



Report of EFACTS project at *euro-ATAXIA* conference October 2010

By Julie Greenfield, Ataxia UK

Professor Massimo Pandolfo, the co-ordinator of the project gave an overview of the EFACTS project to members of *euro-ATAXIA*. This project started a few months ago.

He explained the large role European researchers had played in the FA field and the need to establish such a large network. The network was successful in getting funding from EC of six million euros.

Professor Pandolfo is the overall co-ordinator; Dr Schulz is the clinical co-ordinator and Dr Puccio is the scientific co-ordinator. The project involves 14 partners. It was not possible to include all groups in Europe for practical reasons but the network is not closed and there is some flexibility, such that if good projects are proposed they could be incorporated at a later date.

Work packages that are part of EFACTS:

1. FA database and registry
2. Frataxin function
3. Frataxin gene silencing mechanisms
4. Clinical assessment tools
5. Pathogenesis of FA
6. New models of FA (animal and cell). [There is still a need for a mouse model with a more severe phenotype. A few labs are making iPS cells and differentiation is underway].
7. Identification of biomarkers
8. Identification of modifiers of FA [eg: why do some people with same GAA repeat lengths have different phenotype? Try and find genes that can modify frataxin.]
9. Therapeutic strategies (developing and testing treatments)

In addition to these work packages there is one on management and dissemination of information.

FA database

At the moment they have one reference centre per country involved in EFACTS, with some countries having two (one adult and one paediatric Centre).

The database will include clinical and biological data. Bioinformatics tools would be used to analyse data generated. This aspect will involve a participant at Brunel University, UK. Professor Pandolfo stressed the importance of studying natural history (progression of FA) and to develop good outcome measures to help with future trials and avoid disappointments such as the idebenone trial. They plan to do studies on auditory function, cardiac function and cognitive problems.

The stated goal is to have 600 patients on the database but they are hoping for more (eg: in the euroSCA project they exceeded the anticipated numbers). EFACTS will have open access to any research groups in Europe who apply to become members of the Ataxia Study Group and get ethical approval to include their patients. The idea is for more Centres to be included in each country with time, so there is some flexibility.

Biomarkers

They aim to find biomarkers that correlate with disease status and progression (eg: MRI or blood tests). They will test frataxin levels in cells, ISC enzyme activities, gene expression analysis, oxidative stress markers in blood and urine and cardiac biomarkers.

Development of therapeutics

They will work on drug discovery, understand how the drug works, testing of drugs in preclinical studies. Hope to take two molecules up to the point of being tested in trials. There is no funding for trials in this project (as no funding for trials allowed in the European Commission FP7 programme).

Patient participation

Professor Pandolfo highlighted the importance of taking part in this project, in particular in the database. He also said that you can have patients from countries not in the EFACTS project take part in the future but there would need to be a clinician who approaches the EFACTS Group to take part.

Questions from audience

[Professor Pandolfo left to catch a plane and Dr Caterina Mariotti and Dr Paola Giunti (other EFACTS Group members) took over to answer questions in English and Italian].

1. What do EFACTS researchers expect from patient organisations?

The EFACTS Group wish to a) meet regularly to inform patient groups what is happening (hopefully this will be done at *euro-ATAXIA* meetings) and for this information to be disseminated to all patients and b) encourage recruitment to database. Patients who are included on the database will also take part in biomarker



studies (eg: involving taking blood and urine samples); a few centres will also take part in MRI and cardiac studies.

2. What is the role of Repligen?

The researchers continue to work together with this company to reach phase II trials and ensure structure is in place for trials.

3. Are trials funded in EFACTS?

Trials themselves are not funded by the EC as they are too expensive. If a useful drug emerges during the course of this study the researchers will seek funds to do a trial in parallel. They can use the database to help in recruitment for the trial. The database can help identify patients with specific characteristics (eg: GAA repeat length, ambulant/non ambulant etc).

This report is written by Ataxia UK's Research Projects Manager, Julie Greenfield and approved by the EFACTS Steering Committee. (October 2010)

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