FABRY INTERNATIONAL NETWORK NEWSLETTER

July 2016

Editor's Note

Dear FIN members

It is with regret that it has been a while since our last Newsletter. As many of you may already be aware I joined FIN as Coordinator in December 2015 and for the first part of 2016 I have been focusing my attention on organising the FIN Expert meeting in Japan, which was a great success I might add! Moving forward it is my intention to communicate with you and share up -dates via the FIN Newsletter at least two to three times a year. So should you have any news from your organisation or country which you think may be of interest to others please do forward it to me for the next issue.

Toni Ellerton
toni@fabrynetwork.org

July - 4th Fabry International Network Expert Meeting in Japan 20-22 May 2016

From the evaluation forms and talking to everyone the FIN Expert meeting in Tokyo was as huge success and this was somewhat of a relief for our FIN Co-ordinator, Toni Ellerton and the FIN Board as it was a great challenge to organise this meeting at such a distance. Indeed it would not have been possible without the help we received from Professor Eto, Mr Harada and the Japan Fabry Disease Patients and Association, (JFA) team.

The FIN Board arrived in Japan in time to have a productive full day of one to one face to face meetings with representatives of Shire, Genzyme and Amicus. These were followed by a closed meeting of FIN members who gathered for the FIN Annual General Meeting. Although not many attended the AGM those that did asked valuable questions and scrutinised the Director's Report and Financial Report. The re-election of Directors was held and I am delighted that Lut De Baere, Anna Meriluoto and Jack Johnson were re-elected. Lut took over the Chair to oversee the appointment of Vice President and President. Jack Johnson was duly appointed Vice President and Christine Lavery, President. By the time we all gathered for dinner on the 33rd Floor of the Prince Park Tower Tokyo Hotel nearly all the 51 FIN members and speakers had arrived.

Contents

In this issue:

With a glass of Champagne, donated by the hotel management, in hand the FIN delegates were welcomed to Tokyo by Christine Lavery and Mr Hasio Harada. As the evening came to a close Professor Yoshikatsu Eto, Director, Jikei University, gave an enthusiastic insight into how to enjoy the sights of Tokyo and beyond. Sadly most of us will have to return again if we are to savour these wonderful sights and enjoy the amazing Japanese hospitality.

The FIN Expert Meeting was held at Jikei University and started promptly with an introduction to Fabry disease by Professor Yoshikatsu Eto. This set the scene for presentations by Professor Atul Mehta (UK), Dr Dominique Germain (France), Dr Dau-Ming Niu (Taiwan), Dr Uma Ramaswami (UK), Dr Derralynn Hughes (UK) and Professor James Moon (UK) to speak on the clinical aspects of Fabry disease and there treatment. Professor Moon described some innovative work he is pioneering at University College Hospital, London on advance cardiac imaging of the Fabry heart. Megan Fookes (Australia) shared her experience of Fabry disease in children.

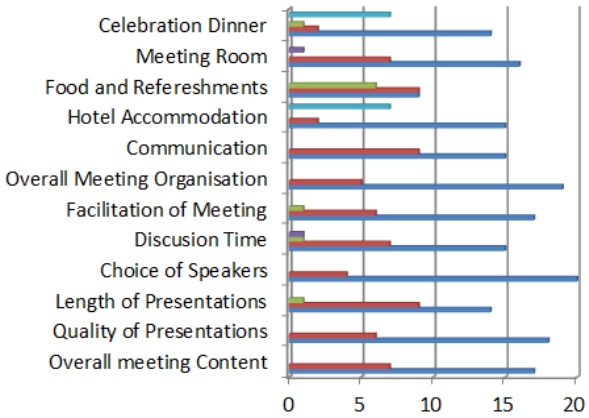
As well as the speakers and FIN members this meeting was opened to 40 Japanese medical students, junior doctors and consultants who chose to give up their Saturday to increase their knowledge of Fabry disease. This initiative came at the request of Mr Harada and is certainly something FIN should consider doing in the future when the programme is medically orientated as part of our educational programme.

On Saturday night a buffet dinner was held at the Green Rattan restaurant in Roppongi Hills a lively part of Tokyo. I would like to say our FIN members then worn out made their way back to the hotel but I can't! Led astray by Mr Harada and some FIN Board Members many headed off to a Karaoke Bar to sing their hearts out and then try and find their way back to the hotel! (Jack and Christine preferred the civilisation of the bar on the 33rd floor back at the hotel!)

On Sunday most of the delegates took early flights or had a well-earned lie in. For many of the FIN Board and some speakers it was back to Jikei University to make presentations at the Fabry Tokyo Symposium 2016.

