation therapy	9	0.1
Vomiting	9	0.1
Arthroscopy	8	0.1
Depression	8	0.1
Drug ineffective	8	0.1
Gastroenteritis	8	0.1
Herpes zoster	8	0.1
Laparoscopic surgery	8	0.1
Pulmonary embolism	8	0.1
Spinal operation	8	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Cardiac failure	7	0.1
Chest pain	7	0.1
Coronary arterial stent insertion	7	0.1
Coronary artery stenosis	7	0.1
Femoral neck fracture	7	0.1
Humerus fracture	7	0.1
Intervertebral disc operation	7	0.1
Multiple fractures	7	0.1
Osteosynthesis	7	0.1
Osteotomy	7	0.1
Postoperative wound infection	7	0.1
Skin ulcer	7	0.1
Synovial cyst	7	0.1
Synovitis	7	0.1
Tendon rupture	7	0.1
Abscess limb	6	0.1
Antibiotic therapy	6	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Arthritis	6	0.1
Arthroscopic surgery	6	0.1
Blood pressure increased	6	0.1
Coronary artery bypass	6	0.1
Dyspnoea	6	0.1
Joint dislocation	6	0.1
Knee operation	6	0.1
Leukopenia	6	0.1
Lumbar vertebral fracture	6	0.1
Pleural effusion	6	0.1
Post procedural infection	6	0.1
Radius fracture	6	0.1
Rheumatoid nodule removal	6	0.1
Rotator cuff syndrome	6	0.1
Sepsis	6	0.1
Ulna fracture	6	0.1
Accident at work	5	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Acquired claw toe	5	0.1
Acute kidney injury	5	0.1
Anaemia	5	0.1
Antibiotic prophylaxis	5	0.1
Aortic valve replacement	5	0.1
Back pain	5	0.1
Benign prostatic hyperplasia	5	0.1
Bursa removal	5	0.1
Cardiac pacemaker insertion	5	0.1
Cellulitis	5	0.1
Cerebral infarction	5	0.1
Cholecystitis acute	5	0.1
Diarrhoea	5	0.1
Foot fracture	5	0.1
Goitre	5	0.1
Haematoma	5	0.1
Headache	5	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Inguinal hernia repair	5	0.1
Liver function test increased	5	0.1
Nausea	5	0.1
Osteoporotic fracture	5	0.1
Pain in extremity	5	0.1
Prostate cancer	5	0.1
Pulmonary fibrosis	5	0.1
Renal failure	5	0.1
Respiratory tract infection	5	0.1
Spinal column stenosis	5	0.1
Thrombosis	5	0.1
Ankle arthroplasty	4	0.1
Ankle fracture	4	0.1
Baker's cyst excision	4	0.1
Bladder cancer	4	0.1
Cataract operation	4	0.1
Cerebellar infarction	4	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Cholecystitis	4	0.1
Chronic obstructive pulmonary disease	4	0.1
Deep vein thrombosis	4	0.1
Device related infection	4	0.1
Dizziness	4	0.1
Endocarditis	4	0.1
Erysipelas	4	0.1
Fatigue	4	0.1
Femur fracture	4	0.1
Fracture displacement	4	0.1
Fracture treatment	4	0.1
Influenza like illness	4	0.1
Lupus-like syndrome	4	0.1
Meningitis	4	0.1
Osteomyelitis	4	0.1
Pain	4	0.1
Perforated ulcer	4	0.1

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Peripheral arterial occlusive disease	4	0.1
Peripheral swelling	4	0.1
Pleurisy	4	0.1
Renal stone removal	4	0.1
Rotator cuff repair	4	0.1
Shoulder operation	4	0.1
Spinal fusion surgery	4	0.1
Squamous cell carcinoma	4	0.1
Subcutaneous abscess	4	0.1
Syncope	4	0.1
Thyroidectomy	4	0.1
Tibia fracture	4	0.1
Upper respiratory tract infection	4	0.1
Urticaria	4	0.1
Abdominal operation	3	0.0
Abdominal pain upper	3	0.0
Abscess	3	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Abscess drainage	3	0.0
Alveolitis	3	0.0
Angina pectoris	3	0.0
Ankle operation	3	0.0
Aortic valve stenosis	3	0.0
Arrhythmia	3	0.0
Basal cell carcinoma	3	0.0
Bile duct stone	3	0.0
Breast conserving surgery	3	0.0
Bronchoscopy	3	0.0
Cancer surgery	3	0.0
Cardiac operation	3	0.0
Coronary angioplasty	3	0.0
Dermatitis allergic	3	0.0
Device dislocation	3	0.0
Diabetes mellitus	3	0.0
Emergency care	3	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Epilepsy	3	0.0
Gallbladder operation	3	0.0
Gastric ulcer	3	0.0
Gastritis	3	0.0
Gastroenteritis norovirus	3	0.0
Haematoma evacuation	3	0.0
Hemiparesis	3	0.0
Hypertensive crisis	3	0.0
Hysterectomy	3	0.0
Inflammation	3	0.0
Inguinal hernia	3	0.0
Intervertebral discitis	3	0.0
Invasive ductal breast carcinoma	3	0.0
Joint surgery	3	0.0
Leukocytosis	3	0.0
Lower limb fracture	3	0.0
Meniscus operation	3	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Metastases to bone	3	0.0
Movement disorder	3	0.0
Musculoskeletal discomfort	3	0.0
Nephrolithiasis	3	0.0
No adverse event	3	0.0
Pain management	3	0.0
Palpitations	3	0.0
Pancreatic carcinoma	3	0.0
Pyelonephritis	3	0.0
Rash	3	0.0
Respiratory distress	3	0.0
Rheumatoid lung	3	0.0
Road traffic accident	3	0.0
Seizure	3	0.0
Septic shock	3	0.0
Shoulder arthroplasty	3	0.0
Sigmoidectomy	3	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Sinusitis	3	0.0
Skin graft	3	0.0
Skin neoplasm excision	3	0.0
Spinal decompression	3	0.0
Spinal osteoarthritis	3	0.0
Spondylolisthesis	3	0.0
Stent placement	3	0.0
Sudden hearing loss	3	0.0
Tendon operation	3	0.0
Thoracic vertebral fracture	3	0.0
Thyroid mass	3	0.0
Toe operation	3	0.0
Tooth extraction	3	0.0
Transient ischaemic attack	3	0.0
Tuberculosis	3	0.0
Viral infection	3	0.0
Weight decreased	3	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Wound infection	3	0.0
Abdominal discomfort	2	0.0
Accident at home	2	0.0
Angina unstable	2	0.0
Aortic aneurysm	2	0.0
Aphasia	2	0.0
Appendicitis perforated	2	0.0
Arterial stent insertion	2	0.0
Arthropathy	2	0.0
Arthropod bite	2	0.0
Asthenia	2	0.0
B-cell lymphoma	2	0.0
Biopsy bone marrow	2	0.0
Biopsy liver	2	0.0
Blepharitis	2	0.0
Breast abscess	2	0.0
Breast reconstruction	2	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Bronchial carcinoma	2	0.0
C-reactive protein increased	2	0.0
Cardiac ablation	2	0.0
Cardiac failure chronic	2	0.0
Carpal tunnel decompression	2	0.0
Cartilage operation	2	0.0
Cerebral ischaemia	2	0.0
Cervix carcinoma	2	0.0
Chemotherapy	2	0.0
Cholangitis	2	0.0
Cholestasis	2	0.0
Chronic sinusitis	2	0.0
Colitis	2	0.0
Colitis microscopic	2	0.0
Computerised tomogram thorax abnormal	2	0.0
Condition aggravated	2	0.0
Cough	2	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Cyst	2	0.0
Dehydration	2	0.0
Diabetic foot	2	0.0
Diverticular perforation	2	0.0
Dizziness postural	2	0.0
Double stranded DNA antibody positive	2	0.0
Drug eruption	2	0.0
Dry mouth	2	0.0
Dysphagia	2	0.0
Emphysema	2	0.0
Enteritis	2	0.0
Erythema	2	0.0
Escherichia sepsis	2	0.0
Facet joint syndrome	2	0.0
Fracture	2	0.0
Gastrectomy	2	0.0
Gastritis erosive	2	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
General physical health deterioration	2	0.0
Genital herpes	2	0.0
Haematochezia	2	0.0
Haematuria	2	0.0
Hernia repair	2	0.0
Hip surgery	2	0.0
Hyperhidrosis	2	0.0
Hyperventilation	2	0.0
Hypoaesthesia	2	0.0
Infectious colitis	2	0.0
Infectious pleural effusion	2	0.0
Infiltration anaesthesia	2	0.0
Injury	2	0.0
Interstitial lung disease	2	0.0
Jaundice	2	0.0
Joint dislocation reduction	2	0.0
Left ventricular failure	2	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Limb injury	2	0.0
Lung infection	2	0.0
Lung infiltration	2	0.0
Lymph node tuberculosis	2	0.0
Lymphadenopathy	2	0.0
Massage	2	0.0
Mastectomy	2	0.0
Medical device removal	2	0.0
Metatarsalgia	2	0.0
Monoparesis	2	0.0
Nasal herpes	2	0.0
Nasal inflammation	2	0.0
Nasal operation	2	0.0
Nasal polypectomy	2	0.0
Nasopharyngitis	2	0.0
Neuroma	2	0.0
Night sweats	2	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Obesity	2	0.0
Open reduction of fracture	2	0.0
Oral herpes	2	0.0
Osteochondrosis	2	0.0
Ovarian cancer	2	0.0
Ovarian cyst	2	0.0
Ovarian cystectomy	2	0.0
Pancreatitis acute	2	0.0
Paraesthesia	2	0.0
Pelvic fracture	2	0.0
Pericarditis	2	0.0
Peritonitis	2	0.0
Pertussis	2	0.0
Plasma cell myeloma	2	0.0
Post procedural complication	2	0.0
Post procedural fistula	2	0.0
Postoperative care	2	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Pregnancy	2	0.0
Prostatic operation	2	0.0
Pseudarthrosis	2	0.0
Pulmonary oedema	2	0.0
Pulmonary resection	2	0.0
Pulmonary tuberculosis	2	0.0
Pustular psoriasis	2	0.0
Radiotherapy	2	0.0
Rectal cancer	2	0.0
Removal of internal fixation	2	0.0
Renal colic	2	0.0
Renal impairment	2	0.0
Rheumatoid nodule	2	0.0
Sciatica	2	0.0
Scoliosis	2	0.0
Sinus node dysfunction	2	0.0
Sinus operation	2	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Sinus tachycardia	2	0.0
Skin cancer	2	0.0
Sleep disorder	2	0.0
Soft tissue infection	2	0.0
Somnolence	2	0.0
Spinal instability	2	0.0
Staphylococcal infection	2	0.0
Stomatitis	2	0.0
Stress	2	0.0
Subarachnoid haemorrhage	2	0.0
Swelling	2	0.0
Tendon sheath incision	2	0.0
Tenoplasty	2	0.0
Thrombocytopenia	2	0.0
Thyroid operation	2	0.0
Tooth abscess	2	0.0
Transitional cell carcinoma	2	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Transurethral prostatectomy	2	0.0
Ureteral stent insertion	2	0.0
Ureterolithiasis	2	0.0
Urinary tract obstruction	2	0.0
Vasculitis	2	0.0
Vertigo	2	0.0
Vertigo positional	2	0.0
Vestibular neuronitis	2	0.0
Wound	2	0.0
Wound treatment	2	0.0
Wrist fracture	2	0.0
Abdominal abscess	1	0.0
Abdominal hernia	1	0.0
Abdominal hernia repair	1	0.0
Abdominal pain lower	1	0.0
Abdominal tenderness	1	0.0
Abscess neck	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Abscess soft tissue	1	0.0
Acetabulum fracture	1	0.0
Acne pustular	1	0.0
Acute myeloid leukaemia	1	0.0
Acute respiratory failure	1	0.0
Acute stress disorder	1	0.0
Adams-Stokes syndrome	1	0.0
Adhesiolysis	1	0.0
Adrenocortical insufficiency acute	1	0.0
Adrenocortical steroid therapy	1	0.0
Adverse drug reaction	1	0.0
Agranulocytosis	1	0.0
Alcohol use	1	0.0
Alopecia	1	0.0
Anal abscess	1	0.0
Aneurysm repair	1	0.0
Angiogram peripheral	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Angioplasty	1	0.0
Animal bite	1	0.0
Ankle impingement	1	0.0
Anogenital warts	1	0.0
Antiallergic therapy	1	0.0
Anticoagulant therapy	1	0.0
Antinuclear antibody positive	1	0.0
Anxiety	1	0.0
Aortic aneurysm repair	1	0.0
Aortic dilatation	1	0.0
Aortic valve incompetence	1	0.0
Aphthous ulcer	1	0.0
Appendectomy	1	0.0
Arterial aneurysm repair	1	0.0
Arterial bypass operation	1	0.0
Arterial catheterisation	1	0.0
Arterial occlusive disease	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Arteriogram coronary	1	0.0
Arteriosclerosis	1	0.0
Arthritis bacterial	1	0.0
Arthritis reactive	1	0.0
Arthrotomy	1	0.0
Asthma	1	0.0
Atrial flutter	1	0.0
Atypical fibroxanthoma	1	0.0
Atypical pneumonia	1	0.0
Autoantibody test	1	0.0
Azotaemia	1	0.0
Basedow's disease	1	0.0
Benign cardiac neoplasm	1	0.0
Bicytopenia	1	0.0
Biliary cirrhosis primary	1	0.0
Biopsy lymph gland	1	0.0
Bladder diverticulum	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Bladder neoplasm	1	0.0
Bladder stenosis	1	0.0
Blood bactericidal activity	1	0.0
Blood calcium	1	0.0
Blood creatine phosphokinase increased	1	0.0
Bone operation	1	0.0
Bowen's disease	1	0.0
Bradycardia	1	0.0
Bradyarrhythmia	1	0.0
Bradycardia	1	0.0
Brain neoplasm	1	0.0
Brain neoplasm malignant	1	0.0
Brain stem infarction	1	0.0
Breast neoplasm	1	0.0
Bronchial lesion excision	1	0.0
Bronchial neoplasm	1	0.0
Bronchiectasis	1	0.0
Bronchiolitis	1	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Bronchitis bacterial	1	0.0
Burns second degree	1	0.0
Bursal haematoma	1	0.0
Bursal operation	1	0.0
Bursitis infective	1	0.0
Calculus urinary	1	0.0
Candida infection	1	0.0
Candida pneumonia	1	0.0
Carbuncle	1	0.0
Cardiac pacemaker replacement	1	0.0
Carotid artery stenosis	1	0.0
Carpal tunnel syndrome	1	0.0
Cataract	1	0.0
Catheterisation cardiac	1	0.0
Cerebral haemorrhage	1	0.0
Cerebrovascular operation	1	0.0
Chest discomfort	1	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Chest wall operation	1	0.0
Cholangiocarcinoma	1	0.0
Cholangitis infective	1	0.0
Cholecystitis chronic	1	0.0
Chondromalacia	1	0.0
Chronic gastritis	1	0.0
Chronic hepatitis C	1	0.0
Chronic lymphocytic leukaemia	1	0.0
Circulatory collapse	1	0.0
Clavicle fracture	1	0.0
Clostridial infection	1	0.0
Cognitive disorder	1	0.0
Colitis ulcerative	1	0.0
Colon cancer	1	0.0
Colon neoplasm	1	0.0
Colonoscopy normal	1	0.0
Compartment syndrome	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Complex regional pain syndrome	1	0.0
Conjunctivitis	1	0.0
Constipation	1	0.0
Contusion	1	0.0
Coronary revascularisation	1	0.0
Craniocerebral injury	1	0.0
Crohn's disease	1	0.0
Cryotherapy	1	0.0
Cyst removal	1	0.0
Cystitis	1	0.0
Cytopenia	1	0.0
DNA antibody positive	1	0.0
Debridement	1	0.0
Decreased appetite	1	0.0
Decubitus ulcer	1	0.0
Delivery	1	0.0
Dermatitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Dermatosis	1	0.0
Developmental hip dysplasia	1	0.0
Device breakage	1	0.0
Diabetes mellitus management	1	0.0
Diabetic gangrene	1	0.0
Diabetic neuropathy	1	0.0
Disseminated tuberculosis	1	0.0
Diverticulum intestinal	1	0.0
Drug hypersensitivity	1	0.0
Drug interaction	1	0.0
Duodenal ulcer	1	0.0
Dysaesthesia	1	0.0
Dyskinesia	1	0.0
Dyspnoea exertional	1	0.0
Ear neoplasm malignant	1	0.0
Ectopic pregnancy	1	0.0
Ejection fraction decreased	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Emergency care examination	1	0.0
Emphysematous cholecystitis	1	0.0
Encephalitis viral	1	0.0
Endocarditis staphylococcal	1	0.0
Endoscopic retrograde cholangiopancreatography	1	0.0
Endoscopy	1	0.0
Epiglottic carcinoma	1	0.0
Epstein-Barr virus antibody positive	1	0.0
Epstein-Barr virus infection	1	0.0
Erosive duodenitis	1	0.0
Erythema multiforme	1	0.0
Erythropenia	1	0.0
Escherichia urinary tract infection	1	0.0
Exercise tolerance decreased	1	0.0
Exostosis	1	0.0
Eye disorder	1	0.0
Eye haemorrhage	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Eye operation	1	0.0
Facial paresis	1	0.0
Faecaloma	1	0.0
Felty's syndrome	1	0.0
Femoral hernia	1	0.0
Femoral hernia repair	1	0.0
Fibrin D dimer increased	1	0.0
Fibromyalgia	1	0.0
Fibula fracture	1	0.0
Fistula repair	1	0.0
Fluid replacement	1	0.0
Flushing	1	0.0
Folliculitis	1	0.0
Forearm fracture	1	0.0
Foreign travel	1	0.0
Fracture debridement	1	0.0
Fractured ischium	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Frontal sinus operation	1	0.0
Furuncle	1	0.0
Gallbladder empyema	1	0.0
Gallbladder perforation	1	0.0
Gamma-glutamyltransferase increased	1	0.0
Gastric cancer stage I	1	0.0
Gastric cancer stage III	1	0.0
Gastric operation	1	0.0
Gastroenteritis viral	1	0.0
Gastrointestinal haemorrhage	1	0.0
Gastrointestinal infection	1	0.0
Gastrointestinal pain	1	0.0
Gastrooesophageal reflux disease	1	0.0
Generalised tonic-clonic seizure	1	0.0
Genital candidiasis	1	0.0
Gingival operation	1	0.0
Gingival recession	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Gingivitis	1	0.0
Glaucoma	1	0.0
Gliosis	1	0.0
Gout	1	0.0
Granuloma	1	0.0
Groin abscess	1	0.0
Groin pain	1	0.0
Haemarthrosis	1	0.0
Haematocrit decreased	1	0.0
Haemoglobin decreased	1	0.0
Haemorrhoids	1	0.0
Haemostasis	1	0.0
Hand dermatitis	1	0.0
Heart rate irregular	1	0.0
Hepatic cirrhosis	1	0.0
Hepatitis cholestatic	1	0.0
Hereditary neuropathic amyloidosis	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Herpes ophthalmic	1	0.0
Herpes simplex encephalitis	1	0.0
Herpes virus infection	1	0.0
Hidradenitis	1	0.0
Hip deformity	1	0.0
Hodgkin's disease	1	0.0
Hodgkin's disease mixed cellularity stage unspecified	1	0.0
Hypercalcaemia	1	0.0
Hyperglycaemia	1	0.0
Hypersensitivity	1	0.0
Hypertensive heart disease	1	0.0
Hyperthyroidism	1	0.0
Hypoaesthesia oral	1	0.0
Hypochromic anaemia	1	0.0
Ileus	1	0.0
Ilium fracture	1	0.0
Immunosuppression	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Implantable defibrillator insertion	1	0.0
Infected seroma	1	0.0
Infection susceptibility increased	1	0.0
Infusion	1	0.0
Injection	1	0.0
Injection site erythema	1	0.0
Injection site pruritus	1	0.0
Injection site reaction	1	0.0
Injection site warmth	1	0.0
Intercostal neuralgia	1	0.0
Intestinal operation	1	0.0
Intestinal stenosis	1	0.0
Intracranial aneurysm	1	0.0
Intracranial venous sinus thrombosis	1	0.0
Intraductal papilloma of breast	1	0.0
Intraductal proliferative breast lesion	1	0.0
Invasive breast carcinoma	1	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Iritis	1	0.0
Iron deficiency anaemia	1	0.0
Jaw operation	1	0.0
Joint debridement	1	0.0
Joint destruction	1	0.0
Joint injection	1	0.0
Joint stabilisation	1	0.0
Joint swelling	1	0.0
Keratouveitis	1	0.0
Kidney rupture	1	0.0
Laboratory test abnormal	1	0.0
Lacunar infarction	1	0.0
Laparoscopy	1	0.0
Laparotomy	1	0.0
Laryngeal oedema	1	0.0
Laryngitis	1	0.0
Leg amputation	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Leukoplakia oral	1	0.0
Lichenoid keratosis	1	0.0
Ligament operation	1	0.0
Ligament pain	1	0.0
Ligament sprain	1	0.0
Limb crushing injury	1	0.0
Limb operation	1	0.0
Limb traumatic amputation	1	0.0
Lip repair	1	0.0
Lipoma	1	0.0
Lithotripsy	1	0.0
Liver abscess	1	0.0
Liver disorder	1	0.0
Lividity	1	0.0
Localised infection	1	0.0
Lung abscess	1	0.0
Lung neoplasm malignant	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Lung squamous cell carcinoma stage III	1	0.0
Lung transplant	1	0.0
Lymphangitis	1	0.0
Lymphatic fistula	1	0.0
Lymphoma	1	0.0
Lymphoma operation	1	0.0
Malignant melanoma	1	0.0
Malignant melanoma in situ	1	0.0
Mania	1	0.0
Mediastinoscopy	1	0.0
Melaena	1	0.0
Meningoencephalitis herpetic	1	0.0
Meniscal degeneration	1	0.0
Meniscus injury	1	0.0
Meniscus removal	1	0.0
Menorrhagia	1	0.0
Menstrual disorder	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Metastases to liver	1	0.0
Metastases to lung	1	0.0
Metastases to lymph nodes	1	0.0
Microembolism	1	0.0
Middle insomnia	1	0.0
Migraine	1	0.0
Mitral valve incompetence	1	0.0
Mucocutaneous ulceration	1	0.0
Multiple injuries	1	0.0
Multiple organ dysfunction syndrome	1	0.0
Muscle strain	1	0.0
Musculoskeletal stiffness	1	0.0
Myalgia	1	0.0
Mycobacterium marinum infection	1	0.0
Mycobacterium tuberculosis complex test positive	1	0.0
Myocarditis	1	0.0
Nasal congestion	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Nasal septal operation	1	0.0
Nasal septum deviation	1	0.0
Nasal ulcer	1	0.0
Neck pain	1	0.0
Necrotising fasciitis	1	0.0
Neoplasm skin	1	0.0
Nephrectomy	1	0.0
Nephroplasty	1	0.0
Nephrostomy	1	0.0
Nerve injury	1	0.0
Nerve root compression	1	0.0
Neurectomy	1	0.0
Neurodermatitis	1	0.0
Neuroendocrine carcinoma	1	0.0
Neurological examination	1	0.0
Neutrophil count decreased	1	0.0
Non-Hodgkin's lymphoma	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Oedema peripheral	1	0.0
Oophorectomy	1	0.0
Ophthalmic vein thrombosis	1	0.0
Organising pneumonia	1	0.0
Orthostatic intolerance	1	0.0
Ossiculoplasty	1	0.0
Ostectomy	1	0.0
Osteonecrosis	1	0.0
Osteoporosis	1	0.0
Otitis media	1	0.0
Otosclerosis	1	0.0
Ovarian adhesion	1	0.0
Pancreatic duct rupture	1	0.0
Pancreatic duct stenosis	1	0.0
Pancreatic mass	1	0.0
Pancreatic operation	1	0.0
Pancreatitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Pancreatitis chronic	1	0.0
Pancytopenia	1	0.0
Panic reaction	1	0.0
Paranasal cyst	1	0.0
Paraplegia	1	0.0
Paronychia	1	0.0
Parotidectomy	1	0.0
Parotitis	1	0.0
Partial seizures	1	0.0
Patella fracture	1	0.0
Pelvic venous thrombosis	1	0.0
Percutaneous coronary intervention	1	0.0
Peripheral artery aneurysm	1	0.0
Peripheral artery occlusion	1	0.0
Peripheral artery thrombosis	1	0.0
Peripheral ischaemia	1	0.0
Peritoneal abscess	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Peritoneal lavage	1	0.0
Petechiae	1	0.0
Pharyngeal operation	1	0.0
Pharyngitis	1	0.0
Photosensitivity reaction	1	0.0
Plasmacytoma	1	0.0
Pleural fibrosis	1	0.0
Pneumococcal sepsis	1	0.0
Pneumonia bacterial	1	0.0
Pneumonia escherichia	1	0.0
Pneumonia fungal	1	0.0
Pneumonia legionella	1	0.0
Pneumonia necrotising	1	0.0
Pneumonia viral	1	0.0
Poliomyelitis	1	0.0
Polyarthritis	1	0.0
Polyneuropathy	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Polypectomy	1	0.0
Post herpetic neuralgia	1	0.0
Post polio syndrome	1	0.0
Post procedural haemorrhage	1	0.0
Postmenopause	1	0.0
Precancerous mucosal lesion	1	0.0
Presyncope	1	0.0
Productive cough	1	0.0
Prostatic dysplasia	1	0.0
Prostatic haemorrhage	1	0.0
Proteus test positive	1	0.0
Pruritus	1	0.0
Psoriasis	1	0.0
Pulmonary hilum mass	1	0.0
Pulmonary mass	1	0.0
Pulmonary sepsis	1	0.0
Pulpitis dental	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Purpura	1	0.0
Purulence	1	0.0
Pyeloplasty	1	0.0
Pyonephrosis	1	0.0
Radical prostatectomy	1	0.0
Radioactive iodine therapy	1	0.0
Rash generalised	1	0.0
Rash pustular	1	0.0
Rash vesicular	1	0.0
Rectal polyp	1	0.0
Rectal polypectomy	1	0.0
Red blood cell sedimentation rate increased	1	0.0
Renal artery arteriosclerosis	1	0.0
Renal artery stenosis	1	0.0
Renal artery stent placement	1	0.0
Renal cell carcinoma recurrent	1	0.0
Resuscitation	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Retinal detachment	1	0.0
Rib fracture	1	0.0
Rosacea	1	0.0
SAPHO syndrome	1	0.0
Salivary gland pain	1	0.0
Salmonellosis	1	0.0
Sarcoidosis	1	0.0
Septic encephalopathy	1	0.0
Shock haemorrhagic	1	0.0
Shock hypoglycaemic	1	0.0
Sjogren's syndrome	1	0.0
Skin abrasion	1	0.0
Skin hypertrophy	1	0.0
Skin lesion removal	1	0.0
Skin necrosis	1	0.0
Skin wound	1	0.0
Sleep apnoea syndrome	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Soft tissue injury	1	0.0
Spinal cord ischaemia	1	0.0
Spinal cord operation	1	0.0
Spondyloarthropathy	1	0.0
Sputum discoloured	1	0.0
Stab wound	1	0.0
Staphylococcal sepsis	1	0.0
Staphylococcus test positive	1	0.0
Sternotomy	1	0.0
Stress cardiomyopathy	1	0.0
Stress urinary incontinence	1	0.0
Subcutaneous emphysema	1	0.0
Subileus	1	0.0
Superinfection	1	0.0
Supraventricular tachycardia	1	0.0
Suture related complication	1	0.0
Swelling face	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Synovial disorder	1	0.0
Systemic lupus erythematosus rash	1	0.0
Tachyarrhythmia	1	0.0
Tachycardia	1	0.0
Tachycardia induced cardiomyopathy	1	0.0
Tenosynovitis	1	0.0
Tenosynovitis stenosans	1	0.0
Testicular abscess	1	0.0
Thalamic infarction	1	0.0
Therapeutic embolisation	1	0.0
Thrombolysis	1	0.0
Thyroid adenoma	1	0.0
Thyroid cancer	1	0.0
Tinnitus	1	0.0
Tobacco abuse	1	0.0
Toe amputation	1	0.0
Tongue operation	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Tonsillectomy	1	0.0
Tonsillitis	1	0.0
Toxic encephalopathy	1	0.0
Tracheitis	1	0.0
Transaminases abnormal	1	0.0
Transfusion	1	0.0
Tuberculosis gastrointestinal	1	0.0
Tuberculosis of genitourinary system	1	0.0
Tuberculosis of intrathoracic lymph nodes	1	0.0
Tuberculous pleurisy	1	0.0
Tumour excision	1	0.0
Type 2 diabetes mellitus	1	0.0
Ulcerative gastritis	1	0.0
Ultrasound abdomen abnormal	1	0.0
Umbilical hernia	1	0.0
Umbilical hernia repair	1	0.0
Unevaluable therapy	1	0.0

