WORLD Symposium 2020

Orlando, Florida, USA. 10th to 14th February 2020

Visit report by Allan Muir,
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Introduction

The WORLD symposium is held every year, alternating between San Diego and Orlando every two or three years. It is an event for all Lysosomal Diseases (LDs) and is an opportunity to hear presentations of the latest research and clinical outcomes for these conditions. A huge variety of posters is presented.

The event is attended by all biotechnology companies with interests in LDs and for that reason is a fantastic opportunity to meet with their advocacy teams and other staff members.

International and National Support Groups

Many patient support groups take advantage of this event, some have posters and displays, and this year there was representation from seven Pompe organisations; namely:

- IPA: International Pompe Association
- UK: Pompe Support Network
- USA: Acid Maltase Deficiency Association
- Canada: Canadian Association of Pompe
- Germany: Pompe Deutschland
- NZ: New Zealand Pompe Network
- Japan: Japan Pompe Association

Representatives from these groups met together for dinner on the first day and regrouped throughout the week to socialise and to exchange experiences and plans for the future.

The Japan Pompe Association were particularly interested in how other national groups encourage Pompe individuals and families to become members of their organisations. They have especially difficult circumstances where families “hide” disabilities, and doctors are so protective of patient confidentiality that they won’t pass on information to families from support groups. Hopefully our advice and encouragement will be of some help to them in the future.

I would encourage more countries to send representatives to this event each year, indeed we may begin to host our own global Pompe meetings at future WORLD Symposia if there is sufficient demand.

Oral Presentations

There were nine presentations directly related to Pompe disease, and several others of relevance to all LDs, on topics such as newborn screening and future therapies. One notable presentation was that of the 2020 Roscoe O. Brady Award for Innovation and Accomplishment to John F. Crowley, Chairman and CEO of Amicus Therapeutics. John followed the award with a

presentation entitled “The Moral Obligation to Ensure Access to Medicines for All Patients in Need”, referring to his family’s journey with Pompe disease.

The Pompe presentations are listed below in Annex A. All will have abstracts referred to in the Poster presentations section of this report of which many will now be published on the affiliated body’s website.

Poster Presentations

Thirty-eight posters were presented referencing Pompe disease; these are listed in Annex B. These illustrate the wide range of research being undertaken in all aspects of biochemistry, treatment, care and support for the condition.

Patient Advocacy Meetings

A number of meetings were arranged for patient advocacy group leaders throughout the week:

Sanofi-Genzyme Patient Advocacy Leader Luncheon

Sanofi organised a luncheon to introduce their senior leadership and advocacy teams. We were informed that 16,000 LD patients are now accessing their therapies and they are working hard to improve access globally; e.g. for Pompe patients in Southeast Asia.

Melody Libby praised the IPA Community Advisory Board (CAB) meeting in San Antonio, saying how it gave an amazing understanding of the lives of patients, and that the executive summary is extremely useful for all their staff.

The Sanofi-Genzyme 2020 PAL Awards will focus on Capability and Capacity Building, although the date for applications is still to be set.

The Humanitarian Programmes were discussed, suggesting that the time from first contact to making a decision should be about five working days.

AVRO-BIO Patient Advocacy Luncheon

Presentations of the AvroBio LD pipeline were given and discussed. The Pompe programme, currently fourth on their list, was not discussed in detail as it is less advanced than the others, they are taking extra steps with it to ensure that their lentiviral therapy reaches the muscles and can cross the Blood-Brain-Barrier (BBB).

The talk highlighted some aspects of the therapy that may require support groups to manage patient expectations; e.g. side effects of the small dose of chemotherapy may have side-effects of hair-loss and vomiting. Also, the FDA are imposing a 15-year follow-up after the therapy is approved, so we would want to have an independent clinical registry in place for Pompe well before such drugs are licensed.

Council of Patient Advocates (COPA)

The COPA meeting was joined with the meetings for scientists and industry this year, and so there was less involvement from patient groups than there was last year.