So you might well ask were does FIN's Expert meeting go from here? It has been agreed we return to Europe in May 2017. The precise country and venue is currently being worked on and will be announced soon.

Results and comments from the Evaluation forms



Lovely meeting & administration of time & speakers variation of themes, love the news within our Fabry disease & looking forward for the Gene therapy

Dominique Germain—very interesting

I liked Jack & Anna's update and would perhaps like to see more on Peer Training between Patient organisations & updates from regions

The role of ERT & emerging therapies in Fabry disease was quite exciting to know the alternative choices for Fabry

Thank you so much for the wonderful meeting

Really enjoyed session 4, I can learn Fabry disease from a patients real voice

Patient expectations ... was a deep and nice discussion.... Impressed

Anne Grimsbo's talk was simple, & honest ... very compelling

Anna & Jack's talk was my favourite session

As a doctor I learned a lot from patients way of thinking which helps me to consider how to communicate with my patients in future

I enjoyed hearing about new treatment options, it's good to know of alternative methods to Fabry. Would like to hear more about pain management in a future meeting

Fabry Disease Research & Treatment

Amicus Therapeutics oral therapy Galafold Previously known as Migalastat, is being appraised through the NICE highly specialised technologies process in England. The UK MPS Society is leading the patient submission for the use of Migalastat in Fabry disease and this may well influence other players in Europe.

Unfortunately the FDA requires more data on Galafold and therefore is not avaialable for reimbursement in the USA

FDA fast-tracks development of Genzyme oral drug, GZ/SAR402671 a new investigational oral substrate reduction therapy for the treatment of Fabry disease.

Japanese ERT to use cloud technology in Fabry research – Medidata, the leading global provider of cloud-based solutions for clinical research in life sciences has announced that its cloud-based technology platform has been adopted by JCR Pharmaceuticals. The pioneer in biotherapeutics is leveraging the Medidata Clinical Cloud to support research on a therapy for the treatment of Fabry disease, bringing greater speed and operational efficiencies to the organisation's development programme in Japan.

Protalix announces positive clinical trial results – Protalix BioTherapeutics has announced interim data from the company's phase I/II clinical trial of 1mg/kg of PRX-102 for a treatment of Fabry disease. PRX-102 is a recombinant plant cell expressing, chemically modified version of the human alpha-Galactosidase-A enzyme. The phase I/II clinical trial of PRX-102 for the treatment of Fabry disease is an open-label, dose-ranging study treating up to 18 naïve male and female adult patients.

Trial to start for moss-made ERT for Fabry disease – Greenovation, a German Biotech company, has announced a phase I clinical trial application for its drug candidate moss-alpha-galactosidase (moss-agal).

Shire's Humanitarian Aid Programme for MPSII and Fabry Disease

Shire
To be as brave as the people we help.

DirectRelief

It is generally accepted that people affected by ultra-rare diseases across the globe face challenges getting reimbursed high cost market approved treatments. Like many LSD patient organisations across the World the MPS Society receives 100 – 200 emails each year from patients and their families pleading for help to access enzyme replacement therapy (ERT) for MPSI, MPSII, MPSIVA, MPSVI and Fabry disease. For most we can only respond with a level of empathy, kindly advising about joining forces with others in their country similarly affected and engaging with clinicians and the Departments of Health. Many of these enquiries come from the Middle East, India, Pakistan and Bangladesh where mistakenly people are under the impression that everyone else in the World is receiving reimbursed ERT unhindered. As many families even in Australia, New Zealand, Canada, South Africa and parts of Europe know this could not be further from the truth. But there is a chink of light for some MPSII and Fabry patients thanks to the Shire Charitable Access Programme which is inviting clinicians in Ecuador, Dominican Republic, Egypt, Albania, Belarus, Tunisia, Malaysia and Pakistan to apply for their patients on line at www.directrelief.org/rarediseases/fabry-disease

If you are a **patient with Fabry disease** in Ecuador, Dominican Republic, Tunisia, Egypt, Albania, Belarus, Malaysia or Pakistan please tell your doctor about the Shire Humanitarian Programme and ask the doctor to apply.

If you are a **patient organisation, doctor or relative** who knows of eligible Fabry patients in these countries please tell them about the Shire Humanitarian Programme.

July - Shire's Humanitarian Aid Programme for MPSII and Fabry Disease

How to Apply

Physicians must complete the online application in order for their patients to be considered for enrolment.

The applications will be reviewed by an independent Medical Expert Committee (MEC) and the physicians will be notified regarding their submissions after the MEC makes their decision. Shire and Direct Relief are not involved in the patient selection process.

