ERA-Net Neuron
NEWSLETTER 12

May 2011, Lake Como, Italy

FROM BENCH TO BEDSIDE – NEURON WORKSHOP ON INVESTIGATOR-DRIVEN MULTINATIONAL CLINICAL TRIALS

The ultimate goal of research in the field of disease-related neuroscience is to advance our understanding of diseases and, eventually, improve patient care. The transfer of results from biomedical research into disease mechanisms to application in clinical practice, however, is still a bottleneck. Clinical trials to study diagnostic or therapeutic measures under controlled clinical conditions are the necessary research step between bench and bedside. Conducting high quality investigator-driven clinical trials with large numbers of patients from several centres requires specific expertise, sufficient resources and comprises a number of formal and legal aspects. This is particularly the case if the patient recruiting centres are distributed over several different countries. On the other hand, financial support for this kind of research is scarce, since cross-border funding poses a problem for most funding agencies. Thus, although with increasing demand on patient stratification transnational multicentre trials become more and more necessary, they are comparably rare. This situation is far from satisfactory and is therefore tackled within the framework of the ERA-Net NEURON.

The second NEURON workshop regarding the topic "Result exploitation from research into brain diseases" examined the field of Multinational Clinical Trials and scrutinized potentials and hurdles for both researchers and research funders. Renowned experts from the field provided information on the rationale and definitions of investigator-driven multinational clinical trials, on the European Clinical Research Infrastructure Network "ECRIN", and on the perspective of clinical researchers. Specific aspects of and differenced between clinical trials to neurological diseases and mental disorders were discussed. Furthermore, since the topic of patient recruitment in multinational multicentre trials is especially relevant to the area of rare diseases, the approach of the Era-Net E-Rare2 in this field was presented.

NEWS FROM ERA NET NEURON

The proposal to the Commission for another 4 year project NEURON II has recently passed the review with very high scores so that we are now confident to be able to continue our work as of January 2012.

The Joint Call secretariat of ERA Net NEURON received 57 applications to its fourth Joint Transnational Call on "European Research Projects on Cerebrovascular Diseases". The applications involve 230 scientists from 11 participating countries, out of them, 19 consortia were asked to submit full proposals until June 15th. Final funding decisions will be made on October 2011, and funding of selected projects will start on early 2012.

The third call for applications for the NEURON Young Scientists Award for Excellent Papers in Neuroscience was published last month. Submission deadline for applications: September 15, 2011.
www.neuron-ernet.org/_media/Announcement_excellent_paper_2011.pdf

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NEED FOR SUPPORT AND FOR FUNDING TO MULTINATIONAL INVESTIGATOR-DRIVEN CLINICAL TRIALS: THE ROLE OF ECRIN | JACQUES DEMOTES

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Creating a single area for clinical research will provide access to patients and expertise all across Europe, but requires defragmentation of infrastructure (the mission of ECRIN, www.ecrin.org), of legislation, and of funding. ERA-net are typical tools for funding multinational trials, but this requires to address critical issues: 1 - critical mass of participating countries. 2 - involve the right partners, as the funding source for clinical trials may differ from the funding for basic neuroscience. 3 - need for signific ant level of funding, minimum 1 to 3M€ for clinical trials, with higher costs in the coordinating country. 4 - can the same panel of experts assess both basic and clinical research (the evaluation is protocol-based and requires expertise in methodology)?. 5 - avoid multiple evaluations (why not use the ECRIN scientific board for access to funding and to infrastructure),6 - avoid parallel trials, and fund a single trial with single sponsor, protocol, management, database, Eudract number, same amendments. 7 - define which category of investigator-driven clinical research will be supported:
only clinical trials comparing treatments?
focus on rare neurological diseases, or common diseases?
which of the three main categories?
a - development of innovative products
b - trials for the repurposing of marketed drugs, exploring new indications?
c - trials for treatment optimisation using already marketed products?

INVESTIGATOR-DRIVEN MULTINATIONAL CLINICAL TRIALS: RATIONAL, DEFINITION AND NEEDS | CHRISTIAN OHMANN

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Innovative medicinal products appear on the market too rarely with a gap between development of drugs and patient's interests and available research is dominated by pharmaceutical interventions. There is a strong need for investigator-driven clinical research in Europe. The main areas to be covered are to establish comparative effectiveness of treatments and therapeutic strategies, to evaluate drugs for rare diseases, to extend variability of treatment to fragile populations and to optimize available treatment. In order to implement investigator-driven multinational clinical trials there is a need for infrastructures at the national, EU and global level as well as a need for funding sources to support multinational and independent assessment of health care strategies. Further aspects are a need for a risk-adapted legislative framework and a need to reinforce transparency for clinical trial data. Multinational clinical trials have the potential to provide an adequate number of patients, it may shorten time for clinical trials and it will improve generalisability of study results. Moreover innovative trial designs are supported by bringing together specific resources and expertise. The role of the European Union in funding multinational clinical trials should be strengthened.

