The acute effects of azithromycin use on cardiovascular mortality, as compared with amoxicillin

First published: 15/04/2015

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Study Finalised

Administrative details

EU PAS number

EUPAS9449

Study ID

37446

DARWIN EU® study

No

Study countries

United States

Study status

Finalised

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Niki Palmetto

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 16/08/2014

Actual: 16/08/2014

Study start date

Planned: 30/04/2015

Actual: 16/04/2015

Date of final study report

Planned: 30/11/2016

Actual: 14/11/2018

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer Inc.

Study protocol

A0661209_PROTOCOL_ 19MAR2015_FINAL_EU PAS REGISTER.pdf (1.39 MB)

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

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

The purpose of this observational study is to examine the effects of azithromycin use on cardiovascular mortality.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

AZITHROMYCIN

AMOXICILLIN

Population studied

Short description of the study population

Patients must meet the following inclusion criteria to be eligible for inclusion in the study:

Inclusion Criteria:

1. Dispensation of an outpatient prescription for azithromycin or amoxicillin

between 01 Jan 1998 and 31 Dec 2012. If a patient had more than one prescription within this period, each exposure will be counted separately (thus, individuals may contribute multiple prescriptions to the analysis).
2. Consistent with the methodology of Ray and Svanstrom, only oral prescriptions will be included (not intravenous or ophthalmic) and amoxicillin-clavulanate prescriptions will also be included in the amoxicillin group
Exclusion criteria
Patients meeting any of the following criteria will not be included in the study:
Exclusion Criteria:
1. Missing date of birth or gender.
2. Age < 30 or >74 years on the index date (the date of the index antibiotic prescription).
3. Not enrolled at KPNC or KPSC during the 365 days prior to the index date (allowing gaps of < 60 days). This criterion ensures capture of potential confounders and effect measure modifiers.
4. Gaps in prescription coverage greater than 60 days during the 365 days prior to the index date, unless there is evidence of a filled prescription in the one year prior to the index date. This criterion ensures opportunities for capturing exposures to the medications of interest, as well as confounders and effect measure modifiers.
5. More than one type of study antibiotic prescribed on the index date, or within 10 days prior (ie, wash-out period).
6. Hospitalization within 30 days prior to the index date. This criterion considers that medication changes and medications administered during hospital stays may not be captured.
7. Residing in a nursing home or other residential institution on the index date or at any time in the preceding 365 days, except for stays of <30 days following hospital discharge. This includes inferred nursing home stays, defined as 2 or more outpatient encounters in the year leading up the index prescription date

with procedure codes indicating nursing home place of service separated by at least 28 days. It also includes external cause of injury diagnosis code indicating place of residence was an institution. This criterion considers that the cause of death information recorded on death certificates within a nursing home setting may be less accurate.

Age groups

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)
- Adults (65 to < 75 years)

Estimated number of subjects

6.900.000

Study design details

Outcomes

Cardiovascular death, sudden cardiac death, cardiovascular death among those with history of CVD, cardiovascular death among those with high CV risk, Non cardiovascular death and all cause death, and cardiovascular death among those with COPD and CAP

Data analysis plan

The regression analysis will allow for heterogeneity in association between exposures and study endpoints over time (eg, 1 – 5 days vs. 6 – 10 days vs. 11-365 days). Candidate models include a fully parametric piecewise exponential survival model and the semi parametric Cox proportional hazards model with treatment * time interaction term, both allowing for occasional right censoring, separate azithromycin/amoxicillin hazard ratios will be estimated for time intervals of interest (eg, 1 – 5 days vs. 6 – 10 days vs. 11-365 days). Propensity

scores will be used to adjust for confounding variables.

Documents

Study results

A0661209 NI Study Report .docx.pdf (3.64 MB)

A0661209 Study Report_FINAL.pdf (1.47 MB)

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 source(s), other

Kaiser Permanente Northern California United States, Kaiser Permanente Southern California United States

Data sources (types)

Drug dispensing/prescription data

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