Eligibility for Fabry Disease

Inclusion Criteria

The applicant must meet the following criteria to be eligible for participation in this Program:

- Applicants must have a genetically confirmed diagnosis of Fabry disease. Patients with a plasma GAL activity 1.5nmol/hr/mL or leukocyte GAL activity 4 nmol/hr/mg are eligible if their Fabry disease can be documented by genetic analysis, positive histopathology, and/or a family history of the disease.
- Applicants must have symptomatic Fabry disease as reported by the treating physician, for example: significant abnormalities in renal function, cardiac function, or cerebrovascular function, peripheral neuropathy, severe proteinuria and/or severe pain or crises.
- Female applicants of childbearing potential must have a negative pregnancy test prior to starting Replagal infusions. Periodic pregnancy testing should be performed as medically indicated. The therapy of pregnant or lactating females should only be considered in severe circumstances.

Exclusion Criteria

- Female applicants who are pregnant or nursing
- Applicants who have a clinical condition or health problem that may prevent any potential benefit of therapy (as assessed by the INCAP Medical Advisory Board)
- Applicants who are currently on another enzyme replacement or substrate inhibition therapy

Lut De Baere becomes a Member of the MetabERN Patient Board

Dear FIN members,

Last year, I followed the workshops held by the European Commission to discuss the services etc of the European Reference Network's (ERN's). Professor Maurizio Scarpa was also there and started to set up a MetabERN. So, he involved me and asked my advice as a patient representative. That was the start of our collaboration!

Normally, you would have received a letter from me to inform you of the submission of a proposal to set up a European Reference Network on Rare Inherited Metabolic Diseases (MetabERN) that will be coordinated by Professor Maurizio Scarpa from Helios Horst Schmidt Klinik Wiesbaden (DE).
MetabERN aims to facilitate access to improved care to all patients with inherited metabolic diseases across Europe.

Patient representatives will be actively involved in the decision-making process and planning activities of the Network. I am also one of the 6 patient advocats in the European Patient Advocacy Groups (ePAG) elected by Eurordis who will be a member of the MetabERN Patient Board, which aims to bring together all patient groups active in the area of rare inherited metabolic diseases. MetabERN has set out a number of key activities that will be conducted during the course of the next 5 years. Patient Groups will work in close collaboration with Healthcare Professionals to map and understand patients' educational and training needs, develop guidelines for patient-involvement in patient care pathways, develop patient-focused outcomes to assess the current standards of care in order to understand gaps and identify solutions. MetabERN is driven by the principle of inclusiveness and it is intended to bring together patient groups from across the EU within the area of inherited metabolic diseases.

If you want more information, you can contact me lut@boks.be

Lut de Baere

Amicus Therapeutics Announces European Commission Approval for Galafold™ (Migalastat) in Patients with Fabry Disease in European Union

On the 31 May 2016 Amicus Therapeutics announced that the European Commission granted full approval for the oral small molecule pharmacological chaperone Galafold™ (migalastat) as a first line therapy for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease (alpha-galactosidase A deficiency) and who have an amenable mutation. Amicus has already begun supplying the market in Germany and has commenced the reimbursement process with NICE and other healthcare authorities in major European countries.

Galafold is the first oral treatment as well as the first precision medicine for Fabry disease. The broad label includes 269 Fabry-causing mutations which represent between 35 and 50 percent of all patients with Fabry disease.

John F Crowley, Chairman and Chief Executive Officer of Amicus Therapeutics, Inc. is quoted as saying, *"This EU approval for Galafold is a significant advancement in the field of precision genetic medicine and a tremendous milestone for the Fabry community."*

The European Commission approval was based on clinical data from two Phase 3 pivotal studies in both treatment naïve Study 011 (FACETS study) and enzyme replacement therapy (ERT) switch patients Study 012 (ATTRACT study), as well as ongoing long-term extension studies. AS it is known Fabry disease is a rare genetic disease and potentially life-threatening condition caused by the accumulation of disease substrate (globotriaosylceramide, GL-3) in the lysosome due to a dysfunctional or deficient enzyme. Galafold works by stabilizing the body's own dysfunctional enzyme, so it can clear the accumulation of disease substrate in patients who have amenable mutations. An amenable mutation is one that is responsive to therapy with Galafold based on predefined criteria.