A PSYCHIATRIST'S PERSPECTIVE ON MULTINATIONAL CLINICAL TRIALS | RENÉ KAHN

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It is clear that conducting large clinical trials outside industry in Europe is difficult. The EUFEST study has been successful for several reasons:
It was able to foster collaboration between the best and scientifically most interested parties. The main basis of the collaboration was to produce good science, not to register a drug. This meant that all researchers were highly motivated. An all success factor was that the question we addressed was limited and focused and we did not allow all different research groups to burden the study with their private scientific interests. Another success factor was that the assessments included in the study were limited in number and frequency. Despite these facts, most patients were recruited in Eastern Europe, the reason being that we paid a flat fee and clearly the amount we paid was worth more in Eastern Europe than it was in the Western part of Europe.

In summary, the success factors for the EUFEST are:

1. It was a highly motivated group of researchers;
2. The study was primarily done for scientific reasons;
3. The research question was extremely focused;
4. The study was not allowed to be burdened by individual interests of researchers;
5. All researchers had the opportunity to publish separately on the data.

A NEUROLOGIST'S PERSPECTIVE ON MULTINATIONAL CLINICAL TRIALS | WOLFGANG OERTEL

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We report on how to establish and maintain a study group, the German Parkinson Study group (GPS - >40 centres with experience in trials on Parkinson syndromes (PD, DLB, MSA, PSP).
GPS also focuses on the premotor phase of PD, i.e. "REM sleep behaviour disorder (RBD)", which converts into PD in 80 % in 20 years – to prepare for trials with disease modifying compounds.
Recommendations:
Identify a core group of 3 to 4 leaders with a proven record of collaboration.
Starting a group from scratch takes >2 years.
Group must have agreed on minimal data set for documentation and used an electronic data capture system.
Protocol should allow any European country to participate. Study design must meet quality criteria for publication. Rules of democratic rotation of group key functions must be defined.
Group must address European diversity in quality of documentation, in rules of ethical committees ,data safety and security, conflict of interest and administration of funding.
The keys to success are
Identify a group of clinician with a European perspective
Identify and sufficiently!! fund one project, so that the group can prove itself as a successful reliable consortium for future funding.

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THE POSITION OF E-RARE, THE ERA-NET FOR RESEARCH IN RARE DISEASES, ON FUNDING CLINICAL TRIALS | SOPHIE KOUTOUZOV

As many other EC-funded ERA-Nets, one of the major activities of the E-Rare consortium – constituted of 12 main European research funding bodies (agencies and ministries) – is to coordinate research programmes (on rare diseases) and to fund, through the launch of Joint Transnational Calls, collaborative research projects on these pathologies.
Through its funding activity, E-Rare has so far favored collaborative, transnational research in rare diseases focused on increasing the knowledge on their etiology, natural history, pathophysiology, and on the development of pre-therapeutical studies. Nevertheless, the Consortium so far has excluded clinical trials from the scope of the calls for several reasons:

1 - the evaluation procedure is already complex due to the great heterogeneity of the proposals; evaluation of proposals on clinical trials would add further complexity and burden;
2 - Funds from participating countries to the calls are limited and would lead to further splitting of resources;
3 - not all E-Rare partners are legally able to fund clinical trials.

However, an important task for the future will be to develop E-Rare projects towards more immediate medical and health benefit for patients suffering from rare diseases. Therefore, we will explore possibilities to expand possible funded research topics towards clinical trials. This will depend on overcoming the bottlenecks described above and developing procedures for funding transnational clinical trials. A workshop organised by E-Rare, foreseen at the end of 2011, will gather the relevant stakeholders to discuss these issues.

German Aerospace Centre, Project Management Agency
Federal Ministry of Education & Research (BMBF), Germany
Austrian Scuence Fund (FWF), Austria
National Authority for Scientific - Ministry of Education, Researc and Youth (ANCS - MECT), Romania
National Centre For Programmes Management, Romania
Ministry of Health (MOH), Italy
Academy of Finland (AKA), Finland
Ministry of Science and Innovation (MICINN), Spain
National Research Agency (ANR), France
National Center for Scientific Research (CNRS), France
Chief Scientist Office, Ministry of Health(CSO-MOH), Israel
National Research Fund (FNR), Luxemburg
Swedish Research Council (SRC), Sweden
Canadian institutes of Health Research, Canada
Québec Health Research Funding Agency (FRSQ), Canada
The National Centre for Research and Development (NCBIR), Poland
Institute of Health Carlos III (ISCII), Spain
Medical Research Council (MRC), UK
National Institute for Medical Research (INSERM), France