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(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Ureterectomy	1	0.0
Ureteric operation	1	0.0
Ureteric stenosis	1	0.0
Urinary hesitation	1	0.0
Urinary incontinence surgery	1	0.0
Urinary tract inflammation	1	0.0
Urticarial vasculitis	1	0.0
Uterine cancer	1	0.0
Uterine leiomyoma	1	0.0
Varicose vein operation	1	0.0
Venous operation	1	0.0
Venous thrombosis	1	0.0
Venous thrombosis limb	1	0.0
Ventricular extrasystoles	1	0.0
Ventricular fibrillation	1	0.0
Vertebral artery dissection	1	0.0
Vertebral body replacement	1	0.0

(Continued)

5. Documented adverse events by patient

5.5 All documented serious adverse events by preferred term

	n	%
Preferred Term		
Vertebral foraminal stenosis	1	0.0
Vulvovaginal mycotic infection	1	0.0
Wolff-Parkinson-White syndrome	1	0.0
Wound closure	1	0.0
Wound drainage	1	0.0
Wound healing normal	1	0.0
Wound infection bacterial	1	0.0
Wrist deformity	1	0.0
Wrist surgery	1	0.0

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Total	405	5.6
	Hospitalisation	110	1.5
	Knee arthroplasty	30	0.4
	Elective surgery	27	0.4
	Arthrodesis	25	0.3
	Hip arthroplasty	24	0.3
	Synovectomy	19	0.3
	Foot operation	18	0.2
	Joint arthroplasty	18	0.2
	Bunion operation	14	0.2
	Cholecystectomy	12	0.2
	Therapy cessation	12	0.2
	Surgery	10	0.1
	Therapy change	10	0.1
	Rehabilitation therapy	9	0.1
	Laparoscopic surgery	8	0.1
Spinal operation	8	0.1	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Coronary arterial stent insertion	7	0.1
	Intervertebral disc operation	7	0.1
	Osteosynthesis	7	0.1
	Osteotomy	7	0.1
	Antibiotic therapy	6	0.1
	Arthroscopic surgery	6	0.1
	Coronary artery bypass	6	0.1
	Knee operation	6	0.1
	Rheumatoid nodule removal	6	0.1
	Antibiotic prophylaxis	5	0.1
	Aortic valve replacement	5	0.1
	Bursa removal	5	0.1
	Cardiac pacemaker insertion	5	0.1
	Inguinal hernia repair	5	0.1
	Ankle arthroplasty	4	0.1
	Baker's cyst excision	4	0.1
	Cataract operation	4	0.1

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Fracture treatment	4	0.1
	Renal stone removal	4	0.1
	Rotator cuff repair	4	0.1
	Shoulder operation	4	0.1
	Spinal fusion surgery	4	0.1
	Thyroidectomy	4	0.1
	Abdominal operation	3	0.0
	Abscess drainage	3	0.0
	Ankle operation	3	0.0
	Breast conserving surgery	3	0.0
	Cancer surgery	3	0.0
	Cardiac operation	3	0.0
	Coronary angioplasty	3	0.0
	Emergency care	3	0.0
	Gallbladder operation	3	0.0
	Haematoma evacuation	3	0.0
	Hysterectomy	3	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Joint surgery	3	0.0
	Meniscus operation	3	0.0
	Pain management	3	0.0
	Shoulder arthroplasty	3	0.0
	Sigmoidectomy	3	0.0
	Skin graft	3	0.0
	Skin neoplasm excision	3	0.0
	Spinal decompression	3	0.0
	Stent placement	3	0.0
	Tendon operation	3	0.0
	Toe operation	3	0.0
	Tooth extraction	3	0.0
	Arterial stent insertion	2	0.0
	Breast reconstruction	2	0.0
	Cardiac ablation	2	0.0
	Carpal tunnel decompression	2	0.0
Cartilage operation	2	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Chemotherapy	2	0.0
	Gastrectomy	2	0.0
	Hernia repair	2	0.0
	Hip surgery	2	0.0
	Infiltration anaesthesia	2	0.0
	Joint dislocation reduction	2	0.0
	Massage	2	0.0
	Mastectomy	2	0.0
	Medical device removal	2	0.0
	Nasal operation	2	0.0
	Nasal polypectomy	2	0.0
	Open reduction of fracture	2	0.0
	Ovarian cystectomy	2	0.0
	Postoperative care	2	0.0
	Prostatic operation	2	0.0
	Pulmonary resection	2	0.0
Radiotherapy	2	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Removal of internal fixation	2	0.0
	Sinus operation	2	0.0
	Tendon sheath incision	2	0.0
	Tenoplasty	2	0.0
	Thyroid operation	2	0.0
	Transurethral prostatectomy	2	0.0
	Ureteral stent insertion	2	0.0
	Wound treatment	2	0.0
	Abdominal hernia repair	1	0.0
	Adhesiolysis	1	0.0
	Adrenocortical steroid therapy	1	0.0
	Aneurysm repair	1	0.0
	Angioplasty	1	0.0
	Antiallergic therapy	1	0.0
	Anticoagulant therapy	1	0.0
	Aortic aneurysm repair	1	0.0
	Appendectomy	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Arterial aneurysm repair	1	0.0
	Arterial bypass operation	1	0.0
	Arterial catheterisation	1	0.0
	Arthrotomy	1	0.0
	Bone operation	1	0.0
	Bronchial lesion excision	1	0.0
	Bursal operation	1	0.0
	Cardiac pacemaker replacement	1	0.0
	Cerebrovascular operation	1	0.0
	Chest wall operation	1	0.0
	Coronary revascularisation	1	0.0
	Cryotherapy	1	0.0
	Cyst removal	1	0.0
	Debridement	1	0.0
	Diabetes mellitus management	1	0.0
	Eye operation	1	0.0
	Femoral hernia repair	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Fistula repair	1	0.0
	Fluid replacement	1	0.0
	Fracture debridement	1	0.0
	Frontal sinus operation	1	0.0
	Gastric operation	1	0.0
	Gingival operation	1	0.0
	Haemostasis	1	0.0
	Implantable defibrillator insertion	1	0.0
	Infusion	1	0.0
	Injection	1	0.0
	Intestinal operation	1	0.0
	Jaw operation	1	0.0
	Joint debridement	1	0.0
	Joint injection	1	0.0
	Joint stabilisation	1	0.0
	Laparotomy	1	0.0
Leg amputation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Ligament operation	1	0.0
	Limb operation	1	0.0
	Lip repair	1	0.0
	Lithotripsy	1	0.0
	Lung transplant	1	0.0
	Lymphoma operation	1	0.0
	Meniscus removal	1	0.0
	Nasal septal operation	1	0.0
	Nephrectomy	1	0.0
	Nephroplasty	1	0.0
	Nephrostomy	1	0.0
	Neurectomy	1	0.0
	Oophorectomy	1	0.0
	Ossiculoplasty	1	0.0
	Ostectomy	1	0.0
	Pancreatic operation	1	0.0
Parotidectomy	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Percutaneous coronary intervention	1	0.0
	Peritoneal lavage	1	0.0
	Pharyngeal operation	1	0.0
	Polypectomy	1	0.0
	Pyeloplasty	1	0.0
	Radical prostatectomy	1	0.0
	Radioactive iodine therapy	1	0.0
	Rectal polypectomy	1	0.0
	Renal artery stent placement	1	0.0
	Resuscitation	1	0.0
	Skin lesion removal	1	0.0
	Spinal cord operation	1	0.0
	Sternotomy	1	0.0
	Therapeutic embolisation	1	0.0
	Thrombolysis	1	0.0
	Toe amputation	1	0.0
Tongue operation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Tonsillectomy	1	0.0
	Transfusion	1	0.0
	Tumour excision	1	0.0
	Umbilical hernia repair	1	0.0
	Unevaluable therapy	1	0.0
	Ureterectomy	1	0.0
	Ureteric operation	1	0.0
	Urinary incontinence surgery	1	0.0
	Varicose vein operation	1	0.0
	Venous operation	1	0.0
	Vertebral body replacement	1	0.0
	Wound closure	1	0.0
	Wound drainage	1	0.0
	Wrist surgery	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Total	267	3.7
	Pneumonia	59	0.8
	Infection	14	0.2
	Bronchitis	13	0.2
	Urosepsis	11	0.2
	Diverticulitis	10	0.1
	Urinary tract infection	10	0.1
	Gastroenteritis	8	0.1
	Herpes zoster	8	0.1
	Postoperative wound infection	7	0.1
	Abscess limb	6	0.1
	Post procedural infection	6	0.1
	Sepsis	6	0.1
	Cellulitis	5	0.1
	Respiratory tract infection	5	0.1
Device related infection	4	0.1	
Endocarditis	4	0.1	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Erysipelas	4	0.1
	Meningitis	4	0.1
	Osteomyelitis	4	0.1
	Subcutaneous abscess	4	0.1
	Upper respiratory tract infection	4	0.1
	Abscess	3	0.0
	Gastroenteritis norovirus	3	0.0
	Intervertebral discitis	3	0.0
	Pyelonephritis	3	0.0
	Septic shock	3	0.0
	Sinusitis	3	0.0
	Tuberculosis	3	0.0
	Viral infection	3	0.0
	Wound infection	3	0.0
	Appendicitis perforated	2	0.0
	Breast abscess	2	0.0
Chronic sinusitis	2	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Escherichia sepsis	2	0.0
	Genital herpes	2	0.0
	Infectious colitis	2	0.0
	Infectious pleural effusion	2	0.0
	Lung infection	2	0.0
	Lymph node tuberculosis	2	0.0
	Nasal herpes	2	0.0
	Nasopharyngitis	2	0.0
	Oral herpes	2	0.0
	Peritonitis	2	0.0
	Pertussis	2	0.0
	Pulmonary tuberculosis	2	0.0
	Soft tissue infection	2	0.0
	Staphylococcal infection	2	0.0
	Tooth abscess	2	0.0
	Vestibular neuronitis	2	0.0
Abdominal abscess	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Abscess neck	1	0.0
	Abscess soft tissue	1	0.0
	Acne pustular	1	0.0
	Anal abscess	1	0.0
	Arthritis bacterial	1	0.0
	Atypical pneumonia	1	0.0
	Bronchiolitis	1	0.0
	Bronchitis bacterial	1	0.0
	Bursitis infective	1	0.0
	Candida infection	1	0.0
	Candida pneumonia	1	0.0
	Carbuncle	1	0.0
	Cholangitis infective	1	0.0
	Chronic hepatitis C	1	0.0
	Clostridial infection	1	0.0
	Conjunctivitis	1	0.0
Cystitis	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Diabetic gangrene	1	0.0
	Disseminated tuberculosis	1	0.0
	Emphysematous cholecystitis	1	0.0
	Encephalitis viral	1	0.0
	Endocarditis staphylococcal	1	0.0
	Epstein-Barr virus infection	1	0.0
	Escherichia urinary tract infection	1	0.0
	Folliculitis	1	0.0
	Furuncle	1	0.0
	Gallbladder empyema	1	0.0
	Gastroenteritis viral	1	0.0
	Gastrointestinal infection	1	0.0
	Genital candidiasis	1	0.0
	Gingivitis	1	0.0
	Groin abscess	1	0.0
	Herpes ophthalmic	1	0.0
Herpes simplex encephalitis	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Herpes virus infection	1	0.0
	Infected seroma	1	0.0
	Infection susceptibility increased	1	0.0
	Keratouveitis	1	0.0
	Laryngitis	1	0.0
	Liver abscess	1	0.0
	Localised infection	1	0.0
	Lung abscess	1	0.0
	Lymphangitis	1	0.0
	Meningoencephalitis herpetic	1	0.0
	Mycobacterium marinum infection	1	0.0
	Necrotising fasciitis	1	0.0
	Otitis media	1	0.0
	Paronychia	1	0.0
	Parotitis	1	0.0
Peritoneal abscess	1	0.0	
Pharyngitis	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Pneumococcal sepsis	1	0.0
	Pneumonia bacterial	1	0.0
	Pneumonia escherichia	1	0.0
	Pneumonia fungal	1	0.0
	Pneumonia legionella	1	0.0
	Pneumonia necrotising	1	0.0
	Pneumonia viral	1	0.0
	Poliomyelitis	1	0.0
	Pulmonary sepsis	1	0.0
	Pulpitis dental	1	0.0
	Purulence	1	0.0
	Pyonephrosis	1	0.0
	Rash pustular	1	0.0
	Salmonellosis	1	0.0
	Septic encephalopathy	1	0.0
	Staphylococcal sepsis	1	0.0
Superinfection	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Testicular abscess	1	0.0
	Tonsillitis	1	0.0
	Tracheitis	1	0.0
	Tuberculosis gastrointestinal	1	0.0
	Tuberculosis of genitourinary system	1	0.0
	Tuberculosis of intrathoracic lymph nodes	1	0.0
	Tuberculous pleurisy	1	0.0
	Vulvovaginal mycotic infection	1	0.0
	Wound infection bacterial	1	0.0
Musculoskeletal and connective tissue disorders	Total	163	2.3
	Rheumatoid arthritis	35	0.5
	Osteoarthritis	15	0.2
	Foot deformity	14	0.2
	Intervertebral disc protrusion	13	0.2
	Bursitis	10	0.1
	Lumbar spinal stenosis	10	0.1
	Arthralgia	9	0.1