There was much talk about advancing research for LDs through NIH and the Genetic and Rare Disease Information Centre (GARD) was promoted for its disease-specific pages; such as Pompe:

https://rarediseases.info.nih.gov/diseases/5714/glycogen-storage-disease-type-2

Registries were discussed as were Novel Explorations in Rare Disease (NERD). A programme to quantify the burden of rare diseases is currently under development.

There was a proposal for a global Uniform LDN Database, which, if realised, could provide an independent registry for Pompe disease; the data would available for all researchers, but would not be owned by patients.

UK LSD Collaborative

It had been hoped to convene a meeting of global support groups for LDs to create a global LSD Collaborative; however, it was not convenient for all parties to meet, and so six members of the UK collaborative members met over dinner to discuss our future plans.

Industry meetings

I had pre-arranged meetings organised with a large number of companies developing therapies for Pompe disease. At least five companies currently have interests in next-generation ERT and eight are considering gene therapies. Our meetings were all informal and were intended to provide each party with an update of each other's progress and future plans. All companies were very interested in the work of our new Pompe Support Network, but I did manage to promote the IPA Community Advisory Board and its plans for International Pompe Day.

As well as meetings with companies engaged with drug development, I met with several others that offer other interesting opportunities for the Pompe community.

Allan Muir
21 February 2020

Annex A, Oral Presentations relevant to Pompe Disease

Jeffrey Y. Huang, Children's Hospital of Orange County, Orange, CA, United States
Longitudinal assessment and immune response to recombinant GAA in CRISPR-Cas9 generated Pompe disease knock-in mice.

Ankit K. Desai, Duke University, Durham, NC, United States
Benefits of prophylactic short-course immunomodulation in patients with infantile Pompe disease: Demonstration of long-term safety and efficacy in a large cohort.

Fulvio Mavilio, Audentes Therapeutics**,** San Francisco, CA, United States
Pre-clinical safety and efficacy findings of AT845, a novel gene replacement therapy for Pompe disease targeting skeletal muscle and heart.

Umut Cagin, Genethon**,** Évry, France
Liver expression of secretable GAA rescues advanced Pompe disease at the biochemical, functional, and transcriptional level in Gaa-/- mice.

David Kronn, New York Medical College**,** Valhalla, NY, United States
Mini-COMET study: Safety, immunogenicity, and preliminary efficacy for repeat avalglucosidase alfa dosing in patients with infantile-onset Pompe disease (IOPD) who were previously treated with alglucosidase alfa and demonstrated clinical decline.

Mazen M. Dimachkie, University of Kansas Medical Center**,** Kansas City, KS, United States
NEO1 and NEO-EXT studies: Long-term safety and exploratory efficacy of repeat avalglucosidase alfa dosing for 5.5 years in late-onset Pompe disease patients.

Stephanie Austin, Duke University**,** Durham, NC, United States
Extended treatment with VAL-1221, a novel protein targeting cytoplasmic glycogen, in patients with late-onset Pompe disease.

Dwight Koeberl, Duke University School of Medicine**,** Durham, NC, United States
A phase 1 study of gene therapy with ACTUS-101 in late-onset Pompe disease.

Sean M. Armour, Spark Therapeutics, Inc., Philadelphia, PA, United States
Preclinical development of SPK-3006, an investigational liver-directed AAV gene therapy for the treatment of Pompe disease.