"As principal investigator in both Galafold pivotal studies, I have experience treating both naïve and treatment-experienced Fabry patients with Galafold," said Derralynn Hughes MA DPhil FRCP FRCPath, Senior Lecturer in Haematology at University College London, UK with clinical responsibilities in haematology and lysosomal storage disorders. *"I am pleased that the European Commission has approved this new treatment option and I believe it has the potential to address unmet needs among Fabry patients who have amenable mutations."*

"The EU approval of the first oral precision medicine for Fabry disease is a major step forward for patients in Europe," said Christine Lavery, President of the Fabry International Network (FIN). *"We appreciate Amicus' commitment to the Fabry community and its dedication to develop high quality therapies for Fabry disease. For the first time in more than a decade, patients with Fabry disease who have amenable mutations now have a choice for an innovative new treatment option."*

This information is taken from a comprehensive Press Release issued by Amicus Therapeutics on 31 May 2016 and published in full on the Fabry International Network (FIN) website www.fabrynetwork.org

My Journey from ERT to Chaperone Migalastat (Galafold)

I learned about Fabry when I was five years old. My father's torso was covered by angiokeratomas. I asked what it was and was told that my father suffered from the same disease that my uncle had recently died from. I remember seeing my uncle in a wheelchair and my grandmother handling a spelling board for him.

When I was eight I had a couple of severe flu attacks with high fever. I had violent pains in my fingers and toes and was told that I suffered from the same disease as my father.

At the age of eighteen a Danish professor wrote to my father asking if he cared to be examined because he knew the disease was in our family. I wanted to be examined as having children was one of my future plans. As expected my father, my sister and I were diagnosed with Fabry.

At the age of 53 my father broke down with kidney failure. He died at 55.

I got pregnant in 1990, had prenatal diagnosis, placenta biopsies, and was told that it was a boy with Fabry. I had an abortion. My second pregnancy had no fetus. My third pregnancy was another boy with Fabry followed by another abortion. My fourth pregnancy I lost. My fifth and sixth pregnancy in 1993 and 1995 were my two boys with no
Fabry.

I never thought of myself as a Fabry patient and I never had any troubles other than the pains when in fever as a young child.

I received annual examinations from 2002. In April 2007 my doctor recommended that I start treatment. In September 2007 I started ERT for the first six months I received treatment at the hospital and after that I had home treatment and my friend or my husband inserted the needle.

My mutation is A156T which means I can receive Migalastat. From 2009 I had a pause in ERT in order to take part in AT 1001. The 16th of December 2010 I had my first Migalastat capsule. The following year I had three kidney biopsies as a part of the trial.

Migalastat continues to work fine for me. This fall my doctor told me that I no longer have microalbuminuria. I have a heart condition and for the time being I have a loop recorder inserted in my chest. I receive medicine for that. For me it is a great advantage to receive Migalastat instead of ERT. I feel less like a patient. I am taking the capsules as if it was vitamins (only every second day, of course).

When you receive ERT you are very much a patient every second weekend and you have to take all kinds of precautions practically, hygienic and planning wise.

It is a great freedom for a Fabry patient to be treated with Migalastat.

The Danish Fabry Patient Organisation was founded in 2002 by my cousin and another patient. Today we have 66 members a mixture of patients and relatives. We have 4 board meetings a year and an AGM. We do a family weekend every second year and a day meeting the opposite year. I became chair in May 2013. In 2014 I joined the board of FIN.

My focus is sharing experiences between Fabry patients, listening to them and show them that a happy life is possible even when diagnosed with Fabry.

Anne Grimsbo

Breaches of the ABPI Code of Practice at the Fabry International Network Expert Meeting 2015

In the interests of transparency and, as reported to the Fabry International Network (FIN) membership at its Annual General Meeting in Japan in May, FIN has inadvertently been linked to a complaint made by Sanofi Genzyme about Amicus to the Prescription Medicines Code of Practice Authority (PMCPA) alleging breaches to the Association of British Pharmaceutical Industry (ABPI) Code of Practice.

The events that led up to this complaint being made occurred at the FIN Expert Meeting held at Latimer House, England, 20-22 November 2015. FIN invited in good faith, and at its own expense, two representatives each from Shire, Sanofi Genzyme and Amicus to present and participate in this meeting.

FIN first became aware that their Expert Meeting had been used in this way when several people saw the 'Fabry International Network' name associated with the case AUTH/2809/12/15: on the PMCPA website www.pmcpa.org.uk Whilst FIN accepts that regulations are in place to protect the reputation of the pharma industry and indeed patients this FIN Expert Meeting was NOT a patient meeting and in the ultra-rare disease field individual pharmaceutical companies play an important role working with the patient organisations to ensure they have accurate and up to date patient relevant information.

