# 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).

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**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 | Educational Institution | ENCePP partner

## The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

**First published:** 07/01/2022

**Last updated:** 24/07/2024

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

## Contact details

### Study institution contact

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Study 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

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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

Drug utilisation

**Data collection methods:**

Secondary use of data

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**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

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**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)

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**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