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Synovial cyst	7	0.1
	Synovitis	7	0.1
	Arthritis	6	0.1
	Rotator cuff syndrome	6	0.1
	Acquired claw toe	5	0.1
	Back pain	5	0.1
	Osteoporotic fracture	5	0.1
	Pain in extremity	5	0.1
	Spinal column stenosis	5	0.1
	Lupus-like syndrome	4	0.1
	Musculoskeletal discomfort	3	0.0
	Spinal osteoarthritis	3	0.0
	Spondylolisthesis	3	0.0
	Arthropathy	2	0.0
	Facet joint syndrome	2	0.0
	Metatarsalgia	2	0.0
	Osteochondrosis	2	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Pseudarthrosis	2	0.0
	Rheumatoid nodule	2	0.0
	Scoliosis	2	0.0
	Spinal instability	2	0.0
	Ankle impingement	1	0.0
	Arthritis reactive	1	0.0
	Bursal haematoma	1	0.0
	Chondromalacia	1	0.0
	Compartment syndrome	1	0.0
	Exostosis	1	0.0
	Felty's syndrome	1	0.0
	Fibromyalgia	1	0.0
	Groin pain	1	0.0
	Haemarthrosis	1	0.0
	Hip deformity	1	0.0
	Joint destruction	1	0.0
Joint swelling	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Ligament pain	1	0.0
	Meniscal degeneration	1	0.0
	Musculoskeletal stiffness	1	0.0
	Myalgia	1	0.0
	Neck pain	1	0.0
	Osteonecrosis	1	0.0
	Osteoporosis	1	0.0
	Polyarthriti	1	0.0
	SAPHO syndrome	1	0.0
	Sjogren's syndrome	1	0.0
	Spondyloarthropathy	1	0.0
	Synovial disorder	1	0.0
	Tenosynovitis	1	0.0
	Tenosynovitis stenosans	1	0.0
	Vertebral foraminal stenosis	1	0.0
Wrist deformity	1	0.0	

(Continued)

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5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Total	96	1.3
	Fall	19	0.3
	Femoral neck fracture	7	0.1
	Humerus fracture	7	0.1
	Multiple fractures	7	0.1
	Tendon rupture	7	0.1
	Joint dislocation	6	0.1
	Lumbar vertebral fracture	6	0.1
	Radius fracture	6	0.1
	Ulna fracture	6	0.1
	Accident at work	5	0.1
	Foot fracture	5	0.1
	Ankle fracture	4	0.1
	Femur fracture	4	0.1
	Fracture displacement	4	0.1
Tibia fracture	4	0.1	
Lower limb fracture	3	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Road traffic accident	3	0.0
	Thoracic vertebral fracture	3	0.0
	Accident at home	2	0.0
	Arthropod bite	2	0.0
	Fracture	2	0.0
	Injury	2	0.0
	Limb injury	2	0.0
	Pelvic fracture	2	0.0
	Post procedural complication	2	0.0
	Post procedural fistula	2	0.0
	Subarachnoid haemorrhage	2	0.0
	Wound	2	0.0
	Wrist fracture	2	0.0
	Acetabulum fracture	1	0.0
	Animal bite	1	0.0
	Burns second degree	1	0.0
Clavicle fracture	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Contusion	1	0.0
	Craniocerebral injury	1	0.0
	Fibula fracture	1	0.0
	Forearm fracture	1	0.0
	Fractured ischium	1	0.0
	Ilium fracture	1	0.0
	Kidney rupture	1	0.0
	Ligament sprain	1	0.0
	Limb crushing injury	1	0.0
	Limb traumatic amputation	1	0.0
	Meniscus injury	1	0.0
	Multiple injuries	1	0.0
	Muscle strain	1	0.0
	Nerve injury	1	0.0
	Pancreatic duct rupture	1	0.0
Patella fracture	1	0.0	
Post procedural haemorrhage	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Rib fracture	1	0.0
	Skin abrasion	1	0.0
	Skin wound	1	0.0
	Soft tissue injury	1	0.0
	Stab wound	1	0.0
	Suture related complication	1	0.0
General disorders and administration site conditions	Total	110	1.5
	Death	16	0.2
	Pyrexia	14	0.2
	Unevaluable event	12	0.2
	Complication associated with device	9	0.1
	Impaired healing	9	0.1
	Drug ineffective	8	0.1
	Chest pain	7	0.1
	Fatigue	4	0.1
	Influenza like illness	4	0.1
	Pain	4	0.1

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Perforated ulcer	4	0.1
	Peripheral swelling	4	0.1
	Inflammation	3	0.0
	No adverse event	3	0.0
	Asthenia	2	0.0
	Condition aggravated	2	0.0
	Cyst	2	0.0
	General physical health deterioration	2	0.0
	Swelling	2	0.0
	Adverse drug reaction	1	0.0
	Chest discomfort	1	0.0
	Drug interaction	1	0.0
	Exercise tolerance decreased	1	0.0
	Granuloma	1	0.0
	Injection site erythema	1	0.0
	Injection site pruritus	1	0.0
Injection site reaction	1	0.0	

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(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Injection site warmth	1	0.0
	Multiple organ dysfunction syndrome	1	0.0
	Oedema peripheral	1	0.0
	Precancerous mucosal lesion	1	0.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Total	90	1.2
	Breast cancer female	15	0.2
	Prostate cancer	5	0.1
	Bladder cancer	4	0.1
	Squamous cell carcinoma	4	0.1
	Basal cell carcinoma	3	0.0
	Invasive ductal breast carcinoma	3	0.0
	Metastases to bone	3	0.0
	Pancreatic carcinoma	3	0.0
	B-cell lymphoma	2	0.0
	Bronchial carcinoma	2	0.0
	Cervix carcinoma	2	0.0
	Neuroma	2	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Ovarian cancer	2	0.0
	Plasma cell myeloma	2	0.0
	Rectal cancer	2	0.0
	Skin cancer	2	0.0
	Transitional cell carcinoma	2	0.0
	Acute myeloid leukaemia	1	0.0
	Anogenital warts	1	0.0
	Atypical fibroxanthoma	1	0.0
	Benign cardiac neoplasm	1	0.0
	Bladder neoplasm	1	0.0
	Bowen's disease	1	0.0
	Brain neoplasm	1	0.0
	Brain neoplasm malignant	1	0.0
	Breast neoplasm	1	0.0
	Bronchial neoplasm	1	0.0
	Cholangiocarcinoma	1	0.0
Chronic lymphocytic leukaemia	1	0.0	

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(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Colon cancer	1	0.0
	Colon neoplasm	1	0.0
	Ear neoplasm malignant	1	0.0
	Epiglottic carcinoma	1	0.0
	Gastric cancer stage I	1	0.0
	Gastric cancer stage III	1	0.0
	Hodgkin's disease	1	0.0
	Hodgkin's disease mixed cellularity stage unspecified	1	0.0
	Intraductal papilloma of breast	1	0.0
	Intraductal proliferative breast lesion	1	0.0
	Invasive breast carcinoma	1	0.0
	Lipoma	1	0.0
	Lung neoplasm malignant	1	0.0
	Lung squamous cell carcinoma stage III	1	0.0
	Lymphoma	1	0.0
	Malignant melanoma	1	0.0
Malignant melanoma in situ	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to liver	1	0.0
	Metastases to lung	1	0.0
	Metastases to lymph nodes	1	0.0
	Neoplasm skin	1	0.0
	Neuroendocrine carcinoma	1	0.0
	Non-Hodgkin's lymphoma	1	0.0
	Plasmacytoma	1	0.0
	Renal cell carcinoma recurrent	1	0.0
	Thyroid adenoma	1	0.0
	Thyroid cancer	1	0.0
	Uterine cancer	1	0.0
	Uterine leiomyoma	1	0.0
Cardiac disorders	Total	80	1.1
	Myocardial infarction	15	0.2
	Coronary artery disease	14	0.2
	Atrial fibrillation	13	0.2
	Acute myocardial infarction	12	0.2

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Cardiac failure	7	0.1
	Coronary artery stenosis	7	0.1
	Angina pectoris	3	0.0
	Aortic valve stenosis	3	0.0
	Arrhythmia	3	0.0
	Palpitations	3	0.0
	Angina unstable	2	0.0
	Cardiac failure chronic	2	0.0
	Left ventricular failure	2	0.0
	Pericarditis	2	0.0
	Sinus node dysfunction	2	0.0
	Sinus tachycardia	2	0.0
	Adams-Stokes syndrome	1	0.0
	Aortic valve incompetence	1	0.0
	Atrial flutter	1	0.0
	Bradyarrhythmia	1	0.0
	Bradycardia	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Hypertensive heart disease	1	0.0
	Mitral valve incompetence	1	0.0
	Myocarditis	1	0.0
	Stress cardiomyopathy	1	0.0
	Supraventricular tachycardia	1	0.0
	Tachyarrhythmia	1	0.0
	Tachycardia	1	0.0
	Tachycardia induced cardiomyopathy	1	0.0
	Ventricular extrasystoles	1	0.0
	Ventricular fibrillation	1	0.0
	Wolff-Parkinson-White syndrome	1	0.0
Nervous system disorders	Total	70	1.0
	Cerebrovascular accident	15	0.2
	Cerebral infarction	5	0.1
	Headache	5	0.1
	Cerebellar infarction	4	0.1
	Dizziness	4	0.1

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Syncope	4	0.1
	Epilepsy	3	0.0
	Hemiparesis	3	0.0
	Movement disorder	3	0.0
	Seizure	3	0.0
	Transient ischaemic attack	3	0.0
	Aphasia	2	0.0
	Cerebral ischaemia	2	0.0
	Dizziness postural	2	0.0
	Hypoaesthesia	2	0.0
	Monoparesis	2	0.0
	Paraesthesia	2	0.0
	Sciatica	2	0.0
	Somnolence	2	0.0
	Brain stem infarction	1	0.0
	Carotid artery stenosis	1	0.0
Carpal tunnel syndrome	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Cerebral haemorrhage	1	0.0
	Cognitive disorder	1	0.0
	Complex regional pain syndrome	1	0.0
	Diabetic neuropathy	1	0.0
	Dysaesthesia	1	0.0
	Dyskinesia	1	0.0
	Facial paresis	1	0.0
	Generalised tonic-clonic seizure	1	0.0
	Gliosis	1	0.0
	Intercostal neuralgia	1	0.0
	Intracranial aneurysm	1	0.0
	Intracranial venous sinus thrombosis	1	0.0
	Lacunar infarction	1	0.0
	Migraine	1	0.0
	Nerve root compression	1	0.0
	Orthostatic intolerance	1	0.0
Paraplegia	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Partial seizures	1	0.0
	Polyneuropathy	1	0.0
	Post herpetic neuralgia	1	0.0
	Post polio syndrome	1	0.0
	Presyncope	1	0.0
	Spinal cord ischaemia	1	0.0
	Thalamic infarction	1	0.0
	Toxic encephalopathy	1	0.0
	Vertebral artery dissection	1	0.0
Gastrointestinal disorders	Total	60	0.8
	Vomiting	9	0.1
	Diarrhoea	5	0.1
	Nausea	5	0.1
	Abdominal pain upper	3	0.0
	Gastric ulcer	3	0.0
	Gastritis	3	0.0
	Inguinal hernia	3	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Abdominal discomfort	2	0.0
	Colitis	2	0.0
	Colitis microscopic	2	0.0
	Diverticular perforation	2	0.0
	Dry mouth	2	0.0
	Dysphagia	2	0.0
	Enteritis	2	0.0
	Gastritis erosive	2	0.0
	Haematochezia	2	0.0
	Pancreatitis acute	2	0.0
	Stomatitis	2	0.0
	Abdominal hernia	1	0.0
	Abdominal pain lower	1	0.0
	Abdominal tenderness	1	0.0
	Aphthous ulcer	1	0.0
	Chronic gastritis	1	0.0
Colitis ulcerative	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Constipation	1	0.0
	Crohn's disease	1	0.0
	Diverticulum intestinal	1	0.0
	Duodenal ulcer	1	0.0
	Erosive duodenitis	1	0.0
	Faecaloma	1	0.0
	Femoral hernia	1	0.0
	Gastrointestinal haemorrhage	1	0.0
	Gastrointestinal pain	1	0.0
	Gastrooesophageal reflux disease	1	0.0
	Gingival recession	1	0.0
	Haemorrhoids	1	0.0
	Hypoaesthesia oral	1	0.0
	Ileus	1	0.0
	Intestinal stenosis	1	0.0
Leukoplakia oral	1	0.0	
Melaena	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Pancreatic duct stenosis	1	0.0
	Pancreatic mass	1	0.0
	Pancreatitis	1	0.0
	Pancreatitis chronic	1	0.0
	Rectal polyp	1	0.0
	Salivary gland pain	1	0.0
	Subileus	1	0.0
	Ulcerative gastritis	1	0.0
	Umbilical hernia	1	0.0
Respiratory, thoracic and mediastinal disorders	Total	59	0.8
	Pulmonary embolism	8	0.1
	Dyspnoea	6	0.1
	Pleural effusion	6	0.1
	Pulmonary fibrosis	5	0.1
	Chronic obstructive pulmonary disease	4	0.1
	Pleurisy	4	0.1
	Alveolitis	3	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Respiratory distress	3	0.0
	Rheumatoid lung	3	0.0
	Cough	2	0.0
	Emphysema	2	0.0
	Hyperventilation	2	0.0
	Interstitial lung disease	2	0.0
	Lung infiltration	2	0.0
	Nasal inflammation	2	0.0
	Pulmonary oedema	2	0.0
	Acute respiratory failure	1	0.0
	Asthma	1	0.0
	Bronchiectasis	1	0.0
	Dyspnoea exertional	1	0.0
	Laryngeal oedema	1	0.0
	Nasal congestion	1	0.0
	Nasal septum deviation	1	0.0
Nasal ulcer	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Organising pneumonia	1	0.0
	Paranasal cyst	1	0.0
	Pleural fibrosis	1	0.0
	Productive cough	1	0.0
	Pulmonary hilum mass	1	0.0
	Pulmonary mass	1	0.0
	Sleep apnoea syndrome	1	0.0
	Sputum discoloured	1	0.0
Investigations	Total	57	0.8
	Arthroscopy	8	0.1
	Blood pressure increased	6	0.1
	Liver function test increased	5	0.1
	Bronchoscopy	3	0.0
	Weight decreased	3	0.0
	Biopsy bone marrow	2	0.0
	Biopsy liver	2	0.0
	C-reactive protein increased	2	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Computerised tomogram thorax abnormal	2	0.0
	Double stranded DNA antibody positive	2	0.0
	Angiogram peripheral	1	0.0
	Antinuclear antibody positive	1	0.0
	Arteriogram coronary	1	0.0
	Autoantibody test	1	0.0
	Biopsy lymph gland	1	0.0
	Blood bactericidal activity	1	0.0
	Blood calcium	1	0.0
	Blood creatine phosphokinase increased	1	0.0
	Catheterisation cardiac	1	0.0
	Colonoscopy normal	1	0.0
	DNA antibody positive	1	0.0
	Ejection fraction decreased	1	0.0
	Emergency care examination	1	0.0
	Endoscopic retrograde cholangiopancreatography	1	0.0
Endoscopy	1	0.0	

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(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Epstein-Barr virus antibody positive	1	0.0
	Fibrin D dimer increased	1	0.0
	Gamma-glutamyltransferase increased	1	0.0
	Haematocrit decreased	1	0.0
	Haemoglobin decreased	1	0.0
	Heart rate irregular	1	0.0
	Laboratory test abnormal	1	0.0
	Laparoscopy	1	0.0
	Mediastinoscopy	1	0.0
	Mycobacterium tuberculosis complex test positive	1	0.0
	Neurological examination	1	0.0
	Neutrophil count decreased	1	0.0
	Proteus test positive	1	0.0
	Red blood cell sedimentation rate increased	1	0.0
	Staphylococcus test positive	1	0.0
	Transaminases abnormal	1	0.0
Ultrasound abdomen abnormal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Wound healing normal	1	0.0
Skin and subcutaneous tissue disorders	Total	49	0.7
	Skin ulcer	7	0.1
	Urticaria	4	0.1
	Dermatitis allergic	3	0.0
	Rash	3	0.0
	Diabetic foot	2	0.0
	Drug eruption	2	0.0
	Erythema	2	0.0
	Hyperhidrosis	2	0.0
	Night sweats	2	0.0
	Pustular psoriasis	2	0.0
	Alopecia	1	0.0
	Decubitus ulcer	1	0.0
	Dermatitis	1	0.0
	Dermatosis	1	0.0
Erythema multiforme	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Hand dermatitis	1	0.0
	Hidradenitis	1	0.0
	Lichenoid keratosis	1	0.0
	Lividity	1	0.0
	Mucocutaneous ulceration	1	0.0
	Neurodermatitis	1	0.0
	Petechiae	1	0.0
	Photosensitivity reaction	1	0.0
	Pruritus	1	0.0
	Psoriasis	1	0.0
	Purpura	1	0.0
	Rash generalised	1	0.0
	Rash vesicular	1	0.0
	Rosacea	1	0.0
	Skin hypertrophy	1	0.0
Skin necrosis	1	0.0	
Subcutaneous emphysema	1	0.0	

