



Drug-induced cardiac arrhythmias, such as those deriving from prolongation of the electrocardiographic QT interval, are a major pharmacological safety concern as they are difficult to predict. Namely, Torsade de Pointes (TdP) and sudden cardiac death are serious side effects of drugs that induce QT prolongation, but these occur very rarely and do not arise with all QT prolonging drugs. As a result of the difficulties in predicting which drugs may result in serious arrhythmic side effects, a number of antipsychotic, antihistaminic and anti-infective drugs have been withdrawn from the market in recent years, and others were restricted in use.

ARITMO aims to investigate the arrhythmia-related risks of antipsychotic, antihistaminic and anti-infective medicines (more than 250 compounds). A multidisciplinary strategy will be applied to create a drug ranked list based on risk of adverse arrhythmogenic outcomes.

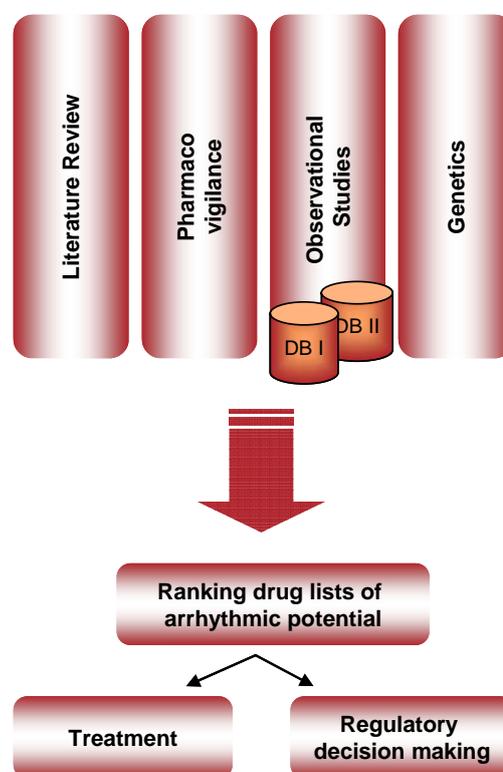
The **ARITMO** Consortium is an international network for the conduct of pharmacovigilance studies, meta-analyses of the literature and large database and surveillance studies in the field. The systematic examination of existing evidence and generation of new evidence by analysis of databases and surveillance systems will generate one of the largest collections of data available. **ARITMO** will have the potential to examine risks arising from differences in prescription patterns between Southern and Northern Europe and assess the genetic susceptibility to arrhythmogenic events.

A multidisciplinary approach will be followed to achieve the **ARITMO** objectives including:

- Critically reviewing the literature on preclinical and clinical evidence
- Conducting in silico modelling to predict the arrhythmic potential through target profiling and docking molecules in existing models and predicting the effects on hERG K+, Na+, and Ca++ channels
- Analyzing the information in national and international pharmacovigilance databases of spontaneous reports of arrhythmias
- Conducting prospective case control surveillance on symptomatic QT prolongation
- Conducting cohort studies in patients receiving antipsychotics or anti-infectives

- Analyzing information on the association between drug use and adverse effects from health care databases on more than 27 million persons
- Collecting blood samples from cases and drug-matched controls to investigate potential effect modification by candidate genes and a hypothesis generating approach including more than 2000 genes

Knowledge integration from the above mentioned actions will provide assistance for the risk/benefit ranking of drugs to aid treatment and regulatory decision making. The comprehensive knowledge database generated will include a score that will be assigned by weighing both the quality and strength of information, and a risk chart for clinicians, which will allow for a more informed treatment and decision making in prescribing drugs.



ARITMO is carried out by an interdisciplinary team of researchers carefully selected by their specific scientific expertise.

- Erasmus University Medical Center, Netherlands. *Project Coordinator.*
- Fundació IMIM, Spain.
- London School of Hygiene & Tropical Medicine, UK.
- Alma Mater Studiorum Università di Bologna, Italy.
- Universitaet Bremen, Germany.
- University of Newcastle, UK.
- Université Victor Segalen-Bordeaux II, France.
- Fondazione Salvatore Maugeri Clinica del Lavoro e Della Riabilitazione, Italy.
- Charité – Universitaetsmedizin Berlin, Germany.
- Università Degli Studi di Verona, Italy.
- St. George's Hospital Medical School, UK.
- AstraZeneca R&D, Sweden.
- Pharmo Coöperatie UA, Netherlands.
- Fondazione Scientifica SIMG-ONLUS, Italy.
- Aarhus University Hospital, Århus Sygehus, Denmark.
- Academisch Medisch Centrum, Amsterdam, Netherlands.
- Drug Safety Research Trust, Southampton, UK.

