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)

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Study Finalised

Administrative details

EU PAS number

EUPAS32437

Study ID

36664

DARWIN EU® study

No

Study countries

- [ ] Denmark
- [ ] Norway
- [ ] Sweden

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.

Study status

Finalised

Research institutions and networks

Institutions

Amgen

- [ ] United States

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Last updated: 21/02/2024

Institution

Contact details

Study institution contact

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Study contact

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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

Study start date

Planned: 01/03/2012

Actual: 01/03/2012

Data analysis start date
Planned: 08/06/2019

Actual: 08/06/2019

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

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

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Data collection methods:

Secondary use of data

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

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: ≥ 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 (≤ 24 IV infusions or ≤ 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.

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)

Special population of interest

Other

Special population of interest, other

Cancer patients

Estimated number of subjects

3098

Study design details

Outcomes

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

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)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

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

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No