



International research team develops new methods for therapy evaluation in rare diseases.

In the EU diseases that affect on average not more than 5 in 10,000 people are called *rare*. Worldwide, more than 7,000 such rare diseases are registered. The resulting groups of patients who are affected by a specific rare disease can be very small. A significant number of diseases occur in only 1-2 patients (e.g. obesity due to prohormone convertase-I deficiency), Orphanet (2012). In the EU 6 to 8 % of the population - that is, from 27 to 36 million people – suffer from at least one of the 5,000 to 8,000 different rare diseases. According to information from the European Society of paediatric oncology, 75% of rare diseases affect children, of whom 30% die before reaching their fifth birthday.

The ability of conventional statistical methods to evaluate new therapeutic approaches for any given rare diseases is limited due to the small number of patients concerned. This means that established statistical approaches to demonstrate the efficacy and safety of therapies may fail in this situation. Thus, there is an urgent need not only to develop new therapeutic approaches to treat diseases, but also to develop new statistical methods to establish which approaches work. The aim is to use and bring together all possible sources of information in order to optimize the process. This is the point of departure for IDEAL ("Integrated Design and Analysis of small population group trials") research project.

The project will explore new methods for design and analysis of clinical studies and to integrate and synthesise these into an effective strategy, so that the efficiency of clinical trials evaluating therapies for rare diseases can be significantly increased.

An international researcher-team under the coordination of Professor Ralf-Dieter Hilgers of the RWTH Aachen will jointly develop new designs and sophisticated analysis methods for the evaluation of therapies for rare diseases, supported by the EU Projectmanagement Office der RWTH Aachen. The research is funded by the 7th Framework Programme of the European Union (FP7-HEALTH-2013-INNOVATION-1, No. 602 552) with 3 million €.

The consortium consist of Professor Ralf-Dieter Hilgers, RWTH Aachen University, Professor Holger Dette, Ruhr University Bochum, Franz König, Medical University of Vienna, Professor France Mentré, Institut National de la Santé et de la Recherche Medicale in Paris, Professor Stephen Senn, Centre de Recherche Public de la Santé Luxembourg, Professor Mats Karlsson, Uppsala University, Uppsala, Professor Malgorzata Bogdan, Polytechnika Wroclawska, Warsaw, Dr. Carl-Fredrik Burman, Chalmers University of Technology, Gothenburg, Professor Geert Molenberghs, University Hasselt, Hasselt and Professor Christoph Male, Medical University of Vienna. The research programme is divided into 11 work packages.

The work packages focus on the assessment of randomization, the extrapolation of dose-response information, the study of adaptive trial designs, the development of optimal experimental designs in mixed models, as well as pharmacokinetic and individualized designs, simulation of clinical studies, the involvement and identification of genetic factors, decision-theoretic considerations, as well as the evaluation of biomarkers.

Two work packages provide support for project management and the dissemination of results. The IDEAL project is accompanied by an advisory board of international experts with different professional backgrounds, representing both patients' interests, the views of the pharmaceutical industry as well as clinical and regulatory aspects.

The ability to use mathematical and statistical techniques for the evaluation of new treatments where standard methods fail to be successful is a challenge and motivation for all of us. We all look forward to this exciting collaboration.

