STUDY SYNOPSIS

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<th>Sponsor</th>
<th>Amgen</th>
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<td>Indication</td>
<td>Metastatic bone disease secondary to solid tumours</td>
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**Study Rationale**

With the approval of XGEVA, there is an SC alternative to bisphosphonate IV formulations available in preventing skeletal related events (SREs) in patients with solid tumours. In addition to XGEVA’s superior efficacy in preventing SREs, switching to a subcutaneous injection (XGEVA) may result in savings of healthcare professional (HCP) time. The savings of HCP time could be allocated to other activities raising the quality of care or increasing the number of patients treated.

Only few published studies reported data on time associated with bisphosphonate IV (including zoledronic acid and pamidronate) infusion in bone metastatic patients.

The present study aims to collect T&M data on the time of XGEVA SC injection and ZOL IV infusion in real-world routine practice.

**Primary Objective**

- To estimate the total time of pre-defined, observable tasks associated with XGEVA SC injection or ZOL IV infusion monotherapy
- To estimate the total active HCP time of pre-defined, observable tasks (i.e. time that HCP is actively dedicating to the task or patient care) associated with XGEVA SC injection or ZOL IV infusion monotherapy

**Secondary Objectives**

- To estimate the impact of concomitant chemotherapy on the total time of pre-defined, observable tasks associated with XGEVA SC injection or ZOL IV infusion
- To estimate the impact of concomitant chemotherapy on the total active HCP time of pre-defined, observable tasks associated with for XGEVA SC injection or ZOL IV infusion
- To estimate patient bed/chair time for XGEVA SC injection or ZOL IV infusion
- To estimate patient treatment unit time for XGEVA SC injection or ZOL IV infusion

**Study Design**

- Prospective, multi-national, multi-site, non-interventional, T&M study to be conducted in approximately 6 European countries
- Focuses on outpatient/ ambulatory/ day treatment unit excluding inpatient setting
- XGEVA SC injection and ZOL IV infusion will be described by 2 sets of predefined tasks and measured by trained observers
- Data collection will occur in 2 settings: treatment unit and pharmacy/drug preparation area
- Observers will record military time of start/stop time of pre-defined tasks.
- Observers will record the active HCP time spent on pre-defined tasks by using a stopwatch
- Observers will record when a patient enters/exits the treatment unit and when a patient enters/leaves the treatment bed/chair in military time
- There will be 4 observation arms:
  - ZOL IV infusion monotherapy
  - XGEVA SC injection monotherapy
  - ZOL IV infusion with same-day chemotherapy IV infusion (concomitant chemotherapy)
  - XGEVA SC injection with same-day chemotherapy IV infusion (concomitant chemotherapy)

### Primary Endpoints

- Time [in minutes] per pre-defined task associated with XGEVA SC injection monotherapy
- Time [in minutes] per pre-defined task associated with ZOL IV infusion monotherapy
- Active HCP time [in minutes] per pre-defined task associated with XGEVA SC injection monotherapy
- Active HCP time [in minutes] per pre-defined task associated with ZOL IV infusion monotherapy

### Secondary Endpoints

- Time [in minutes] per pre-defined task associated with XGEVA SC injection with concomitant chemotherapy
- Time [in minutes] per pre-defined task associated with ZOL IV infusion with concomitant chemotherapy
- Active HCP time [in minutes] per pre-defined task associated with XGEVA SC injection with concomitant chemotherapy
- Active HCP time [in minutes] per pre-defined task associated with ZOL IV infusion with concomitant chemotherapy
- Patient bed/chair time [in minutes] for XGEVA SC injection or ZOL IV infusion with or without concomitant chemotherapy
- Patient time [in minutes] in treatment unit for XGEVA SC injection or ZOL IV infusion with or without concomitant chemotherapy

### Sample Size

The target sample size is 39 observations per monotherapy arm and 78 observations per concomitant therapy arm per country. Crude sample size calculation is based on published data supplemented by assumptions.

### Sampling Frame

At each site, all XGEVA SC injection and ZOL IV infusion administrations being scheduled during the study period constitute the sampling base prior to patient eligibility screening. Then, patients deemed eligible by the study inclusion/ exclusion criteria will form the final sampling frame of the study. From this pool of eligible patients, subjects will be consecutively enrolled for participation and have XGEVA SC injection or ZOL IV infusion treatment sessions observed [following informed consent].

The study period can be up to 12 months at each site and will vary by site.
Data will be collected using the following 3 study data collection forms:

1. **Site Interview:** An interview guide will be developed to map the flow of XGEVA SC injection and ZOL IV treatment processes at study site. Site characteristics including geographical location, number of treatment beds/chairs, number of staff in the treatment unit, number of patients receiving infusions and injections, as well as time estimates for tasks that will not be directly observed (i.e. non-observable tasks\(^1\)) will be collected during this interview.

2. **T&M Observation Data Form:** The T&M observation data form will list pre-defined tasks to be observed in a chronological order reflecting the process flow validated as part of the Site Interview. The observers will record the [military] time, when each task starts and stops and also measure the active HCP time using a stopwatch. Observers will also record the [military] time when a patient enters/leaves the treatment unit and enters/leaves the treatment bed/chair.

3. **A Subject Information Data Form** will be completed by site research staff to collect demographics and baseline clinical characteristics on subjects whose treatment sessions will be observed.

### Data Collection

#### Inclusion Criteria
- Diagnosed with solid tumours
- Scheduled to receive XGEVA SC injection or ZOL IV infusion for metastatic bone disease in out-patient/ ambulatory/ day hospital clinic setting
- Age \( \geq 18 \) years

#### Exclusion criteria
- Currently participating in any interventional trial
- Requiring in-patient admission

### Statistical Considerations

The unit for all outcomes is in minutes and seconds. Descriptive statistics (mean, standard deviation (SD), median, minimum, and maximum) and 95% confidence intervals will be calculated for all variables.

Exploratory multi-level regression analysis will be used to explore the potential impact of covariates such as subject baseline characteristics, site characteristics, country, etc on the time of XGEVA SC injection and ZOL IV infusion in real-world routine practice.

Mean, minimum and maximum of the task time for each non-observable task will be collected during HCP interviews. Analysis will be performed by site and by country. In this T&M study, no formal hypotheses will be tested.

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\(^1\) Non-observable tasks are tasks that are part of the administration day, but cannot be observed since they take place outside the treatment unit/pharmacy.
STUDY DESIGN SCHEMA

STUDY COUNTRY ACTIVITIES

Core T&M Observation Data Form development with country clinical experts

Site Feasibility

Site Selection

Site Initiation

SITE ACTIVITIES

Site interview
- Task mapping to inform potential adjustments to core T&M Observation Data Form
- Collect qualitative data on site practices
- Obtain time estimates for non-observable tasks

Site performs patient eligibility screening

Complete Subject Information Sheet for baseline clinical characteristics

PATIENT ACTIVITY

Providewritten informed consent

OBSERVER ACTIVITIES

Receive training

Conduct T&M measurements and complete respective data forms

Return completed data forms to study coordinating centre

Resolve data queries and complete Data Clarification Forms