Arrhythmogenic Potential of Drugs (ARITMO) project

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Study | Finalised

Administrative details

Contact details

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PURI
https://redirect.ema.europa.eu/resource/20755

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 institution 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

Educational Institution

ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands
First published: 07/01/2022
Last updated 10/01/2022

Institution

Laboratory/Research/Testing facility

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

Arrhythmogenic potential of drugs (ARITMO)

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Network

Study timelines

Date when funding contract was signed
Planned:
04/01/2010
Actual:
04/01/2010

Data collection
Planned:
01/01/1996
Actual:
01/01/1997

Start date of data analysis
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 data collection

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
100000095975
ANTIBACTERIALS FOR SYSTEMIC USE
100000096363
ANTIMYCOTICS FOR SYSTEMIC USE
100000096381
ANTIMYCOBACTERIALS
100000096107
ANTIVIRALS FOR SYSTEMIC USE
100000097789
ANTIPROTOZOALS
100000097449
ANTIPSYCHOTICS
100000098252
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

Results tables
ARITMO_Executive_Summary_08.08.2013.pdf(159.63 KB)

Data management

ENCePP Seal

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
IPCI

Data source(s), other
Emilia Romagna GPs drug prescription

Data sources (types)
Administrative data (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