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Swelling face	1	0.0
	Systemic lupus erythematosus rash	1	0.0
	Urticarial vasculitis	1	0.0
Vascular disorders	Total	45	0.6
	Hypertension	9	0.1
	Haematoma	5	0.1
	Thrombosis	5	0.1
	Deep vein thrombosis	4	0.1
	Peripheral arterial occlusive disease	4	0.1
	Hypertensive crisis	3	0.0
	Aortic aneurysm	2	0.0
	Vasculitis	2	0.0
	Aortic dilatation	1	0.0
	Arterial occlusive disease	1	0.0
	Arteriosclerosis	1	0.0
	Circulatory collapse	1	0.0
	Flushing	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Vascular disorders	Lymphatic fistula	1	0.0
	Microembolism	1	0.0
	Pelvic venous thrombosis	1	0.0
	Peripheral artery aneurysm	1	0.0
	Peripheral artery occlusion	1	0.0
	Peripheral artery thrombosis	1	0.0
	Peripheral ischaemia	1	0.0
	Shock haemorrhagic	1	0.0
	Venous thrombosis	1	0.0
	Venous thrombosis limb	1	0.0
Renal and urinary disorders	Total	29	0.4
	Acute kidney injury	5	0.1
	Renal failure	5	0.1
	Nephrolithiasis	3	0.0
	Haematuria	2	0.0
	Renal colic	2	0.0
	Renal impairment	2	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Renal and urinary disorders	Ureterolithiasis	2	0.0
	Urinary tract obstruction	2	0.0
	Azotaemia	1	0.0
	Bladder diverticulum	1	0.0
	Bladder stenosis	1	0.0
	Calculus urinary	1	0.0
	Renal artery arteriosclerosis	1	0.0
	Renal artery stenosis	1	0.0
	Stress urinary incontinence	1	0.0
	Ureteric stenosis	1	0.0
	Urinary hesitation	1	0.0
	Urinary tract inflammation	1	0.0
Hepatobiliary disorders	Total	23	0.3
	Cholelithiasis	10	0.1
	Cholecystitis acute	5	0.1
	Cholecystitis	4	0.1
	Bile duct stone	3	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Hepatobiliary disorders	Cholangitis	2	0.0
	Cholestasis	2	0.0
	Jaundice	2	0.0
	Biliary cirrhosis primary	1	0.0
	Cholecystitis chronic	1	0.0
	Gallbladder perforation	1	0.0
	Hepatic cirrhosis	1	0.0
	Hepatitis cholestatic	1	0.0
	Liver disorder	1	0.0
Blood and lymphatic system disorders	Total	21	0.3
	Leukopenia	6	0.1
	Anaemia	5	0.1
	Leukocytosis	3	0.0
	Lymphadenopathy	2	0.0
	Thrombocytopenia	2	0.0
	Agranulocytosis	1	0.0
	Bicytopenia	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Blood and lymphatic system disorders	Cytopenia	1	0.0
	Erythropenia	1	0.0
	Hypochromic anaemia	1	0.0
	Iron deficiency anaemia	1	0.0
	Pancytopenia	1	0.0
Psychiatric disorders	Total	17	0.2
	Depression	8	0.1
	Sleep disorder	2	0.0
	Stress	2	0.0
	Acute stress disorder	1	0.0
	Anxiety	1	0.0
	Mania	1	0.0
	Middle insomnia	1	0.0
	Panic reaction	1	0.0
	Tobacco abuse	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Metabolism and nutrition disorders	Total	12	0.2
	Diabetes mellitus	3	0.0
	Dehydration	2	0.0
	Obesity	2	0.0
	Decreased appetite	1	0.0
	Gout	1	0.0
	Hypercalcaemia	1	0.0
	Hyperglycaemia	1	0.0
	Shock hypoglycaemic	1	0.0
	Type 2 diabetes mellitus	1	0.0
Reproductive system and breast disorders	Total	11	0.2
	Benign prostatic hyperplasia	5	0.1
	Ovarian cyst	2	0.0
	Menorrhagia	1	0.0
	Menstrual disorder	1	0.0
	Ovarian adhesion	1	0.0
	Prostatic dysplasia	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Reproductive system and breast disorders	Prostatic haemorrhage	1	0.0
Endocrine disorders	Total	8	0.1
	Goitre	5	0.1
	Thyroid mass	3	0.0
	Adrenocortical insufficiency acute	1	0.0
	Basedow's disease	1	0.0
	Hyperthyroidism	1	0.0
Ear and labyrinth disorders	Total	8	0.1
	Sudden hearing loss	3	0.0
	Vertigo	2	0.0
	Vertigo positional	2	0.0
	Otosclerosis	1	0.0
	Tinnitus	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Eye disorders	Total	7	0.1
	Blepharitis	2	0.0
	Cataract	1	0.0
	Eye disorder	1	0.0
	Eye haemorrhage	1	0.0
	Glaucoma	1	0.0
	Iritis	1	0.0
	Ophthalmic vein thrombosis	1	0.0
	Retinal detachment	1	0.0
Immune system disorders	Total	4	0.1
	Drug hypersensitivity	1	0.0
	Hypersensitivity	1	0.0
	Immunosuppression	1	0.0
	Sarcoidosis	1	0.0

(Continued)

5. Documented adverse events by patient

5.6 All documented serious adverse events by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Product issues	Total	4	0.1
	Device dislocation	3	0.0
	Device breakage	1	0.0
Pregnancy, puerperium and perinatal conditions	Total	3	0.0
	Pregnancy	2	0.0
	Delivery	1	0.0
	Ectopic pregnancy	1	0.0
Social circumstances	Total	3	0.0
	Alcohol use	1	0.0
	Foreign travel	1	0.0
	Postmenopause	1	0.0
Congenital, familial and genetic disorders	Total	2	0.0
	Developmental hip dysplasia	1	0.0
	Hereditary neuropathic amyloidosis	1	0.0

5. Documented adverse events by patient

5.7 All documented adverse events (without SAE) by system organ class

	n	%
System Organ Class		
Total	2324	32.1
Infections and infestations	1071	14.8
General disorders and administration site conditions	523	7.2
Skin and subcutaneous tissue disorders	391	5.4
Surgical and medical procedures	362	5.0
Musculoskeletal and connective tissue disorders	324	4.5
Gastrointestinal disorders	247	3.4
Nervous system disorders	207	2.9
Respiratory, thoracic and mediastinal disorders	204	2.8
Investigations	200	2.8
Injury, poisoning and procedural complications	121	1.7
Vascular disorders	93	1.3
Eye disorders	67	0.9
Psychiatric disorders	67	0.9
Cardiac disorders	64	0.9
Renal and urinary disorders	50	0.7
Metabolism and nutrition disorders	49	0.7

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(Continued)

5. Documented adverse events by patient

5.7 All documented adverse events (without SAE) by system organ class

	n	%
System Organ Class		
Blood and lymphatic system disorders	46	0.6
Ear and labyrinth disorders	36	0.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	31	0.4
Immune system disorders	26	0.4
Reproductive system and breast disorders	26	0.4
Endocrine disorders	16	0.2
Hepatobiliary disorders	16	0.2
Pregnancy, puerperium and perinatal conditions	16	0.2
Product issues	3	0.0
Congenital, familial and genetic disorders	1	0.0

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Total	2324	32.1
Influenza like illness	213	2.9
Bronchitis	177	2.4
Nasopharyngitis	137	1.9
Upper respiratory tract infection	130	1.8
Respiratory tract infection	106	1.5
Infection	88	1.2
Herpes zoster	79	1.1
Therapy cessation	78	1.1
Cough	72	1.0
Rheumatoid arthritis	72	1.0
Pyrexia	70	1.0
Nausea	69	1.0
Urinary tract infection	68	0.9
Diarrhoea	66	0.9
Rash	65	0.9
Sinusitis	63	0.9

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Headache	55	0.8
Pruritus	55	0.8
Dizziness	49	0.7
Elective surgery	48	0.7
Oral herpes	46	0.6
Pneumonia	46	0.6
Drug ineffective	44	0.6
Fatigue	43	0.6
Injection site erythema	40	0.6
Antibiotic therapy	37	0.5
Hypertension	37	0.5
Psoriasis	35	0.5
Cystitis	34	0.5
Erythema	31	0.4
Fall	29	0.4
Liver function test increased	29	0.4
Rash pruritic	29	0.4

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Depression	28	0.4
Alopecia	27	0.4
Arthralgia	27	0.4
Laboratory test abnormal	26	0.4
Pulpitis dental	25	0.3
Back pain	23	0.3
Eczema	22	0.3
Pain in extremity	22	0.3
Tonsillitis	22	0.3
Gastroenteritis	21	0.3
Osteoarthritis	21	0.3
Paraesthesia	21	0.3
Antibiotic prophylaxis	20	0.3
Gastrointestinal infection	20	0.3
Oropharyngeal pain	20	0.3
Vomiting	20	0.3
Erysipelas	19	0.3

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Injection site reaction	19	0.3
Rhinitis	19	0.3
Urticaria	19	0.3
Conjunctivitis	18	0.2
Cystitis noninfective	18	0.2
Dermatitis allergic	18	0.2
Dyspnoea	18	0.2
Hypersensitivity	18	0.2
Injection site pruritus	18	0.2
Joint swelling	18	0.2
Palpitations	18	0.2
Pharyngitis	18	0.2
Unevaluable event	18	0.2
Bursitis	17	0.2
Blood pressure increased	16	0.2
Respiratory distress	16	0.2
Abdominal discomfort	15	0.2

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Arthritis	15	0.2
Hyperhidrosis	15	0.2
Joint surgery	15	0.2
Intervertebral disc protrusion	14	0.2
Sciatica	14	0.2
Skin ulcer	14	0.2
Sleep disorder	14	0.2
Spinal pain	14	0.2
Epistaxis	13	0.2
Otitis media	13	0.2
Pain	13	0.2
Pregnancy	13	0.2
Synovial cyst	13	0.2
Tooth extraction	13	0.2
Angina pectoris	12	0.2
Aphthous ulcer	12	0.2
Cataract operation	12	0.2

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Leukopenia	12	0.2
Rash generalised	12	0.2
Rash pustular	12	0.2
Viral infection	12	0.2
Arthrodesis	11	0.2
Asthenia	11	0.2
Dry mouth	11	0.2
Gamma-glutamyltransferase increased	11	0.2
Influenza	11	0.2
Oedema peripheral	11	0.2
Rhinorrhoea	11	0.2
Synovectomy	11	0.2
Abdominal pain upper	10	0.1
Burning sensation	10	0.1
Dyspnoea exertional	10	0.1
Foot fracture	10	0.1
Gastritis	10	0.1

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Joint effusion	10	0.1
Knee arthroplasty	10	0.1
Knee operation	10	0.1
Osteoporosis	10	0.1
Productive cough	10	0.1
Alanine aminotransferase increased	9	0.1
Arthroscopy	9	0.1
Dental operation	9	0.1
Dermatitis psoriasiform	9	0.1
Laryngitis	9	0.1
Lymphadenopathy	9	0.1
Osteopenia	9	0.1
Peripheral swelling	9	0.1
Pruritus generalised	9	0.1
Subcutaneous abscess	9	0.1
Transaminases increased	9	0.1
Borrelia infection	8	0.1

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Cataract	8	0.1
Foot operation	8	0.1
General physical health deterioration	8	0.1
Hypoaesthesia	8	0.1
Impaired healing	8	0.1
Infection susceptibility increased	8	0.1
Injection site pain	8	0.1
Local reaction	8	0.1
Night sweats	8	0.1
Pyelonephritis	8	0.1
Rheumatoid nodule	8	0.1
Rotator cuff syndrome	8	0.1
Skin disorder	8	0.1
Stomatitis	8	0.1
Tenosynovitis	8	0.1
Tinnitus	8	0.1
Antinuclear antibody increased	7	0.1

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Bacterial infection	7	0.1
Bronchitis bacterial	7	0.1
Chills	7	0.1
Diabetes mellitus	7	0.1
Diverticulitis	7	0.1
Drug intolerance	7	0.1
Eye inflammation	7	0.1
Fungal infection	7	0.1
Gingivitis	7	0.1
Haematoma	7	0.1
Haematuria	7	0.1
Herpes virus infection	7	0.1
Hyperuricaemia	7	0.1
Ligament sprain	7	0.1
Limb injury	7	0.1
Middle ear inflammation	7	0.1
Myalgia	7	0.1

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Polyneuropathy	7	0.1
Rash macular	7	0.1
Rheumatoid nodule removal	7	0.1
Skin reaction	7	0.1
Spinal osteoarthritis	7	0.1
Tendon rupture	7	0.1
Vision blurred	7	0.1
Visual impairment	7	0.1
Vitamin D deficiency	7	0.1
Anxiety	6	0.1
Arthropod bite	6	0.1
Basal cell carcinoma	6	0.1
Carpal tunnel decompression	6	0.1
Carpal tunnel syndrome	6	0.1
Chest discomfort	6	0.1
Cholelithiasis	6	0.1
Dermatitis	6	0.1

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Dry skin	6	0.1
Ear pain	6	0.1
Flushing	6	0.1
Fungal skin infection	6	0.1
Hospitalisation	6	0.1
Hypothyroidism	6	0.1
Injection site swelling	6	0.1
Joint arthroplasty	6	0.1
Migraine	6	0.1
Musculoskeletal pain	6	0.1
Nail bed inflammation	6	0.1
Onychomycosis	6	0.1
Pustular psoriasis	6	0.1
Rheumatoid factor increased	6	0.1
Skin neoplasm excision	6	0.1
Swelling	6	0.1
Tachycardia	6	0.1

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Therapy change	6	0.1
Thrombocytopenia	6	0.1
Abdominal distension	5	0.1
Abscess limb	5	0.1
Arrhythmia	5	0.1
Asthma	5	0.1
Blood creatinine increased	5	0.1
Body temperature increased	5	0.1
Bursa removal	5	0.1
Chronic obstructive pulmonary disease	5	0.1
Coronary artery disease	5	0.1
Dental care	5	0.1
Drug eruption	5	0.1
Dysphagia	5	0.1
Folliculitis	5	0.1
Foot deformity	5	0.1
Gastroenteritis viral	5	0.1

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Goitre	5	0.1
Humerus fracture	5	0.1
Hyperlipidaemia	5	0.1
Inflammation	5	0.1
Iritis	5	0.1
Meniscus operation	5	0.1
Oral candidiasis	5	0.1
Ovarian cyst	5	0.1
Paronychia	5	0.1
Pleurisy	5	0.1
Renal failure	5	0.1
Rosacea	5	0.1
Sudden hearing loss	5	0.1
Thrombosis	5	0.1
Vasculitis	5	0.1
Vulvovaginal mycotic infection	5	0.1
Weight decreased	5	0.1

1282

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Abdominal pain	4	0.1
Abscess drainage	4	0.1
Anaemia	4	0.1
Anxiety disorder	4	0.1
Chronic kidney disease	4	0.1
Chronic sinusitis	4	0.1
Colitis	4	0.1
Depressed mood	4	0.1
Dermatosis	4	0.1
Dry eye	4	0.1
Ear discomfort	4	0.1
Endodontic procedure	4	0.1
Enthesopathy	4	0.1
Erythema migrans	4	0.1
Essential hypertension	4	0.1
Exostosis	4	0.1
Fracture treatment	4	0.1

1283

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Gastrointestinal pain	4	0.1
Gastroesophageal reflux disease	4	0.1
Glaucoma	4	0.1
Haemoptysis	4	0.1
Hip arthroplasty	4	0.1
Hip surgery	4	0.1
Histology normal	4	0.1
Hypercholesterolaemia	4	0.1
Inflammatory marker increased	4	0.1
Injection site hypersensitivity	4	0.1
Injection site urticaria	4	0.1
Joint dislocation	4	0.1
Joint range of motion decreased	4	0.1
Laryngeal inflammation	4	0.1
Lymphoedema	4	0.1
Malaise	4	0.1
Meniscus removal	4	0.1

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Muscle spasms	4	0.1
Musculoskeletal discomfort	4	0.1
Osteitis	4	0.1
Peripheral venous disease	4	0.1
Pleural effusion	4	0.1
Radius fracture	4	0.1
Rash erythematous	4	0.1
Rash papular	4	0.1
Renal colic	4	0.1
Seasonal allergy	4	0.1
Sjogren's syndrome	4	0.1
Skin infection	4	0.1
Skin lesion	4	0.1
Skin papilloma	4	0.1
Somnolence	4	0.1
Surgery	4	0.1
Tooth infection	4	0.1

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Toothache	4	0.1
Type 2 diabetes mellitus	4	0.1
Vertigo	4	0.1
Weight increased	4	0.1
Wisdom teeth removal	4	0.1
Accident	3	0.0
Aortic aneurysm	3	0.0
Atrial fibrillation	3	0.0
Autoimmune thyroiditis	3	0.0
Blood cholesterol increased	3	0.0
Blood pressure measurement	3	0.0
Breast abscess	3	0.0
Bronchitis chronic	3	0.0
Bronchitis viral	3	0.0
Bunion operation	3	0.0
C-reactive protein increased	3	0.0
Campylobacter infection	3	0.0

1286

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Cardiac failure	3	0.0
Cardiovascular disorder	3	0.0
Cerebrovascular disorder	3	0.0
Chest pain	3	0.0
Colitis microscopic	3	0.0
Decreased appetite	3	0.0
Delivery	3	0.0
Dental implantation	3	0.0
Disturbance in attention	3	0.0
Epicondylitis	3	0.0
Epigastric discomfort	3	0.0
Eyelid oedema	3	0.0
Feeling cold	3	0.0
Fracture	3	0.0
Furuncle	3	0.0
Gastroenteritis norovirus	3	0.0
Gingival recession	3	0.0

1287

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Gout	3	0.0
Haematochezia	3	0.0
Haemorrhage	3	0.0
Hand fracture	3	0.0
Hepatic enzyme increased	3	0.0
Hepatic steatosis	3	0.0
Herpes simplex	3	0.0
Hot flush	3	0.0
Hypertonia	3	0.0
Hypoaesthesia oral	3	0.0
Injection site inflammation	3	0.0
Injection site rash	3	0.0
Intervertebral disc operation	3	0.0
Iridocyclitis	3	0.0
Leukocytosis	3	0.0
Localised infection	3	0.0
Lumbar spinal stenosis	3	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Meniscus injury	3	0.0
Menorrhagia	3	0.0
Mouth ulceration	3	0.0
Movement disorder	3	0.0
Myelodysplastic syndrome	3	0.0
Nasal herpes	3	0.0
Noninfective gingivitis	3	0.0
Oedema	3	0.0
Osteochondrosis	3	0.0
Performance status decreased	3	0.0
Photosensitivity reaction	3	0.0
Post procedural infection	3	0.0
Restlessness	3	0.0
Retching	3	0.0
Rib fracture	3	0.0
Road traffic accident	3	0.0
Root canal infection	3	0.0

1289

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Sinus operation	3	0.0
Skin abrasion	3	0.0
Skin burning sensation	3	0.0
Sleep apnoea syndrome	3	0.0
Spinal fracture	3	0.0
Spinal operation	3	0.0
Swelling face	3	0.0
Tendon operation	3	0.0
Thrombophlebitis	3	0.0
Toe operation	3	0.0
Tooth abscess	3	0.0
Tuberculosis	3	0.0
Vertebral foraminal stenosis	3	0.0
Wrist surgery	3	0.0
Abscess	2	0.0
Abscess oral	2	0.0
Accident at home	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Acne	2	0.0
Adrenocortical steroid therapy	2	0.0
Adverse reaction	2	0.0
Agoraphobia	2	0.0
Alcohol detoxification	2	0.0
Allergic sinusitis	2	0.0
Alveolitis allergic	2	0.0
Antinuclear antibody	2	0.0
Apathy	2	0.0
Arthroscopic surgery	2	0.0
Aspartate aminotransferase increased	2	0.0
Baker's cyst excision	2	0.0
Balance disorder	2	0.0
Biliary colic	2	0.0
Blepharitis	2	0.0
Blood creatine phosphokinase increased	2	0.0
Blood pressure decreased	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Blood triglycerides increased	2	0.0
Bone contusion	2	0.0
Bowen's disease	2	0.0
Bradycardia	2	0.0
Cervical conisation	2	0.0
Cholecystitis	2	0.0
Complication associated with device	2	0.0
Computerised tomogram thorax	2	0.0
Computerised tomogram thorax abnormal	2	0.0
Condition aggravated	2	0.0
Contusion	2	0.0
Coronary artery bypass	2	0.0
Cyst	2	0.0
Cyst removal	2	0.0
Deep vein thrombosis	2	0.0
Dental discomfort	2	0.0
Diplopia	2	0.0

1292

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Drug effect decreased	2	0.0
Drug hypersensitivity	2	0.0
Dysaesthesia	2	0.0
Dyspepsia	2	0.0
Dysphonia	2	0.0
Ear infection	2	0.0
Enteritis	2	0.0
Eosinophilia	2	0.0
Epstein-Barr virus infection	2	0.0
Erectile dysfunction	2	0.0
Eye haemorrhage	2	0.0
Eye infection	2	0.0
Eye operation	2	0.0
Eye pain	2	0.0
Eye swelling	2	0.0
Fibromyalgia	2	0.0
Gait disturbance	2	0.0

1293

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Genital herpes	2	0.0
Genital infection fungal	2	0.0
Genitourinary tract infection	2	0.0
Groin abscess	2	0.0
Guttate psoriasis	2	0.0
Gynaecomastia	2	0.0
Haemarthrosis	2	0.0
Haemorrhoids	2	0.0
Hand dermatitis	2	0.0
Hepatic cirrhosis	2	0.0
Herpes dermatitis	2	0.0
Hiatus hernia	2	0.0
Hyperchromic anaemia	2	0.0
Hypertensive crisis	2	0.0
Hypotension	2	0.0
Inguinal hernia	2	0.0
Inguinal hernia repair	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Injection	2	0.0
Injection site abscess	2	0.0
Injection site dermatitis	2	0.0
Injection site induration	2	0.0
Injection site warmth	2	0.0
Intervertebral disc disorder	2	0.0
Jaw operation	2	0.0
Joint warmth	2	0.0
Keratitis	2	0.0
Latent tuberculosis	2	0.0
Leukocyturia	2	0.0
Ligament rupture	2	0.0
Limb discomfort	2	0.0
Lip swelling	2	0.0
Liver disorder	2	0.0
Lumbar vertebral fracture	2	0.0
Lung infection	2	0.0

