

## **FARA Conference – Friedreich’s Ataxia Therapeutics Symposium 2009**

On 17 and 18 July, Friedreich’s Ataxia Research Alliance (FARA; US), held a Therapeutics Symposium in Philadelphia, US. Key scientists and clinicians attended the meeting, where the development of future treatments for Friedreich’s ataxia (FA) was discussed. Two members of Ataxia UK staff also attended; Sue Millman, Chief Executive, and Alison Stevenson, Research Officer.

This is a summary of the clinical research that was presented at the meeting, written by Dr Alison Stevenson.

### **Idebenone**

A clinical trial of idebenone (trade name Catena) in the US has recently been completed. Although treatment with idebenone improved FA symptoms, unfortunately no statistically significant difference was found between treatment and placebo groups. This could be due to unexpected improvements in the placebo group which occurred during the first three months of the six-month study. Despite these results, however, idebenone remains a promising treatment for the cardiac and neurological symptoms of FA; when the results of this study are pooled with those from a previous US trial, a significant improvement in ataxia is seen, compared to placebo.

The US trial has been extended on an open-label basis (where each participant is openly given idebenone) for a further twelve months. There is also currently a clinical trial of idebenone underway in Europe and it is hoped that these two studies will provide satisfactory results for the registration of idebenone in Europe and Switzerland. In the meantime, Santhera, the pharmaceutical company who make Catena, will make the drug available on a named patient basis which will allow healthcare professionals to prescribe it to individual patients.

### **A0001**

A0001 is another antioxidant drug that is similar in its action to idebenone. A small trial of this will take place in the US later this year, looking at its ability to improve energy production within cells.

### **Deferiprone**

Deferiprone (trade name Ferriprox) is a drug that mops up excess iron, an iron chelator. It is prescribed for the treatment of iron overload in some patients with thalassemia, an inherited type of anaemia. In FA, deferiprone improves cardiac function. In experiments using cell models in the laboratory, it reduces the abnormal accumulation of iron that is seen in heart cells and helps to redistribute the iron to other parts of the cell that are iron deficient. It also seems to improve energy function by helping to restore an energy-producing enzyme in the cell.

As the iron accumulation in FA is only seen in some parts of the cell, extra care needs to be taken to ensure that only the excess iron is mopped up and that the iron levels in the iron-deficient parts of the cell are not depleted any further. Therefore, the dosage of the medication is crucial to ensure safety of the treatment and participants in clinical trials need to undergo regular health checks.

A placebo-controlled study looking at deferiprone in FA has recently been completed and the full results of this are expected later this year. Another trial is due to start soon in Europe and will look at the long-term safety and efficacy of deferiprone in FA.

### **Erythropoietin**

Erythropoietin (EPO) is a hormone that promotes red blood cell production in the body. It is also manufactured as a drug and is prescribed for the treatment of anaemia, cancer and other critical illnesses. Its potential for use in FA is based on the fact that it increases frataxin protein levels. Its mode of action is unknown, but is not thought to involve direct changes to the gene or the way it is read.

A small pilot study of EPO (eight participants) showed increased frataxin protein and reduced markers of oxidative damage in participants. Preliminary results from a more recent clinical trial show that EPO increased frataxin protein in all participants, although significant increases in frataxin protein were not seen until approximately three months after a single injection of the drug. The increase in frataxin protein was more noticeable at higher doses of EPO.

However, EPO treatment can also cause increased red blood cell production and lowered iron levels in the blood. Further investigation of EPO, in larger, placebo-controlled studies, is therefore required before it can be confidently recommended as a treatment for FA. Future work will also investigate whether higher concentrations of EPO can slow the progression of ataxia in FA and look at alternative ways of administering the drug (it is currently done by injection).

### **Histone deacetylase inhibitors**

Good progress is being made with histone deacetylase inhibitors (HDAC inhibitors) in moving them towards clinical trials. These compounds act by switching back on the frataxin gene, which is abnormally switched off in FA. Current laboratory research is aimed at determining the best dosage and timings for administration of the drug. HDAC inhibitors are being developed for clinical trials and it is hoped that these will commence in one to two years' time.

In addition to the new HDAC inhibitor compounds that are being developed, a commercially available HDAC inhibitor is also being studied. It is hoped that a pilot trial of this compound can also be undertaken soon.

### **Other drugs**

Sometimes, drugs licensed for treatment of one condition show beneficial effects in another condition. Using a drug that has already been licensed often means that it is easier and quicker to get to market because safety and toxicity studies have already been done. Pioglitazone and varenicline are two such drugs.

**Pioglitazone** (trade name Actos) is prescribed for type II diabetes. It has also shown positive effects in multiple sclerosis and may have a general neuroprotective effect, by promoting natural antioxidants. A placebo-controlled trial recently started in France and will be open to UK participants in 2010. People with FA who are aged 7-24 and are ambulatory will be able to take part. Please contact the Ataxia UK office for further details of this.

**Varenicline** (trade names Chantix in US, Champix in Europe) is an anti-smoking drug. However, when one clinician from Florida, US, gave it to some people with ataxia (two people with FA, one person with spinocerebellar ataxia type 3, one person with spinocerebellar ataxia 14 and one person with Fragile X tremor/ataxia syndrome) she noticed improvements in their ataxia. How varenicline might affect ataxia is not yet understood. The first clinical trial of varenicline in ataxia will be a short, placebo-controlled study in people with Friedreich's ataxia. The trial is planned to start soon and will take place in the US.

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