

# A Non-interventional Pharmacovigilance Study of Osteonecrosis of the Jaw and Infection Leading to Hospitalization Among Patients With Cancer Treated With XGEVA™ or Zoledronic Acid in Sweden, Denmark, and Norway (20101363)

**First published:** 11/02/2020

**Last updated:** 05/08/2020

Study

Finalised

## Administrative details

### **PURI**

<https://redirect.ema.europa.eu/resource/36664>

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### **EU PAS number**

EUPAS32437

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### **Study ID**

36664

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## **DARWIN EU® study**

No

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### **Study countries**

Denmark

Norway

Sweden

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### **Study description**

This study aims to describe occurrence of two adverse events of special interest (AESIs) related to XGEVA (denosumab) use, osteonecrosis of the jaw (ONJ) and infection leading to hospitalization, in a postmarketing environment. The study was conducted using data linked from nationwide administrative and health registries in Sweden, Denmark, and Norway, in combination with abstraction of data from patients' medical records. Patients were identified from 01 October 2011 through 31 December 2013 in Sweden and Norway and through 31 December 2014 in Denmark, and eligible patients were included in one of the three treatment cohorts: the XGEVA inception cohort, the zoledronic acid inception cohort, and the XGEVA-switch cohort. Incidence of medically confirmed ONJ and infections leading to hospitalization were estimated for the three treatment cohorts, overall and stratified by primary cancer site, country, and calendar year of index date.

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### **Study status**

Finalised

## **Research institutions and networks**

### **Institutions**

# Amgen

United States

**First published:** 01/02/2024

**Last updated:** 21/02/2024

Institution

## Contact details

### Study institution contact

Global Development Leader Amgen Inc.

Study contact

[medinfo@amgen.com](mailto:medinfo@amgen.com)

### Primary lead investigator

Global Development Leader Amgen Inc.

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 01/01/2012

Actual: 01/01/2012

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### Study start date

Planned: 01/03/2012

Actual: 01/03/2012

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### **Data analysis start date**

Planned: 08/06/2019

Actual: 08/06/2019

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### **Date of final study report**

Planned: 24/01/2020

Actual: 07/01/2020

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Amgen

## Study protocol

[20101363\\_01.02.06 Public Redacted Protocol Ver 1.0 2016-06-29 English.pdf](#)  
(417.83 KB)

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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### **Is the study required by a Risk Management Plan (RMP)?**

EU RMP category 3 (required)

## Methodological aspects

Study type

**Study topic:**

Human medicinal product

Disease /health condition

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

**Data collection methods:**

Secondary use of data

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**Main study objective:**

- Estimate, by treatment cohort, the yearly incidence proportions and 95% confidence intervals (CIs) for medically confirmed ONJ among patients with cancer whose initial antiresorptive treatment is XGEVA or IV zoledronic acid
- Estimate, by treatment cohort, the yearly incidence proportions and 95% CIs for infection leading to hospitalization for XGEVA and zoledronic acid inception cohorts

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

## **Name of medicine**

XGEVA

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## **Medical condition to be studied**

Osteonecrosis of jaw

Pneumonia

Skin infection

Cellulitis

Endocarditis

Encephalitis

Myelitis

Encephalomyelitis

Urinary tract infection

Pyelonephritis

## **Population studied**

### **Short description of the study population**

Eligibility criteria are:  $\geq 18$  years old, diagnosed with cancer, and, subsequent to cancer diagnosis, initiating antiresorptive treatment for SRE prevention during the treatment cohort identification period with XGEVA or zoledronic acid or switching to XGEVA from treatment for SRE prevention with oral or IV bisphosphonates of no more than 2 years duration ( $\leq 24$  IV infusions or  $\leq 24$  monthly oral prescriptions).

The exclusion criteria are: radiation therapy to the head and neck region before a subject's potential index date or having hypercalcemia of malignancy as the sole

indication for treatment with an anti-resorptive agent. Patients with a history of

ONJ before the start of follow-up will be excluded when calculating incidence proportions and incidence rates of ONJ.

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### **Age groups**

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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### **Special population of interest**

Other

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### **Special population of interest, other**

Cancer patients

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### **Estimated number of subjects**

3098

## Study design details

### **Outcomes**

Medically confirmed osteonecrosis of the jaw (ONJ) and infection leading to hospitalization

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### **Data analysis plan**

The 1-, 2-, 3-, 4-, and 5-year incidence proportions of medically confirmed ONJ in the three treatment cohorts were computed overall and stratified by primary cancer site, country, and calendar year of index date (2012, 2013, 2014).

Patients who started follow-up in the zoledronic acid inception cohort and

switched to XGEVA during the study period stopped contributing time to the zoledronic acid inception cohort and started contributing time to the XGEVA-switch cohort at the time of the switch. Binomial exact 95% CIs were computed for incidence proportions, and exact Poisson 95% CIs were computed for incidence rates. For infection leading to hospitalization, follow-up started on the cohort entry date. Only patients who had the opportunity to accrue full 1, 2, 3, 4, or 5 years after index date were included in the calculation of the respective incidence proportions. This restriction was not applied to incidence rate calculation.

## Documents

### Study results

[Clinical Study Report 2020-01-07 20101363 ORSR Abstract.pdf\(340.91 KB\)](#)

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## Data management

### Data sources

#### Data sources (types)

[Disease registry](#)

[Electronic healthcare records \(EHR\)](#)

### Use of a Common Data Model (CDM)

#### CDM mapping

No

### Data quality specifications



**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No