1295

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Lupus-like syndrome	2	0.0
Macular degeneration	2	0.0
Mediastinoscopy	2	0.0
Metrorrhagia	2	0.0
Middle insomnia	2	0.0
Mood swings	2	0.0
Mucosal dryness	2	0.0
Musculoskeletal stiffness	2	0.0
Myocarditis	2	0.0
Nasal inflammation	2	0.0
Neuralgia	2	0.0
Neutropenia	2	0.0
Nodal osteoarthritis	2	0.0
Ocular discomfort	2	0.0
Osteoporotic fracture	2	0.0
Osteotomy	2	0.0
Painful respiration	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Papule	2	0.0
Paranasal sinus discomfort	2	0.0
Parkinson's disease	2	0.0
Patella fracture	2	0.0
Pelvic fracture	2	0.0
Periodontitis	2	0.0
Peripheral arterial occlusive disease	2	0.0
Pharyngeal inflammation	2	0.0
Pneumonitis	2	0.0
Poor quality sleep	2	0.0
Post procedural complication	2	0.0
Postoperative wound infection	2	0.0
Pulmonary embolism	2	0.0
Rash maculo-papular	2	0.0
Rash vesicular	2	0.0
Renal impairment	2	0.0
Renal pain	2	0.0

1297

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Restless legs syndrome	2	0.0
Rheumatoid lung	2	0.0
Salmonellosis	2	0.0
Sensory disturbance	2	0.0
Shoulder operation	2	0.0
Sinobronchitis	2	0.0
Skin exfoliation	2	0.0
Skin fissures	2	0.0
Soft tissue infection	2	0.0
Somatic symptom disorder	2	0.0
Spinal fusion surgery	2	0.0
Sputum discoloured	2	0.0
Syncope	2	0.0
Synovial rupture	2	0.0
Synovitis	2	0.0
Tendon sheath incision	2	0.0
Tendonitis	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Thoracic vertebral fracture	2	0.0
Tinea versicolour	2	0.0
Tongue discomfort	2	0.0
Transient ischaemic attack	2	0.0
Tremor	2	0.0
Ulcerative keratitis	2	0.0
Urticarial vasculitis	2	0.0
Vaginal infection	2	0.0
Vascular graft	2	0.0
Venous thrombosis limb	2	0.0
Visual acuity reduced	2	0.0
Vitamin B12 deficiency	2	0.0
Vocal cord inflammation	2	0.0
Vulvovaginal candidiasis	2	0.0
Vulvovaginal inflammation	2	0.0
White blood cell count increased	2	0.0
Wound	2	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Wrist fracture	2	0.0
Abdominal operation	1	0.0
Abdominal pain lower	1	0.0
Abdominal wall abscess	1	0.0
Abortion spontaneous	1	0.0
Abscess jaw	1	0.0
Abscess neck	1	0.0
Abscess of eyelid	1	0.0
Accident at work	1	0.0
Accidental death	1	0.0
Acinetobacter infection	1	0.0
Activated partial thromboplastin time normal	1	0.0
Acute coronary syndrome	1	0.0
Acute kidney injury	1	0.0
Acute myeloid leukaemia	1	0.0
Acute myocardial infarction	1	0.0
Acute sinusitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Adjustment disorder with depressed mood	1	0.0
Agitation	1	0.0
Alcoholism	1	0.0
Allergic cough	1	0.0
Amenorrhoea	1	0.0
Anaemia vitamin B12 deficiency	1	0.0
Anal erosion	1	0.0
Analgesic therapy	1	0.0
Anaphylactic reaction	1	0.0
Angina unstable	1	0.0
Angioedema	1	0.0
Animal bite	1	0.0
Anti-cyclic citrullinated peptide antibody positive	1	0.0
Antiallergic therapy	1	0.0
Antibody test abnormal	1	0.0
Antinuclear antibody positive	1	0.0
Aortic aneurysm repair	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Aortic dilatation	1	0.0
Aortic valve incompetence	1	0.0
Apicectomy	1	0.0
Apnoea	1	0.0
Appendicectomy	1	0.0
Application site reaction	1	0.0
Arteritis	1	0.0
Arthritis infective	1	0.0
Arthropathy	1	0.0
Aspartate aminotransferase normal	1	0.0
Atelectasis	1	0.0
Auditory disorder	1	0.0
Auricular swelling	1	0.0
Autoimmune pancreatitis	1	0.0
Autonomic ganglionectomy	1	0.0
Autonomic nervous system imbalance	1	0.0
Axonal neuropathy	1	0.0

1302

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Bacterial vaginosis	1	0.0
Bacteriuria	1	0.0
Bartholin's cyst	1	0.0
Biopsy	1	0.0
Biopsy liver	1	0.0
Bladder irritation	1	0.0
Blister infected	1	0.0
Blood bilirubin increased	1	0.0
Blood count abnormal	1	0.0
Blood glucose fluctuation	1	0.0
Blood immunoglobulin M increased	1	0.0
Blood lactate dehydrogenase	1	0.0
Blood pressure abnormal	1	0.0
Blood urea increased	1	0.0
Blood uric acid	1	0.0
Bone densitometry	1	0.0
Bone disorder	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Bone fissure	1	0.0
Bone graft	1	0.0
Bone pain	1	0.0
Bordetella infection	1	0.0
Borrelia test positive	1	0.0
Breast cancer female	1	0.0
Breast mass	1	0.0
Breast neoplasm	1	0.0
Breast pain	1	0.0
Bronchial carcinoma	1	0.0
Bronchoscopy abnormal	1	0.0
Calcific deposits removal	1	0.0
Candida infection	1	0.0
Candida test positive	1	0.0
Cardiac failure chronic	1	0.0
Cardiac flutter	1	0.0
Carotid arteriosclerosis	1	0.0

1304

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Cartilage injury	1	0.0
Cast application	1	0.0
Cellulitis	1	0.0
Central obesity	1	0.0
Cerebral microangiopathy	1	0.0
Cerebrovascular accident	1	0.0
Cervical dysplasia	1	0.0
Cervical laser therapy	1	0.0
Cervical spinal stenosis	1	0.0
Cervicobrachial syndrome	1	0.0
Cervix carcinoma stage 0	1	0.0
Chest X-ray abnormal	1	0.0
Chillblains	1	0.0
Chlamydia test positive	1	0.0
Chlamydial infection	1	0.0
Cholestasis	1	0.0
Chronic tonsillitis	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Clostridial sepsis	1	0.0
Colitis ulcerative	1	0.0
Colonoscopy	1	0.0
Computerised tomogram abdomen abnormal	1	0.0
Computerised tomogram kidney abnormal	1	0.0
Congenital tongue anomaly	1	0.0
Constipation	1	0.0
Craniocerebral injury	1	0.0
Crohn's disease	1	0.0
Cutaneous leishmaniasis	1	0.0
Cutaneous lupus erythematosus	1	0.0
Decubitus ulcer	1	0.0
Demyelinating polyneuropathy	1	0.0
Dermatophytosis	1	0.0
Device breakage	1	0.0
Device dislocation	1	0.0
Device expulsion	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Device related infection	1	0.0
Diabetic foot	1	0.0
Diabetic neuropathy	1	0.0
Diarrhoea haemorrhagic	1	0.0
Diffuse alopecia	1	0.0
Dizziness postural	1	0.0
Double stranded DNA antibody positive	1	0.0
Drug reaction with eosinophilia and systemic symptoms	1	0.0
Drug specific antibody present	1	0.0
Duodenitis haemorrhagic	1	0.0
Dysgeusia	1	0.0
Dyspareunia	1	0.0
Dysphonia psychogenic	1	0.0
Dysplasia	1	0.0
Dysuria	1	0.0
Ear operation	1	0.0
Echocardiogram	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Eczema asteatotic	1	0.0
Eczema weeping	1	0.0
Electrolyte imbalance	1	0.0
Endometriosis	1	0.0
Endoscopy normal	1	0.0
Endoscopy upper gastrointestinal tract	1	0.0
Enterocolitis bacterial	1	0.0
Enterovirus infection	1	0.0
Epiglottic cyst	1	0.0
Epilepsy	1	0.0
Erythema of eyelid	1	0.0
Eschar	1	0.0
Exfoliative rash	1	0.0
External ear pain	1	0.0
Extrasystoles	1	0.0
Extravasation	1	0.0
Eye infection bacterial	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Eye infection viral	1	0.0
Feeling abnormal	1	0.0
Feeling hot	1	0.0
Femur fracture	1	0.0
Fibrosis	1	0.0
Fibula fracture	1	0.0
Fine motor skill dysfunction	1	0.0
Finger deformity	1	0.0
Fistula	1	0.0
Flatulence	1	0.0
Food poisoning	1	0.0
Forced expiratory volume	1	0.0
Fractured ischium	1	0.0
Gait inability	1	0.0
Gamma-glutamyltransferase abnormal	1	0.0
Gastric antral vascular ectasia	1	0.0
Gastric ulcer	1	0.0

1309

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Gastric ulcer haemorrhage	1	0.0
Gastrointestinal mucosal disorder	1	0.0
Gastrointestinal viral infection	1	0.0
Genital candidiasis	1	0.0
Genital herpes zoster	1	0.0
Giardiasis	1	0.0
Gingival bleeding	1	0.0
Gingival discomfort	1	0.0
Gingival graft	1	0.0
Gingival operation	1	0.0
Glaucoma surgery	1	0.0
Glossodynia	1	0.0
Gynaecological examination	1	0.0
Gynaecological examination normal	1	0.0
Haemochromatosis	1	0.0
Haemoglobin decreased	1	0.0
Haemorrhagic diathesis	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Hallucination	1	0.0
Hallucination, auditory	1	0.0
Hand-foot-and-mouth disease	1	0.0
Head discomfort	1	0.0
Head injury	1	0.0
Heart rate increased	1	0.0
Heart valve replacement	1	0.0
Heat stroke	1	0.0
Helicobacter gastritis	1	0.0
Helicobacter infection	1	0.0
Hemiparesis	1	0.0
Henoch-Schonlein purpura	1	0.0
Hepatic enzyme abnormal	1	0.0
Hepatic fibrosis	1	0.0
Herpes ophthalmic	1	0.0
Hordeolum	1	0.0
Hyperaesthesia	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Hypercalcaemia	1	0.0
Hyperferritinaemia	1	0.0
Hyperglycaemia	1	0.0
Hyperkalaemia	1	0.0
Hypertensive heart disease	1	0.0
Hyperthyroidism	1	0.0
Hypertriglyceridaemia	1	0.0
Hypochloraemia	1	0.0
Hypokalaemia	1	0.0
Hypophosphataemia	1	0.0
Hyposmia	1	0.0
Hypoventilation	1	0.0
Hysterectomy	1	0.0
Illusion	1	0.0
Immunosuppression	1	0.0
Impetigo	1	0.0
Increased bronchial secretion	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Increased tendency to bruise	1	0.0
Induration	1	0.0
Infected bite	1	0.0
Infected dermal cyst	1	0.0
Infected skin ulcer	1	0.0
Infectious mononucleosis	1	0.0
Inflammation of lacrimal passage	1	0.0
Inflammation of wound	1	0.0
Ingrowing nail	1	0.0
Injection related reaction	1	0.0
Injection site bruising	1	0.0
Injection site infection	1	0.0
Injection site oedema	1	0.0
Insomnia	1	0.0
Intertrigo	1	0.0
Intervertebral disc degeneration	1	0.0
Intestinal resection	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Intraocular lens implant	1	0.0
Iron deficiency	1	0.0
Iron deficiency anaemia	1	0.0
Irritable bowel syndrome	1	0.0
Jaundice	1	0.0
Jaw cyst	1	0.0
Joint fluid drainage	1	0.0
Joint injection	1	0.0
Joint injury	1	0.0
Joint stabilisation	1	0.0
Joint stiffness	1	0.0
Keratoplasty	1	0.0
Kidney infection	1	0.0
Laboratory test	1	0.0
Lactose intolerance	1	0.0
Left ventricular dysfunction	1	0.0
Leg amputation	1	0.0

1314

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Ligament operation	1	0.0
Limb crushing injury	1	0.0
Limb mass	1	0.0
Limb operation	1	0.0
Lip injury	1	0.0
Lip oedema	1	0.0
Lipoatrophy	1	0.0
Lipoma	1	0.0
Liver function test	1	0.0
Loss of consciousness	1	0.0
Low density lipoprotein increased	1	0.0
Lower limb fracture	1	0.0
Lower respiratory tract infection	1	0.0
Lung disorder	1	0.0
Lymphadenitis	1	0.0
Lymphocyte count decreased	1	0.0
Lymphocytosis	1	0.0

1315

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Lymphopenia	1	0.0
Macular cyst	1	0.0
Madarosis	1	0.0
Mammoplasty	1	0.0
Mastoiditis	1	0.0
Mean cell volume abnormal	1	0.0
Memory impairment	1	0.0
Meniere's disease	1	0.0
Menstrual disorder	1	0.0
Menstruation irregular	1	0.0
Metastases to thorax	1	0.0
Metastatic neoplasm	1	0.0
Mitral valve incompetence	1	0.0
Mole excision	1	0.0
Mouth cyst	1	0.0
Mucosal inflammation	1	0.0
Mucous membrane disorder	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Muscle contractions involuntary	1	0.0
Muscle fatigue	1	0.0
Muscle spasticity	1	0.0
Muscular weakness	1	0.0
Myocardial infarction	1	0.0
Myoclonus	1	0.0
Myofascial pain syndrome	1	0.0
Nail disorder	1	0.0
Nail operation	1	0.0
Nasal congestion	1	0.0
Nasal dryness	1	0.0
Nasal mucosal disorder	1	0.0
Nasal operation	1	0.0
Neck pain	1	0.0
Neoplasm skin	1	0.0
Nephrolithiasis	1	0.0
Nerve compression	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Neuritis cranial	1	0.0
Neurodermatitis	1	0.0
Neurological symptom	1	0.0
Neurolysis	1	0.0
Neuropathy peripheral	1	0.0
Neurostimulator removal	1	0.0
Neutrophil count increased	1	0.0
Nightmare	1	0.0
No adverse event	1	0.0
Nocturnal dyspnoea	1	0.0
Noninfective sialoadenitis	1	0.0
Nystagmus	1	0.0
Obesity	1	0.0
Ocular hyperaemia	1	0.0
Ocular hypertension	1	0.0
Odynophagia	1	0.0
Oedema mucosal	1	0.0

1318

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Oesophageal candidiasis	1	0.0
Oesophagitis	1	0.0
Off label use	1	0.0
Onychoclasia	1	0.0
Optic neuritis	1	0.0
Oral discomfort	1	0.0
Oral fungal infection	1	0.0
Oral mucosa erosion	1	0.0
Oral mucosal blistering	1	0.0
Orchitis	1	0.0
Orchitis noninfective	1	0.0
Oropharyngitis fungal	1	0.0
Ostectomy	1	0.0
Osteomyelitis	1	0.0
Osteonecrosis	1	0.0
Osteosynthesis	1	0.0
Otitis externa bacterial	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Otitis externa fungal	1	0.0
Otitis media acute	1	0.0
Overdose	1	0.0
Pain in jaw	1	0.0
Pain management	1	0.0
Pancreatitis acute	1	0.0
Panic attack	1	0.0
Panic disorder	1	0.0
Papilloedema	1	0.0
Papilloma excision	1	0.0
Papilloma viral infection	1	0.0
Paradoxical drug reaction	1	0.0
Parkinsonism	1	0.0
Parotitis	1	0.0
Pathological fracture	1	0.0
Pericardial effusion	1	0.0
Pericarditis	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Periodontal disease	1	0.0
Periodontal inflammation	1	0.0
Periostitis	1	0.0
Peripheral artery occlusion	1	0.0
Peripheral artery stenosis	1	0.0
Peripheral sensorimotor neuropathy	1	0.0
Peritoneal abscess	1	0.0
Peritonsillitis	1	0.0
Perivascular dermatitis	1	0.0
Pertussis	1	0.0
Pharyngitis streptococcal	1	0.0
Phlebectomy	1	0.0
Photophobia	1	0.0
Physiotherapy	1	0.0
Pigmentation disorder	1	0.0
Plantar erythema	1	0.0
Platelet count normal	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Platelet disorder	1	0.0
Pleural decortication	1	0.0
Pleurodesis	1	0.0
Pneumonia pseudomonal	1	0.0
Polypectomy	1	0.0
Precancerous mucosal lesion	1	0.0
Proctitis	1	0.0
Product intolerance	1	0.0
Prostate cancer	1	0.0
Prostatic dysplasia	1	0.0
Prostatitis	1	0.0
Prothrombin time normal	1	0.0
Prurigo	1	0.0
Pseudomonas infection	1	0.0
Psoriatic arthropathy	1	0.0
Psychomotor retardation	1	0.0
Pulmonary congestion	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Pulmonary fibrosis	1	0.0
Pulmonary mycosis	1	0.0
Pulmonary tuberculoma	1	0.0
Pulmonary tuberculosis	1	0.0
Purpura	1	0.0
Purulence	1	0.0
Pyelocystitis	1	0.0
Pyoderma	1	0.0
Raynaud's phenomenon	1	0.0
Rectal haemorrhage	1	0.0
Red blood cell sedimentation rate increased	1	0.0
Refractory cytopenia with unilineage dysplasia	1	0.0
Removal of internal fixation	1	0.0
Renal cell carcinoma recurrent	1	0.0
Renal function test abnormal	1	0.0
Renal infarct	1	0.0
Rheumatic disorder	1	0.0

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Rhinitis allergic	1	0.0
Rhonchi	1	0.0
Right ventricular failure	1	0.0
Rubber sensitivity	1	0.0
Sacroiliitis	1	0.0
Salivary gland neoplasm	1	0.0
Salpingo-oophorectomy	1	0.0
Scar	1	0.0
Secretion discharge	1	0.0
Sepsis	1	0.0
Serum ferritin decreased	1	0.0
Serum ferritin increased	1	0.0
Shock hypoglycaemic	1	0.0
Single functional kidney	1	0.0
Skin atrophy	1	0.0
Skin cancer	1	0.0
Skin cyst excision	1	0.0

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Skin discomfort	1	0.0
Skin hypertrophy	1	0.0
Skin induration	1	0.0
Skin irritation	1	0.0
Skin lesion removal	1	0.0
Skin tightness	1	0.0
Skin wound	1	0.0
Soft tissue swelling	1	0.0
Spermatocele	1	0.0
Spinal decompression	1	0.0
Spinal nerve stimulator implantation	1	0.0
Spontaneous haematoma	1	0.0
Sputum purulent	1	0.0
Staphylococcus test positive	1	0.0
Stasis dermatitis	1	0.0
Stent placement	1	0.0
Steroid therapy	1	0.0

1325

(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Stress fracture	1	0.0
Subileus	1	0.0
Superinfection bacterial	1	0.0
Suture related complication	1	0.0
Swollen tongue	1	0.0
Synovial cyst removal	1	0.0
Synoviorthesis	1	0.0
Systemic lupus erythematosus	1	0.0
Temporomandibular joint surgery	1	0.0
Tendon disorder	1	0.0
Tendon injury	1	0.0
Thirst	1	0.0
Thoracic cavity drainage	1	0.0
Throat clearing	1	0.0
Throat irritation	1	0.0
Throat tightness	1	0.0
Thrombophlebitis septic	1	0.0

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Thyroid cancer recurrent	1	0.0
Thyroidectomy	1	0.0
Thyroiditis	1	0.0
Thyroiditis subacute	1	0.0
Tinea pedis	1	0.0
Tongue blistering	1	0.0
Tonsillar inflammation	1	0.0
Tonsillectomy	1	0.0
Tonsillitis bacterial	1	0.0
Tonsillitis streptococcal	1	0.0
Tooth fracture	1	0.0
Tooth loss	1	0.0
Tracheobronchitis	1	0.0
Transurethral prostatectomy	1	0.0
Traumatic fracture	1	0.0
Trigeminal neuralgia	1	0.0
Tuberculin test positive	1	0.0