Immediately prior to the start of the FIN Expert meeting, members of the FIN Board attended the Amicus opening of their European Office. Amicus had some leftover over champagne and offered it to me for FIN. As I was not driving, for health reasons and could not lift, it was agreed the Champagne was transported to the FIN Expert meeting where it was used at the FIN 10th Anniversary dinner on Saturday night to provide each delegate, including the pharma industry delegates, one glass each. Genzyme reported this as a breach of the ABPI Code but in inter alia company discussions Genzyme accepted an apology from Amicus that this was a one off and would not happen again! Nevertheless this left a 'trust' issue in many of our minds. In monetary terms each delegate technically received a gift of less than £5! I am sure there is not one FIN member who felt this one glass of champagne was an inducement. I think we are made of stronger morals than that!

More seriously, Genzyme alleged further breaches against Amicus including promotion of an unlicensed medicine and failure to show reference numbers on the presentation raising concerns over a robust review and approval process from appropriately qualified personnel. Genzyme also alleged that the breaches were broad and gross in scope constituting a failure to maintain high standards and undermine the standing of the pharmaceutical industry.

Amicus provided the PMCPA with a detailed response in which it refuted the allegations made by Genzyme stating that no clinical results from the studies were given in the presentation and the audience was high level representatives from global Fabry patient associations.

On appeal, the PMCPA Panel considered the statements and discussion about amenable mutations and the implied positive regulatory status of Migalastat. Although much of the information is in the public domain, on balance the appeal board considered that the presentation had raised the prospect of a new treatment for Fabry patients with amenable mutations and, in that regard, had promoted Migalastat prior to the granting of a marketing authorisation.

The appeal board noted its ruling above and considered that as the promotional presentation was not formally certified it upheld a breach of the Code. The appeal panel also considered that as the presentation was aimed at patient organisations and had not been formally certified it also upheld a breach of the Code.

The appeal board noted its comments and rulings above and considered that high standards had not been maintained and consequently upheld a breach of the Code.

Although noting its comments above, **THE APPEAL BOARD HOWEVER DID NOT CONSIDER THAT IN THE PARTICULAR CIRCUMSTANCES OF THE CASE A RULING OF A BREACH OF CLAUSE 2 - DISCREDIT TO, AND REDUCTION OF CONFIDENCE IN, THE INDUSTRY - HAD TAKEN PLACE**

Not directly related to the matters above, to those of us working in the ultra-rare disease field, patient organisations want to embrace and welcome further drug development and a professional working relationship is essential. Increasingly, this means new generations of drugs whereas ten years ago there was only one drug per disease or none at all. It is therefore an anathema that the ABPI Code can be used as a vehicle for anti-competitive behaviour by bigger and stronger pharmaceutical companies against smaller pharma companies

Breaches of the ABPI Code of Practice at the Fabry International Network Expert Meeting 2015

doing their best to find treatments for ultra-rare diseases in this important rapidly emerging field for patients affected.

In truth nothing was shown or said by Amicus back in November that most of the Fabry patient organisation leaders didn't already know! Has the ABPI and PMCPA not heard of the internet and social media? Today we don't need to travel on the Queen Mary to gather information from across the Atlantic. How can it be that American ultra-rare disease patients can access all the information they need on current treatments and clinical trials but in Europe we are all considered so corruptible that we need protecting from ourselves through a flawed ABPI Code of Practice?

History has shown that regulation of the pharmaceutical industry is necessary for patient safety but for ultra-rare disease patients and their patient organisations perhaps this should be left to the Medicines and Healthcare Products Regulatory Agency (MHRA), a professional organisation and equipped for the role, and compliance with the Medicines Act 1968.

If I was the CEO of a Biotech Company or small pharmaceutical company with an eye to the European market for ultra-rare diseases today one thing is for certain I would not commit to complying with the ABPI Code of Practice or join the self-regulating ABPI relying on the funds of big pharma and the fines of penalised smaller pharma for its existence.

Christine Lavery

President of the Fabry International Network

FINAL CALL For New FIN Board Member

At the AGM in Tokyo the FIN Board communicated that there one vacant place on the FIN Board. Members were invited to write to the FIN President, Christine Lavery.

If you are interested in joining the FIN Board please send your expression of interest to Christine Lavery, email: info@fabrynetwork.org no later than 8 August 2016. The FIN Board will then hold teleconference interviews with all applicants. They will then make a final decision in September 2016.

5th FABRY INTERNATIONAL NETWORK EXPERT MEETING TO BE HELD IN EUROPE

MAY 2017

FURTHER DETAILS TO FOLLOW

The primary aim of the Fabry International Network is to facilitate collaboration between Patient Organisations around the world to support those affected by Fabry Disease.

Contact FIN for:

Membership
Latest News
Information
Connection
Support

Board of Directors:

Christine Lavery
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