Arrhythmogenic Potential of Drugs (ARITMO) project

First published: 13/04/2012

Last updated: 22/02/2024

Study Finalised

Administrative details

EU PAS number

EUPAS2361

Study ID

20755

DARWIN EU® study

No

Study countries

- Denmark
- Germany
- Italy
- Netherlands
- United Kingdom

Study description

Cardiac ventricular arrhythmia as a side effect of anti-arrhythmic and non-antiarrhythmic drugs has become a major pharmacological safety concern for the pharmaceutical industry and the health regulatory authorities.The overall objective of the ARITMO project is to analyse the ventricular arrhythmogenic potential of individual drugs belonging to the following classes (> 400 compounds): antipsychotics (ATC - Anatomical Therapeutic Chemical classification: N05A), anti-infectives (antibacterials (J01), antimycotics (J02), antivirals (J05), and antiprotozoals (P01)) and H1-antihistamines (R06). The aim of observational database study is to investigate the pro-arrhitmic risk associated to the medications belonging to the following classes: anti-infectives, antihistamines and antipsychotics. In detail, the primary objective is to estimate the rates and relative risks of (a) ventricular arrhythmia (VA) and (b) sudden unexpected death (SUD)/sudden cardiac death (SCD) associated with the most frequently prescribed individual anti-infectives, antihistamines and antipsychotics. To estimate the comparative risks of the study drugs, different comparators will be selected for each drug class of interest.Secondary objectives of the study are:- to explore the effect of dose and duration of use and route of administration on the association between study outcomes and drugs of interest,- to identify demographic and clinical predictors for the specific drug-induced arrhythmias- to describe the prescribing pattern of the study drugs in different databases For each of the two outcomes (VA and SCD/SUD) matched, nested case control studies will be conducted separately to assess the rates and the relative risk associated with anti-infectives, antihistamines and antipsychotics. As regard the anti-infectives, different case control subsets will be created for each drug subgroup (i.e. antibiotics, antivirals, antimycotics and antiprotozoals).

Study status

Finalised

Research institutions and networks

Institutions

Erasmus Medical Centre Rotterdam

First published: 01/02/2024

Last updated: 01/02/2024

Institution

N/A

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution | Educational Institution | ENCePP partner

Department of Pharmacology, University of Bologna (UNIBO)

Italy

First published: 25/06/2010

Last updated: 13/02/2012

Institution | Outdated | Educational Institution | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 19/12/2025

Institution | Non-Pharmaceutical company | ENCePP partner

Società Italiana di Medicina Generale e delle Cure Primarie (SIMG)

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Patient organisation/association

AARHUS university Denmark, Uni-HB Germany

Networks

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Network

Contact details

Study institution contact

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Primary lead investigator

Miriam Sturkenboom

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 04/01/2010

Actual: 04/01/2010

Study start date

Planned: 01/01/1996

Actual: 01/01/1997

Data analysis start date

Planned: 04/01/2010

Actual: 04/01/2010

Date of final study report
Planned: 30/09/2013

Actual: 08/08/2013

Sources of funding

- EU institutional research programme

More details on funding

VII Framework Programme

Study protocol

Aritmo_Deliverable5.2.pdf (1.07 MB)

Aritmo_Deliverable5.2_amended.pdf (1.99 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Not applicable

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

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

The aim of this observational database study is to investigate the pro-arrhitmic risk associated with medications belonging to the following classes: anti-infectives, antihistamines and antipsychotics.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J01) ANTIBACTERIALS FOR SYSTEMIC USE

ANTIBACTERIALS FOR SYSTEMIC USE

(J02) ANTIMYCOTICS FOR SYSTEMIC USE

ANTIMYCOTICS FOR SYSTEMIC USE

(J04) ANTIMYCOBACTERIALS

ANTIMYCOBACTERIALS

(J05) ANTIVIRALS FOR SYSTEMIC USE

ANTIVIRALS FOR SYSTEMIC USE

(P01) ANTIPROTOZOALS

ANTIPROTOZOALS

(N05A) ANTIPSYCHOTICS

ANTIPSYCHOTICS

(R06) ANTIHISTAMINES FOR SYSTEMIC USE

ANTIHISTAMINES FOR SYSTEMIC USE

Medical condition to be studied

Ventricular arrhythmia

Sudden cardiac death

Population studied

Short description of the study population

Patients who had:

1. At least one study drug prescription/dispensing during the study period

2. At least 12 months of continuous enrolment before initial prescription/dispensing of a study drug. This period is required to characterize the subject in relation to previous occurrence of study outcomes or previous exposure to study drugs. Patients with ventricular arrhythmias registered within the year prior the study entry will be identified and analysed in a specific sub-group analysis

3. For each drug class, no use of any drug belonging to that class for six months before initial prescription/dispensing. This wash-out period is required to avoid selection of prevalent users and potential depletion of suceptibles

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Age groups

- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- 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)

Estimated number of subjects

27000000

Study design details

Outcomes

primary objective is to estimate the incidence rates and incidence rate ratios of (a) ventricular arrhythmia (VA) and (b) sudden unexpected death (SUD)/sudden cardiac death (SCD) associated with the most frequently prescribed individual anti-infectives, antihistamines and antipsychotics. - to explore the effect of dose and duration of use and route of administration on the association between study outcomes and drugs of interest,- to identify demographic and clinical predictors for the specific drug-induced arrhythmias- to describe the prescribing pattern of the study drugs in different databases

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Data analysis plan

Crude incidence rate together with 95% Confidence Interval (CI) for each study outcome will be separately calculated for each drug class and individual medication dividing the number of events occurring during the exposure to the study drug(s) by the total number of person-years of exposure.Age and gender specific incidence rates will also be assessed in an external reference group from general population in order to estimate the background incidence rate for study ouctomes.Case control studies will be conducted separately within each inception cohort of new users of the study drug classes. By means of conditional logistic regression analyses, odds ratios (ORs) together with 95% CI will be calculated for each individual study drug as compared to corresponding reference category, adjusted for potential confounders. All analyses will first be performed for each database separately and the heterogeneity between databases will be examined.

Documents

Study results

ARITMO_Executive_Summary_08.08.2013.pdf (159.63 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.

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

Conflict of Interests.pdf (97.48 KB)

Composition of steering group and observers

Steering Commitee ARITMO.pdf (61.8 KB)

Data sources

Data source(s)

THIN® (The Health Improvement Network®)

Drug claims information system

Health Search/IQVIA Health Longitudinal Patient Database

Integrated Primary Care Information (IPCI)

Data source(s), other

Emilia Romagna GPs drug prescription

Data sources (types)

Administrative healthcare records (e.g., claims)

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