

The IMIM Foundation is an important participant in this project financed with 2.7 million euros by the European Commission

The ARITMO Project Researches the Risk of Arrhythmia that May Be Caused by Some Antipsychotic, Antihistamine and Anti-Infective Drugs

- More than 250 pharmacological compounds will be studied
- The medical data of more than 27 million Europeans will be analysed
- The objective is to provide doctors with better guidance when making drug prescription decisions

Barcelona, 26 April 2010. - Cardiac arrhythmia caused by medications is a priority in pharmacological safety as they are difficult to predict. Sudden cardiac death and Torsades de Pointes (TDP) are serious side effects of some antipsychotic, antihistamine and anti-infective drugs that induce prolonged QT intervals. The QT interval is a measure of the time between the Q and T cardiac waves that are recorded in electrocardiograms. If it is abnormally prolonged, arrhythmias may be caused. The normal value is between 0.30 and 0.44 seconds in men and 0.45 seconds in women.

Although its incidence is not very frequent and not all medications that prolong the QT interval cause these side effects, the difficulty of determining which of them can cause serious arrhythmic side effects in recent years has led to the removal of some of these medications from the market or restrictions on their use.

ARITMO arose out of the need to identify not only which medications prolong the QT interval, but also those that can cause serious side effects as well as discover the factors that are associated with this risk. The project, which will last a total of 36 months, will analyse the arrhythmogenic potential of more than 250 antipsychotic, antihistamine and anti-infective drug compounds on the initiative of the European Medicines Agency Pharmacovigilance Group.

The ARITMO project (the complete title is "Arrhythmogenic Potential of Medicines") has received a 2.7 million euro subsidy from the European Commission (7th Framework Programme). It will be carried out by a consortium of 17 internationally renowned research institutions, led by Dr. Miriam Sturkenboom from the Erasmus Medical Centre of Rotterdam (Holland) who will create a common protocol for the participating databases and will conduct surveillance studies. Combining the databases and surveillance systems will make it possible to study one of the largest data collections available and be equipped with great potential to examine the risks deriving from the differences in prescription patterns between southern and northern Europe.

The IMIM Foundation, through its European Project Coordination Office, will be responsible for coordinating this management and the IMIM (Hospital del Mar Research Institute) Chemical

Genomics Laboratory, led by Jordi Mestres, will be responsible for preparing the cardiac safety profiles for the medications.

A multi-disciplinary approach will be used to achieve the ARITMO objectives such as:

- Critically evaluating the literature on clinical and pre-clinical scientific evidence
- In silico modelling to predict arrhythmogenic potentials using the target profile and molecular docking in existing models and predicting the effects on ion channels
- Analysing the information in spontaneous reports of arrhythmias in national and international pharmaco-surveillance databases
- Conducting prospective surveillance studies on the symptomatic prolongation of the QT interval
- Conducting cohort studies with patients who take antipsychotic and anti-infective drugs
- Analysing information on the association between the use of medications and their adverse effects based on health databases with more than 27 million people
- Analysing information from ongoing clinical studies to evaluate the association between the use of medications and some arrhythmogenic results
- Gathering blood samples to research the possible effects of modifying candidate genes

Integrating all of the knowledge from all of these actions will help evaluate the risks and benefits of the medications in order to make treatment decisions. The database gathering all the knowledge generated will include a score assigned based on the weight of the quality and soundness of the information as well as a risk classification aimed at doctors so as to enable improved informed treatments and decision making when prescribing drugs.

About the IMIM Foundation

The IMIM Foundation is a private, non-profit entity that was created in 1992, the objective of which is research and post-graduate education in the fields of biomedicine and health and living sciences and their promotion within the Mar Health Park.

The European Project Coordination Office (EPCO) is responsible for managing the ARITMO project. EPCO specialises in complex research project management, supporting the project coordination of the work plan follow-up tasks, administrative, legal and financial management as well as aspects related to the dissemination and exploitation of the project activities and results. Currently, EPCO is managing 6 R+D projects financed by the European Commission.

About IMIM (Hospital del Mar Research Institute)

The IMIM is a public research institute created 60 years ago by the City of Barcelona which is dedicated to scientific research in the fields of biomedicine and health sciences as well as to training highly qualified research personnel in these areas. It is organized into 5 research programmes: cancer, neuropsychopharmacology, epidemiology and public health, inflammatory and cardiovascular processes and biomedical information science. Director: Miguel López-Botet. www.imim.es The IMIM Chemical Genomics Laboratory, directed by Mr. Jordi Mestres, has developed its own methodology which enables predicting the molecular affinity for more than 2700 proteins.

In recent years, the Chemical Genomics Laboratory has applied this methodology in the assisted design of molecules with specific pharmacological profiles for various therapeutic areas (cardiovascular, central

nervous system, cancer and pain). With this capacity, the laboratory's contribution to the project will be to identify the affinity signatures related to the arrhythmogenic potential of medications.

Additional information:

Participating institutions:

- Erasmus University Medical Center, Netherlands
- Fundació IMIM, Spain
- London School for Hygiene and Tropical Medicine, United Kingdom
- Alma Mater Studiorum-Università di Bologna, Italy
- Universitaet Bremen, Germany
- University of Newcastle, United Kingdom
- Université Victor-Segalen Bordeaux 2, France
- Fondazione Salvatore Maugeri Clinica del Lavoro e Della Riabilitazione – IRCCS, Pavia, Italy
- Charite – Universitaetsmedizin Berlin, Germany
- Università Degli Studi di Verona, Italy
- St. George's Hospital Medical School, United Kingdom
- AstraZeneca, Sweden
- PHARMO Institute, Netherlands
- Fondazione Scientifica SIMG-ONLUS, Italy
- Aarhus Universitetshospital, Aarhus Sygehus, Denmark
- Academisch Medisch Centrum bij de Universiteit van Amsterdam, Netherlands
- Drug Safety Research Trust, United Kingdom

Project website: www.aritmo-project.org

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