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Tuberculosis of intrathoracic lymph nodes	1	0.0
Twin pregnancy	1	0.0
Tympanomastoidectomy	1	0.0
Ultrasound abdomen normal	1	0.0
Ultrasound scan	1	0.0
Ultrasound scan normal	1	0.0
Upper limb fracture	1	0.0
Urinary incontinence	1	0.0
Urinary sediment present	1	0.0
Urinary tract neoplasm	1	0.0
Urogenital haemorrhage	1	0.0
Urogenital infection bacterial	1	0.0
Uterine dilation and curettage	1	0.0
Uterine leiomyoma	1	0.0
Uterine polyp	1	0.0
Uterine polypectomy	1	0.0
Uveitis	1	0.0

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(Continued)

5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
Varicella	1	0.0
Varicella zoster virus infection	1	0.0
Varicose vein	1	0.0
Varicose vein operation	1	0.0
Vascular stenosis	1	0.0
Vascular stent insertion	1	0.0
Ventricular extrasystoles	1	0.0
Vertebral column mass	1	0.0
Vertebroplasty	1	0.0
Vestibular migraine	1	0.0
Vocal cord polyp	1	0.0
Vocal cord thickening	1	0.0
Vulval abscess	1	0.0
Weight bearing difficulty	1	0.0
White blood cell analysis abnormal	1	0.0
White blood cell count	1	0.0

(Continued)

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5. Documented adverse events by patient

5.8 All documented adverse events (without SAE) by preferred term

	n	%
Preferred Term		
White blood cell count decreased	1	0.0
Wound infection	1	0.0

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Total	1071	14.8
	Bronchitis	177	2.4
	Nasopharyngitis	137	1.9
	Upper respiratory tract infection	130	1.8
	Respiratory tract infection	106	1.5
	Infection	88	1.2
	Herpes zoster	79	1.1
	Urinary tract infection	68	0.9
	Sinusitis	63	0.9
	Oral herpes	46	0.6
	Pneumonia	46	0.6
	Cystitis	34	0.5
	Pulpitis dental	25	0.3
	Tonsillitis	22	0.3
	Gastroenteritis	21	0.3
Gastrointestinal infection	20	0.3	
Erysipelas	19	0.3	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Rhinitis	19	0.3
	Conjunctivitis	18	0.2
	Pharyngitis	18	0.2
	Otitis media	13	0.2
	Rash pustular	12	0.2
	Viral infection	12	0.2
	Influenza	11	0.2
	Laryngitis	9	0.1
	Subcutaneous abscess	9	0.1
	Borrelia infection	8	0.1
	Infection susceptibility increased	8	0.1
	Pyelonephritis	8	0.1
	Bacterial infection	7	0.1
	Bronchitis bacterial	7	0.1
	Diverticulitis	7	0.1
	Fungal infection	7	0.1
Gingivitis	7	0.1	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Herpes virus infection	7	0.1
	Fungal skin infection	6	0.1
	Onychomycosis	6	0.1
	Abscess limb	5	0.1
	Folliculitis	5	0.1
	Gastroenteritis viral	5	0.1
	Oral candidiasis	5	0.1
	Paronychia	5	0.1
	Vulvovaginal mycotic infection	5	0.1
	Chronic sinusitis	4	0.1
	Erythema migrans	4	0.1
	Skin infection	4	0.1
	Tooth infection	4	0.1
	Breast abscess	3	0.0
	Bronchitis viral	3	0.0
	Campylobacter infection	3	0.0
	Furuncle	3	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Gastroenteritis norovirus	3	0.0
	Herpes simplex	3	0.0
	Localised infection	3	0.0
	Nasal herpes	3	0.0
	Post procedural infection	3	0.0
	Root canal infection	3	0.0
	Tooth abscess	3	0.0
	Tuberculosis	3	0.0
	Abscess	2	0.0
	Abscess oral	2	0.0
	Ear infection	2	0.0
	Epstein-Barr virus infection	2	0.0
	Eye infection	2	0.0
	Genital herpes	2	0.0
	Genital infection fungal	2	0.0
	Genitourinary tract infection	2	0.0
	Groin abscess	2	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Herpes dermatitis	2	0.0
	Injection site abscess	2	0.0
	Latent tuberculosis	2	0.0
	Lung infection	2	0.0
	Periodontitis	2	0.0
	Postoperative wound infection	2	0.0
	Salmonellosis	2	0.0
	Sinobronchitis	2	0.0
	Soft tissue infection	2	0.0
	Tinea versicolour	2	0.0
	Vaginal infection	2	0.0
	Vulvovaginal candidiasis	2	0.0
	Abdominal wall abscess	1	0.0
	Abscess jaw	1	0.0
	Abscess neck	1	0.0
	Abscess of eyelid	1	0.0
Acinetobacter infection	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Acute sinusitis	1	0.0
	Arthritis infective	1	0.0
	Bacterial vaginosis	1	0.0
	Bacteriuria	1	0.0
	Blister infected	1	0.0
	Bordetella infection	1	0.0
	Candida infection	1	0.0
	Cellulitis	1	0.0
	Chlamydial infection	1	0.0
	Chronic tonsillitis	1	0.0
	Clostridial sepsis	1	0.0
	Cutaneous leishmaniasis	1	0.0
	Dermatophytosis	1	0.0
	Device related infection	1	0.0
	Enterocolitis bacterial	1	0.0
	Enterovirus infection	1	0.0
Eye infection bacterial	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Eye infection viral	1	0.0
	Gastrointestinal viral infection	1	0.0
	Genital candidiasis	1	0.0
	Genital herpes zoster	1	0.0
	Giardiasis	1	0.0
	Hand-foot-and-mouth disease	1	0.0
	Helicobacter gastritis	1	0.0
	Helicobacter infection	1	0.0
	Herpes ophthalmic	1	0.0
	Hordeolum	1	0.0
	Impetigo	1	0.0
	Infected bite	1	0.0
	Infected dermal cyst	1	0.0
	Infected skin ulcer	1	0.0
	Infectious mononucleosis	1	0.0
Injection site infection	1	0.0	
Kidney infection	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Lower respiratory tract infection	1	0.0
	Mastoiditis	1	0.0
	Oesophageal candidiasis	1	0.0
	Oral fungal infection	1	0.0
	Orchitis	1	0.0
	Oropharyngitis fungal	1	0.0
	Osteomyelitis	1	0.0
	Otitis externa bacterial	1	0.0
	Otitis externa fungal	1	0.0
	Otitis media acute	1	0.0
	Papilloma viral infection	1	0.0
	Parotitis	1	0.0
	Peritoneal abscess	1	0.0
	Peritonitis	1	0.0
	Pertussis	1	0.0
Pharyngitis streptococcal	1	0.0	
Pneumonia pseudomonal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Pseudomonas infection	1	0.0
	Pulmonary mycosis	1	0.0
	Pulmonary tuberculoma	1	0.0
	Pulmonary tuberculosis	1	0.0
	Purulence	1	0.0
	Pyelocystitis	1	0.0
	Pyoderma	1	0.0
	Sepsis	1	0.0
	Sputum purulent	1	0.0
	Superinfection bacterial	1	0.0
	Thrombophlebitis septic	1	0.0
	Tinea pedis	1	0.0
	Tonsillitis bacterial	1	0.0
	Tonsillitis streptococcal	1	0.0
	Tracheobronchitis	1	0.0
Tuberculosis of intrathoracic lymph nodes	1	0.0	
Urogenital infection bacterial	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Infections and infestations	Varicella	1	0.0
	Varicella zoster virus infection	1	0.0
	Vulval abscess	1	0.0
	Wound infection	1	0.0
General disorders and administration site conditions	Total	523	7.2
	Influenza like illness	213	2.9
	Pyrexia	70	1.0
	Drug ineffective	44	0.6
	Fatigue	43	0.6
	Injection site erythema	40	0.6
	Injection site reaction	19	0.3
	Injection site pruritus	18	0.2
	Unevaluable event	18	0.2
	Pain	13	0.2
	Asthenia	11	0.2
	Oedema peripheral	11	0.2
	Peripheral swelling	9	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	General physical health deterioration	8	0.1
	Impaired healing	8	0.1
	Injection site pain	8	0.1
	Local reaction	8	0.1
	Chills	7	0.1
	Drug intolerance	7	0.1
	Chest discomfort	6	0.1
	Injection site swelling	6	0.1
	Swelling	6	0.1
	Inflammation	5	0.1
	Injection site hypersensitivity	4	0.1
	Injection site urticaria	4	0.1
	Malaise	4	0.1
	Chest pain	3	0.0
	Feeling cold	3	0.0
	Injection site inflammation	3	0.0
Injection site rash	3	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Oedema	3	0.0
	Performance status decreased	3	0.0
	Adverse reaction	2	0.0
	Complication associated with device	2	0.0
	Condition aggravated	2	0.0
	Cyst	2	0.0
	Drug effect decreased	2	0.0
	Gait disturbance	2	0.0
	Injection site dermatitis	2	0.0
	Injection site induration	2	0.0
	Injection site warmth	2	0.0
	Mucosal dryness	2	0.0
	Accidental death	1	0.0
	Application site reaction	1	0.0
	Dysplasia	1	0.0
	Extravasation	1	0.0
Feeling abnormal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
General disorders and administration site conditions	Feeling hot	1	0.0
	Fibrosis	1	0.0
	Gait inability	1	0.0
	Induration	1	0.0
	Injection site bruising	1	0.0
	Injection site oedema	1	0.0
	Mucosal inflammation	1	0.0
	Mucous membrane disorder	1	0.0
	No adverse event	1	0.0
	Oedema mucosal	1	0.0
	Paradoxical drug reaction	1	0.0
	Precancerous mucosal lesion	1	0.0
	Product intolerance	1	0.0
	Secretion discharge	1	0.0
Thirst	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Total	391	5.4
	Rash	65	0.9
	Pruritus	55	0.8
	Psoriasis	35	0.5
	Erythema	31	0.4
	Rash pruritic	29	0.4
	Alopecia	27	0.4
	Eczema	22	0.3
	Urticaria	19	0.3
	Dermatitis allergic	18	0.2
	Hyperhidrosis	15	0.2
	Skin ulcer	14	0.2
	Rash generalised	12	0.2
	Dermatitis psoriasiform	9	0.1
	Pruritus generalised	9	0.1
Night sweats	8	0.1	
Skin disorder	8	0.1	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Rash macular	7	0.1
	Skin reaction	7	0.1
	Dermatitis	6	0.1
	Dry skin	6	0.1
	Nail bed inflammation	6	0.1
	Pustular psoriasis	6	0.1
	Drug eruption	5	0.1
	Rosacea	5	0.1
	Dermatosis	4	0.1
	Rash erythematous	4	0.1
	Rash papular	4	0.1
	Skin lesion	4	0.1
	Photosensitivity reaction	3	0.0
	Skin burning sensation	3	0.0
	Swelling face	3	0.0
	Acne	2	0.0
Guttate psoriasis	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Hand dermatitis	2	0.0
	Papule	2	0.0
	Rash maculo-papular	2	0.0
	Rash vesicular	2	0.0
	Skin exfoliation	2	0.0
	Skin fissures	2	0.0
	Urticarial vasculitis	2	0.0
	Angioedema	1	0.0
	Cutaneous lupus erythematosus	1	0.0
	Decubitus ulcer	1	0.0
	Diabetic foot	1	0.0
	Diffuse alopecia	1	0.0
	Drug reaction with eosinophilia and systemic symptoms	1	0.0
	Eczema asteatotic	1	0.0
	Eczema weeping	1	0.0
Exfoliative rash	1	0.0	
Henoch-Schonlein purpura	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Ingrowing nail	1	0.0
	Intertrigo	1	0.0
	Lipoatrophy	1	0.0
	Madarosis	1	0.0
	Nail disorder	1	0.0
	Neurodermatitis	1	0.0
	Onychoclasia	1	0.0
	Perivascular dermatitis	1	0.0
	Pigmentation disorder	1	0.0
	Plantar erythema	1	0.0
	Prurigo	1	0.0
	Purpura	1	0.0
	Skin atrophy	1	0.0
	Skin discomfort	1	0.0
	Skin hypertrophy	1	0.0
Skin induration	1	0.0	
Skin irritation	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Skin and subcutaneous tissue disorders	Skin tightness	1	0.0
	Stasis dermatitis	1	0.0
Surgical and medical procedures	Total	362	5.0
	Therapy cessation	78	1.1
	Elective surgery	48	0.7
	Antibiotic therapy	37	0.5
	Antibiotic prophylaxis	20	0.3
	Joint surgery	15	0.2
	Tooth extraction	13	0.2
	Cataract operation	12	0.2
	Arthrodesis	11	0.2
	Synovectomy	11	0.2
	Knee arthroplasty	10	0.1
	Knee operation	10	0.1
	Dental operation	9	0.1
	Foot operation	8	0.1
Rheumatoid nodule removal	7	0.1	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Carpal tunnel decompression	6	0.1
	Hospitalisation	6	0.1
	Joint arthroplasty	6	0.1
	Skin neoplasm excision	6	0.1
	Therapy change	6	0.1
	Bursa removal	5	0.1
	Dental care	5	0.1
	Meniscus operation	5	0.1
	Abscess drainage	4	0.1
	Endodontic procedure	4	0.1
	Fracture treatment	4	0.1
	Hip arthroplasty	4	0.1
	Hip surgery	4	0.1
	Meniscus removal	4	0.1
	Surgery	4	0.1
	Wisdom teeth removal	4	0.1
	Bunion operation	3	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Dental implantation	3	0.0
	Intervertebral disc operation	3	0.0
	Sinus operation	3	0.0
	Spinal operation	3	0.0
	Tendon operation	3	0.0
	Toe operation	3	0.0
	Wrist surgery	3	0.0
	Adrenocortical steroid therapy	2	0.0
	Alcohol detoxification	2	0.0
	Arthroscopic surgery	2	0.0
	Baker's cyst excision	2	0.0
	Cervical conisation	2	0.0
	Coronary artery bypass	2	0.0
	Cyst removal	2	0.0
	Eye operation	2	0.0
	Inguinal hernia repair	2	0.0
Injection	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Jaw operation	2	0.0
	Osteotomy	2	0.0
	Shoulder operation	2	0.0
	Spinal fusion surgery	2	0.0
	Tendon sheath incision	2	0.0
	Vascular graft	2	0.0
	Abdominal operation	1	0.0
	Analgesic therapy	1	0.0
	Antiallergic therapy	1	0.0
	Aortic aneurysm repair	1	0.0
	Apicectomy	1	0.0
	Appendicectomy	1	0.0
	Autonomic ganglionectomy	1	0.0
	Bone graft	1	0.0
	Calcific deposits removal	1	0.0
	Cast application	1	0.0
Cervical laser therapy	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Ear operation	1	0.0
	Gingival graft	1	0.0
	Gingival operation	1	0.0
	Glaucoma surgery	1	0.0
	Heart valve replacement	1	0.0
	Hysterectomy	1	0.0
	Intestinal resection	1	0.0
	Intraocular lens implant	1	0.0
	Joint fluid drainage	1	0.0
	Joint injection	1	0.0
	Joint stabilisation	1	0.0
	Keratoplasty	1	0.0
	Leg amputation	1	0.0
	Ligament operation	1	0.0
	Limb operation	1	0.0
	Mammoplasty	1	0.0
Mole excision	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Nail operation	1	0.0
	Nasal operation	1	0.0
	Neurolysis	1	0.0
	Neurostimulator removal	1	0.0
	Ostectomy	1	0.0
	Osteosynthesis	1	0.0
	Pain management	1	0.0
	Papilloma excision	1	0.0
	Phlebectomy	1	0.0
	Physiotherapy	1	0.0
	Pleural decortication	1	0.0
	Pleurodesis	1	0.0
	Polypectomy	1	0.0
	Removal of internal fixation	1	0.0
	Salpingo-oophorectomy	1	0.0
	Skin cyst excision	1	0.0
Skin lesion removal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Surgical and medical procedures	Spinal decompression	1	0.0
	Spinal nerve stimulator implantation	1	0.0
	Stent placement	1	0.0
	Steroid therapy	1	0.0
	Synovial cyst removal	1	0.0
	Synoviorthesis	1	0.0
	Temporomandibular joint surgery	1	0.0
	Thoracic cavity drainage	1	0.0
	Thyroidectomy	1	0.0
	Tonsillectomy	1	0.0
	Transurethral prostatectomy	1	0.0
	Tympanomastoidectomy	1	0.0
	Uterine dilation and curettage	1	0.0
	Uterine polypectomy	1	0.0
	Varicose vein operation	1	0.0
	Vascular stent insertion	1	0.0
Vertebroplasty	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Total	324	4.5
	Rheumatoid arthritis	72	1.0
	Arthralgia	27	0.4
	Back pain	23	0.3
	Pain in extremity	22	0.3
	Osteoarthritis	21	0.3
	Joint swelling	18	0.2
	Bursitis	17	0.2
	Arthritis	15	0.2
	Intervertebral disc protrusion	14	0.2
	Spinal pain	14	0.2
	Synovial cyst	13	0.2
	Joint effusion	10	0.1
	Osteoporosis	10	0.1
	Osteopenia	9	0.1
	Rheumatoid nodule	8	0.1
Rotator cuff syndrome	8	0.1	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Tenosynovitis	8	0.1
	Myalgia	7	0.1
	Spinal osteoarthritis	7	0.1
	Musculoskeletal pain	6	0.1
	Foot deformity	5	0.1
	Enthesopathy	4	0.1
	Exostosis	4	0.1
	Joint range of motion decreased	4	0.1
	Muscle spasms	4	0.1
	Musculoskeletal discomfort	4	0.1
	Osteitis	4	0.1
	Sjogren's syndrome	4	0.1
	Lumbar spinal stenosis	3	0.0
	Osteochondrosis	3	0.0
	Vertebral foraminal stenosis	3	0.0
	Fibromyalgia	2	0.0
	Haemarthrosis	2	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Intervertebral disc disorder	2	0.0
	Joint warmth	2	0.0
	Limb discomfort	2	0.0
	Lupus-like syndrome	2	0.0
	Musculoskeletal stiffness	2	0.0
	Nodal osteoarthritis	2	0.0
	Osteoporotic fracture	2	0.0
	Synovitis	2	0.0
	Tendonitis	2	0.0
	Arthropathy	1	0.0
	Bone disorder	1	0.0
	Bone pain	1	0.0
	Cervical spinal stenosis	1	0.0
	Finger deformity	1	0.0
	Fistula	1	0.0
	Intervertebral disc degeneration	1	0.0
Jaw cyst	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Joint stiffness	1	0.0
	Limb mass	1	0.0
	Muscle fatigue	1	0.0
	Muscular weakness	1	0.0
	Myofascial pain syndrome	1	0.0
	Neck pain	1	0.0
	Osteonecrosis	1	0.0
	Pain in jaw	1	0.0
	Pathological fracture	1	0.0
	Periostitis	1	0.0
	Psoriatic arthropathy	1	0.0
	Rheumatic disorder	1	0.0
	Sacroiliitis	1	0.0
	Soft tissue swelling	1	0.0
	Systemic lupus erythematosus	1	0.0
	Tendon disorder	1	0.0
Vertebral column mass	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Musculoskeletal and connective tissue disorders	Weight bearing difficulty	1	0.0
Gastrointestinal disorders	Total	247	3.4
	Nausea	69	1.0
	Diarrhoea	66	0.9
	Vomiting	20	0.3
	Abdominal discomfort	15	0.2
	Aphthous ulcer	12	0.2
	Dry mouth	11	0.2
	Abdominal pain upper	10	0.1
	Gastritis	10	0.1
	Stomatitis	8	0.1
	Abdominal distension	5	0.1
	Dysphagia	5	0.1
	Abdominal pain	4	0.1
	Colitis	4	0.1
	Gastrointestinal pain	4	0.1
Gastroesophageal reflux disease	4	0.1	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Toothache	4	0.1
	Colitis microscopic	3	0.0
	Epigastric discomfort	3	0.0
	Gingival recession	3	0.0
	Haematochezia	3	0.0
	Hypoaesthesia oral	3	0.0
	Mouth ulceration	3	0.0
	Noninfective gingivitis	3	0.0
	Retching	3	0.0
	Dental discomfort	2	0.0
	Dyspepsia	2	0.0
	Enteritis	2	0.0
	Haemorrhoids	2	0.0
	Hiatus hernia	2	0.0
	Inguinal hernia	2	0.0
	Lip swelling	2	0.0
Tongue discomfort	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Abdominal pain lower	1	0.0
	Anal erosion	1	0.0
	Autoimmune pancreatitis	1	0.0
	Colitis ulcerative	1	0.0
	Constipation	1	0.0
	Crohn's disease	1	0.0
	Diarrhoea haemorrhagic	1	0.0
	Duodenitis haemorrhagic	1	0.0
	Flatulence	1	0.0
	Food poisoning	1	0.0
	Gastric antral vascular ectasia	1	0.0
	Gastric ulcer	1	0.0
	Gastric ulcer haemorrhage	1	0.0
	Gastrointestinal mucosal disorder	1	0.0
	Gingival bleeding	1	0.0
	Gingival discomfort	1	0.0
Glossodynia	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Irritable bowel syndrome	1	0.0
	Lip oedema	1	0.0
	Mouth cyst	1	0.0
	Noninfective sialoadenitis	1	0.0
	Odynophagia	1	0.0
	Oesophagitis	1	0.0
	Oral discomfort	1	0.0
	Oral mucosa erosion	1	0.0
	Oral mucosal blistering	1	0.0
	Pancreatitis acute	1	0.0
	Periodontal disease	1	0.0
	Periodontal inflammation	1	0.0
	Proctitis	1	0.0
	Rectal haemorrhage	1	0.0
	Subileus	1	0.0
Swollen tongue	1	0.0	
Tongue blistering	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Gastrointestinal disorders	Tooth loss	1	0.0
Respiratory, thoracic and mediastinal disorders	Total	204	2.8
	Cough	72	1.0
	Oropharyngeal pain	20	0.3
	Dyspnoea	18	0.2
	Respiratory distress	16	0.2
	Epistaxis	13	0.2
	Rhinorrhoea	11	0.2
	Dyspnoea exertional	10	0.1
	Productive cough	10	0.1
	Asthma	5	0.1
	Chronic obstructive pulmonary disease	5	0.1
	Pleurisy	5	0.1
	Haemoptysis	4	0.1
	Laryngeal inflammation	4	0.1
	Pleural effusion	4	0.1
Bronchitis chronic	3	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	3	0.0
	Allergic sinusitis	2	0.0
	Alveolitis allergic	2	0.0
	Dysphonia	2	0.0
	Nasal inflammation	2	0.0
	Painful respiration	2	0.0
	Paranasal sinus discomfort	2	0.0
	Pharyngeal inflammation	2	0.0
	Pneumonitis	2	0.0
	Pulmonary embolism	2	0.0
	Rheumatoid lung	2	0.0
	Sputum discoloured	2	0.0
	Vocal cord inflammation	2	0.0
	Allergic cough	1	0.0
	Apnoea	1	0.0
Atelectasis	1	0.0	
Epiglottic cyst	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Respiratory, thoracic and mediastinal disorders	Hypoventilation	1	0.0
	Increased bronchial secretion	1	0.0
	Lung disorder	1	0.0
	Nasal congestion	1	0.0
	Nasal dryness	1	0.0
	Nasal mucosal disorder	1	0.0
	Nocturnal dyspnoea	1	0.0
	Pulmonary congestion	1	0.0
	Pulmonary fibrosis	1	0.0
	Rhinitis allergic	1	0.0
	Rhonchi	1	0.0
	Throat clearing	1	0.0
	Throat irritation	1	0.0
	Throat tightness	1	0.0
	Tonsillar inflammation	1	0.0
Vocal cord polyp	1	0.0	
Vocal cord thickening	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Total	207	2.9
	Headache	55	0.8
	Dizziness	49	0.7
	Paraesthesia	21	0.3
	Sciatica	14	0.2
	Burning sensation	10	0.1
	Hypoaesthesia	8	0.1
	Polyneuropathy	7	0.1
	Carpal tunnel syndrome	6	0.1
	Migraine	6	0.1
	Somnolence	4	0.1
	Cerebrovascular disorder	3	0.0
	Disturbance in attention	3	0.0
	Hypertonia	3	0.0
	Movement disorder	3	0.0
	Balance disorder	2	0.0
Dysaesthesia	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Neuralgia	2	0.0
	Parkinson's disease	2	0.0
	Poor quality sleep	2	0.0
	Restless legs syndrome	2	0.0
	Sensory disturbance	2	0.0
	Syncope	2	0.0
	Transient ischaemic attack	2	0.0
	Tremor	2	0.0
	Autonomic nervous system imbalance	1	0.0
	Axonal neuropathy	1	0.0
	Carotid arteriosclerosis	1	0.0
	Cerebral microangiopathy	1	0.0
	Cerebrovascular accident	1	0.0
	Cervicobrachial syndrome	1	0.0
	Demyelinating polyneuropathy	1	0.0
	Diabetic neuropathy	1	0.0
	Dizziness postural	1	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Dysgeusia	1	0.0
	Dysphonia psychogenic	1	0.0
	Epilepsy	1	0.0
	Fine motor skill dysfunction	1	0.0
	Head discomfort	1	0.0
	Hemiparesis	1	0.0
	Hyperaesthesia	1	0.0
	Hyposmia	1	0.0
	Loss of consciousness	1	0.0
	Memory impairment	1	0.0
	Muscle contractions involuntary	1	0.0
	Muscle spasticity	1	0.0
	Myoclonus	1	0.0
	Nerve compression	1	0.0
	Neuritis cranial	1	0.0
	Neurological symptom	1	0.0
Neuropathy peripheral	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Nervous system disorders	Nystagmus	1	0.0
	Optic neuritis	1	0.0
	Parkinsonism	1	0.0
	Peripheral sensorimotor neuropathy	1	0.0
	Trigeminal neuralgia	1	0.0
	Vestibular migraine	1	0.0
Investigations	Total	200	2.8
	Liver function test increased	29	0.4
	Laboratory test abnormal	26	0.4
	Blood pressure increased	16	0.2
	Gamma-glutamyltransferase increased	11	0.2
	Alanine aminotransferase increased	9	0.1
	Arthroscopy	9	0.1
	Transaminases increased	9	0.1
	Antinuclear antibody increased	7	0.1
	Rheumatoid factor increased	6	0.1
	Blood creatinine increased	5	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Body temperature increased	5	0.1
	Weight decreased	5	0.1
	Histology normal	4	0.1
	Inflammatory marker increased	4	0.1
	Weight increased	4	0.1
	Blood cholesterol increased	3	0.0
	Blood pressure measurement	3	0.0
	C-reactive protein increased	3	0.0
	Hepatic enzyme increased	3	0.0
	Antinuclear antibody	2	0.0
	Aspartate aminotransferase increased	2	0.0
	Blood creatine phosphokinase increased	2	0.0
	Blood pressure decreased	2	0.0
	Blood triglycerides increased	2	0.0
	Computerised tomogram thorax	2	0.0
	Computerised tomogram thorax abnormal	2	0.0
	Mediastinoscopy	2	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	White blood cell count increased	2	0.0
	Activated partial thromboplastin time normal	1	0.0
	Anti-cyclic citrullinated peptide antibody positive	1	0.0
	Antibody test abnormal	1	0.0
	Antinuclear antibody positive	1	0.0
	Aspartate aminotransferase normal	1	0.0
	Biopsy	1	0.0
	Biopsy liver	1	0.0
	Blood bilirubin increased	1	0.0
	Blood count abnormal	1	0.0
	Blood glucose fluctuation	1	0.0
	Blood immunoglobulin M increased	1	0.0
	Blood lactate dehydrogenase	1	0.0
	Blood pressure abnormal	1	0.0
	Blood urea increased	1	0.0
	Blood uric acid	1	0.0
Bone densitometry	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Borrelia test positive	1	0.0
	Bronchoscopy abnormal	1	0.0
	Candida test positive	1	0.0
	Chest X-ray abnormal	1	0.0
	Chlamydia test positive	1	0.0
	Colonoscopy	1	0.0
	Computerised tomogram abdomen abnormal	1	0.0
	Computerised tomogram kidney abnormal	1	0.0
	Double stranded DNA antibody positive	1	0.0
	Drug specific antibody present	1	0.0
	Echocardiogram	1	0.0
	Endoscopy normal	1	0.0
	Endoscopy upper gastrointestinal tract	1	0.0
	Forced expiratory volume	1	0.0
	Gamma-glutamyltransferase abnormal	1	0.0
	Gynaecological examination	1	0.0
Gynaecological examination normal	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Haemoglobin decreased	1	0.0
	Heart rate increased	1	0.0
	Hepatic enzyme abnormal	1	0.0
	Laboratory test	1	0.0
	Liver function test	1	0.0
	Low density lipoprotein increased	1	0.0
	Lymphocyte count decreased	1	0.0
	Mean cell volume abnormal	1	0.0
	Neutrophil count increased	1	0.0
	Platelet count normal	1	0.0
	Prothrombin time normal	1	0.0
	Red blood cell sedimentation rate increased	1	0.0
	Renal function test abnormal	1	0.0
	Serum ferritin decreased	1	0.0
	Serum ferritin increased	1	0.0
Staphylococcus test positive	1	0.0	
Tuberculin test positive	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Investigations	Ultrasound abdomen normal	1	0.0
	Ultrasound scan	1	0.0
	Ultrasound scan normal	1	0.0
	Urinary sediment present	1	0.0
	White blood cell analysis abnormal	1	0.0
	White blood cell count	1	0.0
	White blood cell count decreased	1	0.0
Injury, poisoning and procedural complications	Total	121	1.7
	Fall	29	0.4
	Foot fracture	10	0.1
	Ligament sprain	7	0.1
	Limb injury	7	0.1
	Tendon rupture	7	0.1
	Arthropod bite	6	0.1
	Humerus fracture	5	0.1
	Joint dislocation	4	0.1
	Radius fracture	4	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Accident	3	0.0
	Epicondylitis	3	0.0
	Fracture	3	0.0
	Hand fracture	3	0.0
	Meniscus injury	3	0.0
	Rib fracture	3	0.0
	Road traffic accident	3	0.0
	Skin abrasion	3	0.0
	Spinal fracture	3	0.0
	Accident at home	2	0.0
	Bone contusion	2	0.0
	Contusion	2	0.0
	Ligament rupture	2	0.0
	Lumbar vertebral fracture	2	0.0
	Patella fracture	2	0.0
	Pelvic fracture	2	0.0
Post procedural complication	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Synovial rupture	2	0.0
	Thoracic vertebral fracture	2	0.0
	Wound	2	0.0
	Wrist fracture	2	0.0
	Accident at work	1	0.0
	Animal bite	1	0.0
	Bone fissure	1	0.0
	Cartilage injury	1	0.0
	Chillblains	1	0.0
	Craniocerebral injury	1	0.0
	Eschar	1	0.0
	Femur fracture	1	0.0
	Fibula fracture	1	0.0
	Fractured ischium	1	0.0
	Head injury	1	0.0
Heat stroke	1	0.0	
Inflammation of wound	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Injury, poisoning and procedural complications	Injection related reaction	1	0.0
	Joint injury	1	0.0
	Limb crushing injury	1	0.0
	Lip injury	1	0.0
	Lower limb fracture	1	0.0
	Off label use	1	0.0
	Overdose	1	0.0
	Scar	1	0.0
	Skin wound	1	0.0
	Stress fracture	1	0.0
	Suture related complication	1	0.0
	Tendon injury	1	0.0
	Tooth fracture	1	0.0
	Traumatic fracture	1	0.0
Upper limb fracture	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Vascular disorders	Total	93	1.3
	Hypertension	37	0.5
	Haematoma	7	0.1
	Flushing	6	0.1
	Thrombosis	5	0.1
	Vasculitis	5	0.1
	Essential hypertension	4	0.1
	Lymphoedema	4	0.1
	Peripheral venous disease	4	0.1
	Aortic aneurysm	3	0.0
	Haemorrhage	3	0.0
	Hot flush	3	0.0
	Thrombophlebitis	3	0.0
	Deep vein thrombosis	2	0.0
	Hypertensive crisis	2	0.0
	Hypotension	2	0.0
Peripheral arterial occlusive disease	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Vascular disorders	Venous thrombosis limb	2	0.0
	Aortic dilatation	1	0.0
	Arteritis	1	0.0
	Peripheral artery occlusion	1	0.0
	Peripheral artery stenosis	1	0.0
	Raynaud's phenomenon	1	0.0
	Varicose vein	1	0.0
	Vascular stenosis	1	0.0
Psychiatric disorders	Total	67	0.9
	Depression	28	0.4
	Sleep disorder	14	0.2
	Anxiety	6	0.1
	Anxiety disorder	4	0.1
	Depressed mood	4	0.1
	Restlessness	3	0.0
	Agoraphobia	2	0.0
	Apathy	2	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Psychiatric disorders	Middle insomnia	2	0.0
	Mood swings	2	0.0
	Somatic symptom disorder	2	0.0
	Adjustment disorder with depressed mood	1	0.0
	Agitation	1	0.0
	Alcoholism	1	0.0
	Hallucination	1	0.0
	Hallucination, auditory	1	0.0
	Illusion	1	0.0
	Insomnia	1	0.0
	Nightmare	1	0.0
	Panic attack	1	0.0
	Panic disorder	1	0.0
	Psychomotor retardation	1	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Eye disorders	Total	67	0.9
	Cataract	8	0.1
	Eye inflammation	7	0.1
	Vision blurred	7	0.1
	Visual impairment	7	0.1
	Iritis	5	0.1
	Dry eye	4	0.1
	Glaucoma	4	0.1
	Eyelid oedema	3	0.0
	Iridocyclitis	3	0.0
	Blepharitis	2	0.0
	Diplopia	2	0.0
	Eye haemorrhage	2	0.0
	Eye pain	2	0.0
	Eye swelling	2	0.0
Keratitis	2	0.0	
Macular degeneration	2	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Eye disorders	Ocular discomfort	2	0.0
	Ulcerative keratitis	2	0.0
	Visual acuity reduced	2	0.0
	Erythema of eyelid	1	0.0
	Inflammation of lacrimal passage	1	0.0
	Macular cyst	1	0.0
	Ocular hyperaemia	1	0.0
	Ocular hypertension	1	0.0
	Papilloedema	1	0.0
	Photophobia	1	0.0
	Uveitis	1	0.0
Cardiac disorders	Total	64	0.9
	Palpitations	18	0.2
	Angina pectoris	12	0.2
	Tachycardia	6	0.1
	Arrhythmia	5	0.1
	Coronary artery disease	5	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Atrial fibrillation	3	0.0
	Cardiac failure	3	0.0
	Cardiovascular disorder	3	0.0
	Bradycardia	2	0.0
	Myocarditis	2	0.0
	Acute coronary syndrome	1	0.0
	Acute myocardial infarction	1	0.0
	Angina unstable	1	0.0
	Aortic valve incompetence	1	0.0
	Cardiac failure chronic	1	0.0
	Cardiac flutter	1	0.0
	Extrasystoles	1	0.0
	Hypertensive heart disease	1	0.0
	Left ventricular dysfunction	1	0.0
	Mitral valve incompetence	1	0.0
	Myocardial infarction	1	0.0
Pericardial effusion	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Cardiac disorders	Pericarditis	1	0.0
	Right ventricular failure	1	0.0
	Ventricular extrasystoles	1	0.0
Metabolism and nutrition disorders	Total	49	0.7
	Diabetes mellitus	7	0.1
	Hyperuricaemia	7	0.1
	Vitamin D deficiency	7	0.1
	Hyperlipidaemia	5	0.1
	Hypercholesterolaemia	4	0.1
	Type 2 diabetes mellitus	4	0.1
	Decreased appetite	3	0.0
	Gout	3	0.0
	Vitamin B12 deficiency	2	0.0
	Central obesity	1	0.0
	Electrolyte imbalance	1	0.0
	Haemochromatosis	1	0.0
Hypercalcaemia	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Metabolism and nutrition disorders	Hyperferritinaemia	1	0.0
	Hyperglycaemia	1	0.0
	Hyperkalaemia	1	0.0
	Hypertriglyceridaemia	1	0.0
	Hypochloraemia	1	0.0
	Hypokalaemia	1	0.0
	Hypophosphataemia	1	0.0
	Iron deficiency	1	0.0
	Lactose intolerance	1	0.0
	Obesity	1	0.0
	Shock hypoglycaemic	1	0.0
Renal and urinary disorders	Total	50	0.7
	Cystitis noninfective	18	0.2
	Haematuria	7	0.1
	Renal failure	5	0.1
	Chronic kidney disease	4	0.1
	Renal colic	4	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Renal and urinary disorders	Leukocyturia	2	0.0
	Renal impairment	2	0.0
	Renal pain	2	0.0
	Acute kidney injury	1	0.0
	Bladder irritation	1	0.0
	Dysuria	1	0.0
	Nephrolithiasis	1	0.0
	Renal infarct	1	0.0
	Single functional kidney	1	0.0
	Urinary incontinence	1	0.0
	Urogenital haemorrhage	1	0.0
Blood and lymphatic system disorders	Total	46	0.6
	Leukopenia	12	0.2
	Lymphadenopathy	9	0.1
	Thrombocytopenia	6	0.1
	Anaemia	4	0.1
	Leukocytosis	3	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Blood and lymphatic system disorders	Eosinophilia	2	0.0
	Hyperchromic anaemia	2	0.0
	Neutropenia	2	0.0
	Anaemia vitamin B12 deficiency	1	0.0
	Haemorrhagic diathesis	1	0.0
	Increased tendency to bruise	1	0.0
	Iron deficiency anaemia	1	0.0
	Lymphadenitis	1	0.0
	Lymphocytosis	1	0.0
	Lymphopenia	1	0.0
	Platelet disorder	1	0.0
	Spontaneous haematoma	1	0.0
Ear and labyrinth disorders	Total	36	0.5
	Tinnitus	8	0.1
	Middle ear inflammation	7	0.1
	Ear pain	6	0.1
	Sudden hearing loss	5	0.1

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Ear and labyrinth disorders	Ear discomfort	4	0.1
	Vertigo	4	0.1
	Auditory disorder	1	0.0
	Auricular swelling	1	0.0
	External ear pain	1	0.0
	Meniere's disease	1	0.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Total	31	0.4
	Basal cell carcinoma	6	0.1
	Skin papilloma	4	0.1
	Myelodysplastic syndrome	3	0.0
	Bowen's disease	2	0.0
	Acute myeloid leukaemia	1	0.0
	Breast cancer female	1	0.0
	Breast neoplasm	1	0.0
	Bronchial carcinoma	1	0.0
	Cervix carcinoma stage 0	1	0.0
	Lipoma	1	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to thorax	1	0.0
	Metastatic neoplasm	1	0.0
	Neoplasm skin	1	0.0
	Prostate cancer	1	0.0
	Refractory cytopenia with unilineage dysplasia	1	0.0
	Renal cell carcinoma recurrent	1	0.0
	Salivary gland neoplasm	1	0.0
	Skin cancer	1	0.0
	Thyroid cancer recurrent	1	0.0
	Urinary tract neoplasm	1	0.0
	Uterine leiomyoma	1	0.0
Reproductive system and breast disorders	Total	26	0.4
	Ovarian cyst	5	0.1
	Menorrhagia	3	0.0
	Erectile dysfunction	2	0.0
	Gynaecomastia	2	0.0
	Metrorrhagia	2	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Reproductive system and breast disorders	Vulvovaginal inflammation	2	0.0
	Amenorrhoea	1	0.0
	Bartholin's cyst	1	0.0
	Breast mass	1	0.0
	Breast pain	1	0.0
	Cervical dysplasia	1	0.0
	Dyspareunia	1	0.0
	Endometriosis	1	0.0
	Menstrual disorder	1	0.0
	Menstruation irregular	1	0.0
	Orchitis noninfective	1	0.0
	Prostatic dysplasia	1	0.0
	Prostatitis	1	0.0
	Spermatocele	1	0.0
Uterine polyp	1	0.0	

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Immune system disorders	Total	26	0.4
	Hypersensitivity	18	0.2
	Seasonal allergy	4	0.1
	Drug hypersensitivity	2	0.0
	Anaphylactic reaction	1	0.0
	Immunosuppression	1	0.0
	Rubber sensitivity	1	0.0
Hepatobiliary disorders	Total	16	0.2
	Cholelithiasis	6	0.1
	Hepatic steatosis	3	0.0
	Biliary colic	2	0.0
	Cholecystitis	2	0.0
	Hepatic cirrhosis	2	0.0
	Liver disorder	2	0.0
	Cholestasis	1	0.0
	Hepatic fibrosis	1	0.0
	Jaundice	1	0.0

(Continued)

5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Pregnancy, puerperium and perinatal conditions	Total	16	0.2
	Pregnancy	13	0.2
	Delivery	3	0.0
	Abortion spontaneous	1	0.0
	Twin pregnancy	1	0.0
Endocrine disorders	Total	16	0.2
	Hypothyroidism	6	0.1
	Goitre	5	0.1
	Autoimmune thyroiditis	3	0.0
	Hyperthyroidism	1	0.0
	Thyroiditis	1	0.0
	Thyroiditis subacute	1	0.0
Product issues	Total	3	0.0
	Device breakage	1	0.0
	Device dislocation	1	0.0
	Device expulsion	1	0.0

(Continued)

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5. Documented adverse events by patient

5.9 All documented adverse events (without SAE) by system organ class and preferred term

		n	%
System Organ Class	Preferred Term		
Congenital, familial and genetic disorders	Total	1	0.0
	Congenital tongue anomaly	1	0.0

6. Documented adverse events by patient and key comorbidities

6.1 All documented adverse events by system organ class and arterial hypertension

	Arterial hypertension			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	1102	45.0	1662	34.8
Infections and infestations	506	20.7	746	15.6
Surgical and medical procedures	312	12.8	386	8.1
General disorders and administration site conditions	244	10.0	376	7.9
Musculoskeletal and connective tissue disorders	197	8.1	262	5.5
Skin and subcutaneous tissue disorders	154	6.3	272	5.7
Gastrointestinal disorders	117	4.8	180	3.8
Nervous system disorders	122	5.0	150	3.1
Respiratory, thoracic and mediastinal disorders	105	4.3	150	3.1
Investigations	113	4.6	137	2.9
Injury, poisoning and procedural complications	103	4.2	105	2.2
Cardiac disorders	73	3.0	66	1.4
Vascular disorders	63	2.6	71	1.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	49	2.0	67	1.4
Psychiatric disorders	34	1.4	46	1.0

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(Continued)

6. Documented adverse events by patient and key comorbidities

6.1 All documented adverse events by system organ class and arterial hypertension

	Arterial hypertension			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	42	1.7	33	0.7
Eye disorders	24	1.0	47	1.0
Blood and lymphatic system disorders	21	0.9	43	0.9
Metabolism and nutrition disorders	33	1.3	27	0.6
Ear and labyrinth disorders	15	0.6	27	0.6
Hepatobiliary disorders	17	0.7	19	0.4
Reproductive system and breast disorders	12	0.5	21	0.4
Immune system disorders	12	0.5	18	0.4
Endocrine disorders	7	0.3	16	0.3
Pregnancy, puerperium and perinatal conditions	1	0.0	17	0.4
Product issues	5	0.2	2	0.0
Congenital, familial and genetic disorders	2	0.1	1	0.0
Social circumstances	3	0.1	0	0

6. Documented adverse events by patient and key comorbidities

6.2 All documented adverse events by system organ class and coronary heart disease

	Coronary heart disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	184	46.6	2580	37.8
Infections and infestations	83	21.0	1169	17.1
Surgical and medical procedures	53	13.4	645	9.4
General disorders and administration site conditions	44	11.1	576	8.4
Musculoskeletal and connective tissue disorders	30	7.6	429	6.3
Skin and subcutaneous tissue disorders	27	6.8	399	5.8
Gastrointestinal disorders	30	7.6	267	3.9
Nervous system disorders	22	5.6	250	3.7
Respiratory, thoracic and mediastinal disorders	25	6.3	230	3.4
Investigations	20	5.1	230	3.4
Injury, poisoning and procedural complications	19	4.8	189	2.8
Cardiac disorders	27	6.8	112	1.6
Vascular disorders	8	2.0	126	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	9	2.3	107	1.6
Psychiatric disorders	4	1.0	76	1.1

(Continued)

6. Documented adverse events by patient and key comorbidities

6.2 All documented adverse events by system organ class and coronary heart disease

	Coronary heart disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	9	2.3	66	1.0
Eye disorders	3	0.8	68	1.0
Blood and lymphatic system disorders	5	1.3	59	0.9
Metabolism and nutrition disorders	7	1.8	53	0.8
Ear and labyrinth disorders	2	0.5	40	0.6
Hepatobiliary disorders	3	0.8	33	0.5
Reproductive system and breast disorders	2	0.5	31	0.5
Immune system disorders	2	0.5	28	0.4
Endocrine disorders	3	0.8	20	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	1	0.3	6	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	0	0	3	0.0

6. Documented adverse events by patient and key comorbidities

6.3 All documented adverse events by system organ class and hyperlipidemia

	Hyperlipidemia			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	281	50.3	2483	37.2
Infections and infestations	127	22.7	1125	16.9
Surgical and medical procedures	78	14.0	620	9.3
General disorders and administration site conditions	59	10.6	561	8.4
Musculoskeletal and connective tissue disorders	60	10.7	399	6.0
Skin and subcutaneous tissue disorders	46	8.2	380	5.7
Gastrointestinal disorders	32	5.7	265	4.0
Nervous system disorders	31	5.5	241	3.6
Respiratory, thoracic and mediastinal disorders	28	5.0	227	3.4
Investigations	37	6.6	213	3.2
Injury, poisoning and procedural complications	21	3.8	187	2.8
Cardiac disorders	22	3.9	117	1.8
Vascular disorders	14	2.5	120	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	14	2.5	102	1.5
Psychiatric disorders	10	1.8	70	1.0

(Continued)

6. Documented adverse events by patient and key comorbidities

6.3 All documented adverse events by system organ class and hyperlipidemia

	Hyperlipidemia			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	10	1.8	65	1.0
Eye disorders	8	1.4	63	0.9
Blood and lymphatic system disorders	4	0.7	60	0.9
Metabolism and nutrition disorders	12	2.1	48	0.7
Ear and labyrinth disorders	5	0.9	37	0.6
Hepatobiliary disorders	5	0.9	31	0.5
Reproductive system and breast disorders	2	0.4	31	0.5
Immune system disorders	3	0.5	27	0.4
Endocrine disorders	5	0.9	18	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	3	0.5	4	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	1	0.2	2	0.0

6. Documented adverse events by patient and key comorbidities

6.4 All documented adverse events by system organ class and diabetes type I

	Diabetes Type I			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	41	40.6	2723	38.2
Infections and infestations	16	15.8	1236	17.3
Surgical and medical procedures	5	5.0	693	9.7
General disorders and administration site conditions	8	7.9	612	8.6
Musculoskeletal and connective tissue disorders	3	3.0	456	6.4
Skin and subcutaneous tissue disorders	9	8.9	417	5.9
Gastrointestinal disorders	5	5.0	292	4.1
Nervous system disorders	3	3.0	269	3.8
Respiratory, thoracic and mediastinal disorders	7	6.9	248	3.5
Investigations	7	6.9	243	3.4
Injury, poisoning and procedural complications	1	1.0	207	2.9
Cardiac disorders	0	0	139	2.0
Vascular disorders	1	1.0	133	1.9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	2.0	114	1.6
Psychiatric disorders	2	2.0	78	1.1

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(Continued)

6. Documented adverse events by patient and key comorbidities

6.4 All documented adverse events by system organ class and diabetes type I

	Diabetes Type I			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	1	1.0	74	1.0
Eye disorders	1	1.0	70	1.0
Blood and lymphatic system disorders	0	0	64	0.9
Metabolism and nutrition disorders	2	2.0	58	0.8
Ear and labyrinth disorders	0	0	42	0.6
Hepatobiliary disorders	1	1.0	35	0.5
Reproductive system and breast disorders	1	1.0	32	0.4
Immune system disorders	0	0	30	0.4
Endocrine disorders	1	1.0	22	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	0	0	7	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	0	0	3	0.0

6. Documented adverse events by patient and key comorbidities

6.5 All documented adverse events by system organ class and diabetes type II

	Diabetes Type II			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	266	44.6	2498	37.7
Infections and infestations	123	20.6	1129	17.0
Surgical and medical procedures	76	12.8	622	9.4
General disorders and administration site conditions	55	9.2	565	8.5
Musculoskeletal and connective tissue disorders	41	6.9	418	6.3
Skin and subcutaneous tissue disorders	34	5.7	392	5.9
Gastrointestinal disorders	23	3.9	274	4.1
Nervous system disorders	28	4.7	244	3.7
Respiratory, thoracic and mediastinal disorders	24	4.0	231	3.5
Investigations	26	4.4	224	3.4
Injury, poisoning and procedural complications	22	3.7	186	2.8
Cardiac disorders	16	2.7	123	1.9
Vascular disorders	12	2.0	122	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	15	2.5	101	1.5
Psychiatric disorders	5	0.8	75	1.1

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(Continued)

6. Documented adverse events by patient and key comorbidities

6.5 All documented adverse events by system organ class and diabetes type II

	Diabetes Type II			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	12	2.0	63	0.9
Eye disorders	5	0.8	66	1.0
Blood and lymphatic system disorders	4	0.7	60	0.9
Metabolism and nutrition disorders	10	1.7	50	0.8
Ear and labyrinth disorders	2	0.3	40	0.6
Hepatobiliary disorders	3	0.5	33	0.5
Reproductive system and breast disorders	3	0.5	30	0.5
Immune system disorders	3	0.5	27	0.4
Endocrine disorders	2	0.3	21	0.3
Pregnancy, puerperium and perinatal conditions	1	0.2	17	0.3
Product issues	2	0.3	5	0.1
Congenital, familial and genetic disorders	1	0.2	2	0.0
Social circumstances	0	0	3	0.0

6. Documented adverse events by patient and key comorbidities

6.6 All documented adverse events by system organ class and chronic inflammatory disease

	Chronic inflammatory disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	78	53.8	2686	37.9
Infections and infestations	38	26.2	1214	17.1
Surgical and medical procedures	27	18.6	671	9.5
General disorders and administration site conditions	21	14.5	599	8.5
Musculoskeletal and connective tissue disorders	14	9.7	445	6.3
Skin and subcutaneous tissue disorders	11	7.6	415	5.9
Gastrointestinal disorders	20	13.8	277	3.9
Nervous system disorders	7	4.8	265	3.7
Respiratory, thoracic and mediastinal disorders	4	2.8	251	3.5
Investigations	11	7.6	239	3.4
Injury, poisoning and procedural complications	11	7.6	197	2.8
Cardiac disorders	5	3.4	134	1.9
Vascular disorders	3	2.1	131	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3	2.1	113	1.6
Psychiatric disorders	2	1.4	78	1.1

6. Documented adverse events by patient and key comorbidities

6.6 All documented adverse events by system organ class and chronic inflammatory disease

	Chronic inflammatory disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	4	2.8	71	1.0
Eye disorders	3	2.1	68	1.0
Blood and lymphatic system disorders	4	2.8	60	0.8
Metabolism and nutrition disorders	3	2.1	57	0.8
Ear and labyrinth disorders	0	0	42	0.6
Hepatobiliary disorders	1	0.7	35	0.5
Reproductive system and breast disorders	0	0	33	0.5
Immune system disorders	0	0	30	0.4
Endocrine disorders	1	0.7	22	0.3
Pregnancy, puerperium and perinatal conditions	1	0.7	17	0.2
Product issues	0	0	7	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	0	0	3	0.0

6. Documented adverse events by patient and key comorbidities

6.7 All documented adverse events by system organ class and chronic obstructive pulmonary disease

	Chronic obstructive pulmonary disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	163	49.5	2601	37.7
Infections and infestations	80	24.3	1172	17.0
Surgical and medical procedures	42	12.8	656	9.5
General disorders and administration site conditions	44	13.4	576	8.3
Musculoskeletal and connective tissue disorders	25	7.6	434	6.3
Skin and subcutaneous tissue disorders	22	6.7	404	5.9
Gastrointestinal disorders	11	3.3	286	4.1
Nervous system disorders	15	4.6	257	3.7
Respiratory, thoracic and mediastinal disorders	22	6.7	233	3.4
Investigations	7	2.1	243	3.5
Injury, poisoning and procedural complications	11	3.3	197	2.9
Cardiac disorders	5	1.5	134	1.9
Vascular disorders	7	2.1	127	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	0.6	114	1.7
Psychiatric disorders	4	1.2	76	1.1

6. Documented adverse events by patient and key comorbidities

6.7 All documented adverse events by system organ class and chronic obstructive pulmonary disease

	Chronic obstructive pulmonary disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	4	1.2	71	1.0
Eye disorders	4	1.2	67	1.0
Blood and lymphatic system disorders	4	1.2	60	0.9
Metabolism and nutrition disorders	11	3.3	49	0.7
Ear and labyrinth disorders	0	0	42	0.6
Hepatobiliary disorders	0	0	36	0.5
Reproductive system and breast disorders	3	0.9	30	0.4
Immune system disorders	3	0.9	27	0.4
Endocrine disorders	0	0	23	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	1	0.3	6	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	1	0.3	2	0.0

6. Documented adverse events by patient and key comorbidities

6.8 All documented adverse events by system organ class and osteoporosis

	Osteoporosis			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	447	42.9	2317	37.4
Infections and infestations	205	19.7	1047	16.9
Surgical and medical procedures	151	14.5	547	8.8
General disorders and administration site conditions	86	8.3	534	8.6
Musculoskeletal and connective tissue disorders	83	8.0	376	6.1
Skin and subcutaneous tissue disorders	62	6.0	364	5.9
Gastrointestinal disorders	45	4.3	252	4.1
Nervous system disorders	58	5.6	214	3.5
Respiratory, thoracic and mediastinal disorders	49	4.7	206	3.3
Investigations	50	4.8	200	3.2
Injury, poisoning and procedural complications	52	5.0	156	2.5
Cardiac disorders	27	2.6	112	1.8
Vascular disorders	26	2.5	108	1.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	22	2.1	94	1.5
Psychiatric disorders	7	0.7	73	1.2

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(Continued)

6. Documented adverse events by patient and key comorbidities

6.8 All documented adverse events by system organ class and osteoporosis

	Osteoporosis			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	19	1.8	56	0.9
Eye disorders	12	1.2	59	1.0
Blood and lymphatic system disorders	13	1.2	51	0.8
Metabolism and nutrition disorders	14	1.3	46	0.7
Ear and labyrinth disorders	6	0.6	36	0.6
Hepatobiliary disorders	6	0.6	30	0.5
Reproductive system and breast disorders	4	0.4	29	0.5
Immune system disorders	5	0.5	25	0.4
Endocrine disorders	4	0.4	19	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	1	0.1	6	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	1	0.1	2	0.0

6. Documented adverse events by patient and key comorbidities

6.9 All documented adverse events by system organ class and degenerative joint disease

	Degenerative joint disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	536	42.4	2228	37.4
Infections and infestations	229	18.1	1023	17.2
Surgical and medical procedures	167	13.2	531	8.9
General disorders and administration site conditions	119	9.4	501	8.4
Musculoskeletal and connective tissue disorders	120	9.5	339	5.7
Skin and subcutaneous tissue disorders	73	5.8	353	5.9
Gastrointestinal disorders	52	4.1	245	4.1
Nervous system disorders	64	5.1	208	3.5
Respiratory, thoracic and mediastinal disorders	56	4.4	199	3.3
Investigations	45	3.6	205	3.4
Injury, poisoning and procedural complications	49	3.9	159	2.7
Cardiac disorders	34	2.7	105	1.8
Vascular disorders	42	3.3	92	1.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	28	2.2	88	1.5
Psychiatric disorders	14	1.1	66	1.1

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(Continued)

6. Documented adverse events by patient and key comorbidities

6.9 All documented adverse events by system organ class and degenerative joint disease

	Degenerative joint disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	19	1.5	56	0.9
Eye disorders	22	1.7	49	0.8
Blood and lymphatic system disorders	16	1.3	48	0.8
Metabolism and nutrition disorders	18	1.4	42	0.7
Ear and labyrinth disorders	12	0.9	30	0.5
Hepatobiliary disorders	7	0.6	29	0.5
Reproductive system and breast disorders	8	0.6	25	0.4
Immune system disorders	5	0.4	25	0.4
Endocrine disorders	6	0.5	17	0.3
Pregnancy, puerperium and perinatal conditions	1	0.1	17	0.3
Product issues	2	0.2	5	0.1
Congenital, familial and genetic disorders	1	0.1	2	0.0
Social circumstances	0	0	3	0.1

6. Documented adverse events by patient and key comorbidities

6.10 All documented adverse events by system organ class and degenerative spinal disease

	Degenerative spinal disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	428	41.8	2336	37.6
Infections and infestations	192	18.8	1060	17.1
Surgical and medical procedures	137	13.4	561	9.0
General disorders and administration site conditions	83	8.1	537	8.7
Musculoskeletal and connective tissue disorders	87	8.5	372	6.0
Skin and subcutaneous tissue disorders	61	6.0	365	5.9
Gastrointestinal disorders	47	4.6	250	4.0
Nervous system disorders	52	5.1	220	3.5
Respiratory, thoracic and mediastinal disorders	48	4.7	207	3.3
Investigations	39	3.8	211	3.4
Injury, poisoning and procedural complications	38	3.7	170	2.7
Cardiac disorders	38	3.7	101	1.6
Vascular disorders	24	2.3	110	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	15	1.5	101	1.6
Psychiatric disorders	10	1.0	70	1.1

(Continued)

6. Documented adverse events by patient and key comorbidities

6.10 All documented adverse events by system organ class and degenerative spinal disease

	Degenerative spinal disease			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	18	1.8	57	0.9
Eye disorders	12	1.2	59	1.0
Blood and lymphatic system disorders	8	0.8	56	0.9
Metabolism and nutrition disorders	14	1.4	46	0.7
Ear and labyrinth disorders	10	1.0	32	0.5
Hepatobiliary disorders	4	0.4	32	0.5
Reproductive system and breast disorders	2	0.2	31	0.5
Immune system disorders	3	0.3	27	0.4
Endocrine disorders	3	0.3	20	0.3
Pregnancy, puerperium and perinatal conditions	0	0	18	0.3
Product issues	2	0.2	5	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	0	0	3	0.0

6. Documented adverse events by patient and key comorbidities

6.11 All documented adverse events by system organ class and mental illness (e.g. depression)

	Mental illness (e.g. depression)			
	Yes		No	
	n	%	n	%
System Organ Class				
Total	199	43.5	2565	37.9
Infections and infestations	90	19.7	1162	17.2
Surgical and medical procedures	46	10.1	652	9.6
General disorders and administration site conditions	41	9.0	579	8.5
Musculoskeletal and connective tissue disorders	33	7.2	426	6.3
Skin and subcutaneous tissue disorders	31	6.8	395	5.8
Gastrointestinal disorders	31	6.8	266	3.9
Nervous system disorders	19	4.2	253	3.7
Respiratory, thoracic and mediastinal disorders	16	3.5	239	3.5
Investigations	20	4.4	230	3.4
Injury, poisoning and procedural complications	11	2.4	197	2.9
Cardiac disorders	7	1.5	132	1.9
Vascular disorders	9	2.0	125	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10	2.2	106	1.6
Psychiatric disorders	17	3.7	63	0.9

6. Documented adverse events by patient and key comorbidities

6.11 All documented adverse events by system organ class and mental illness (e.g. depression)

	Mental illness (e.g. depression)			
	Yes		No	
	n	%	n	%
System Organ Class				
Renal and urinary disorders	6	1.3	69	1.0
Eye disorders	2	0.4	69	1.0
Blood and lymphatic system disorders	5	1.1	59	0.9
Metabolism and nutrition disorders	4	0.9	56	0.8
Ear and labyrinth disorders	2	0.4	40	0.6
Hepatobiliary disorders	6	1.3	30	0.4
Reproductive system and breast disorders	2	0.4	31	0.5
Immune system disorders	5	1.1	25	0.4
Endocrine disorders	2	0.4	21	0.3
Pregnancy, puerperium and perinatal conditions	1	0.2	17	0.3
Product issues	2	0.4	5	0.1
Congenital, familial and genetic disorders	0	0	3	0.0
Social circumstances	0	0	3	0.0

AbbVie Inc. (AbbVie)

Post Marketing Observational Study

Protocol P11-973

**Long-term Documentation of the Safety,
Effectiveness, and Effects on Quality of Life and
Work Productivity in Patients with Rheumatoid
Arthritis during HUMIRA® (Adalimumab) Therapy in
Routine Clinical Practice (AGIL) and Supplementary
Documentation to Record Cardiovascular and
Metabolic Risk Factors (AGIL-CV)**

Final Report

Approved by:

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