Annex B. Poster presentations relevant to Pompe disease

2	Mary-Alice Abbott	Characteristics of Pompe disease patients with and without the c. 32 13T>G (IVS1) variant: data from the Pompe Registry
19	Carolina Aranda	Infantile-onset Pompe disease and CRIM negative status: Immunomodulation with intravenous immunoglobulin as an alternative for regular immune tolerance induction
23	Stephanie Austin	Complicated cases and the need for individualized follow up plans for children diagnosed with Pompe disease via newborn screening
24	Stephanie Austin	Extended treatment with VAL-1221, a novel protein targeting cytoplasmic glycogen, in patients with late-onset Pompe disease
25	Mahima Avanti	Effects of enzyme replacement therapy on bone density in late onset Pompe disease
30	Anneliese Barth	Early enzyme replacement therapy in a CRIM positive classic infantile Pompe patient: 11-year follow-up of a still progressive disease
61	Umut Cagin	Liver expression of secretable GAA rescues advanced Pompe disease at the biochemical, functional, and transcriptional level in Gaa-/- mice
98	Mazen Dimachkie	NEO1 and NEO-EXT studies: Long-term safety and exploratory efficacy of repeat avalglucosidase alfa dosing for 5.5 years in late-onset Pompe disease patients
116	Luca Fierro	Newborn screening for Pompe disease in New York state: Results from 6 year single center experience
117	Niamh Finnegan	Promoting independence and empowering patients on enzyme replacement therapy
131	Michael Gelb	A universal newborn and diagnostic screening platform for lysosomal diseases and beyond
156	Sang-oh Han	Comparisons of infant and adult mice reveal age effects for liver depot gene therapy in Pompe disease
170	Sinead Horgan	Chart review of the management of late-onset Pompe patients diagnosed through newborn screening
173	Caoimhe Howard	Adherence to international and local guidelines in Irish Morquio syndrome type A patients
175	Leroy Hubert	Molecular diagnostic findings of lysosomal diseases as a result of "Detect Lysosomal Storage Diseases", a no-charge sponsored testing program
199	David Kasper	Challenges for newborn screening and rare disease diagnostic initiatives in Europe
200	David Kasper	Combined biochemical and targeted-next generation sequencing panel for differential diagnosis of inherited myopathies
201	David Kasper	The value of biochemical enzymatic testing for the rapid identification of early-onset Pompe disease in newborns and children

208	Brian Kevany	Intravenous delivery of a novel AAV capsid with improved PNS tropism reduces underlying Pompe disease pathology
209	Aleena Khan	Whole-body MRI in late-onset Pompe disease: Clinical utility and correlation with functional measures
210	Aleena Khan	Higher dosing of alglucosidase alfa improves outcomes in children with Pompe disease
215	Virginia Kimonis	Antisense oligonucleotide targeting glycogen synthase (GYS1) in a Pompe disease mouse model
218	Dwight Koeberl	A phase 1 study of gene therapy with ACTUS-101 in late-onset Pompe disease
221	Aditi Korlimarla	A new look at an old disease: Is Pompe disease a neuromuscular disorder with CNS involvement?
222	David Kronn	Mini-COMET study: Safety, immunogenicity, and preliminary efficacy for repeat avalglucosidase alfa dosing in patients with infantile-onset Pompe disease (IOPD) who were previously treated with alglucosidase alfa and demonstrated clinical decline
225	Francyne Kubaski	Quantification of glycosaminoglycan species in patients with multiple sulfatase deficiency by liquid chromatography tandem mass spectrometry: A potential biomarker for this condition
226	Francyne Kubaski	Newborn screening for six lysosomal diseases: Pilot study in Brazil
263	Fulvio Mavilio	Pre-clinical safety and efficacy findings of AT845, a novel gene replacement therapy for Pompe disease targeting skeletal muscle and heart
282	Marta Morado	Pompe disease: PAS-positive lymphocyte vacuoles as diagnostic screening test
287	Juana Navarrete	Use of biomarkers to follow up positive lysosomal diseases in newborn screening
323	Loren Pena	Impact of early diagnosis by NBS on existing genotype phenotype correlations for Pompe disease
336	Ana Puhl	Combining machine learning and in vitro approaches to identify potential chaperones for lysosomal diseases
369	Emilie Sandfeld	Genomic correction of Pompe disease knock-in mouse myoblasts via CRISPR-Cas9 homology-directed repair
390	Satowa Tanaka	A novel approach to CNS dysfunction of Pompe disease with a fusion protein consisting of anti-transferrin receptor antibody and GAA enzyme
LB-04	Elfrida Benjamin	Humoral immune responses to ATB200 in the first-in-human study of ATB200/AT2221 in patients with Pompe disease: Results from the phase 1/2 ATB200-02 trial
LB-09	Yu-Ting Chiu	Natural product inspired combinatorial chemistry enables us to discover small molecules for the potential treatment of lysosomal disorders
LB-19	Harrison Jones	Determining the diagnostic utility of the identification of tongue involvement in late-onset Pompe disease
LB-32	Matthijs Raaben	Identification of genetic modifiers as therapeutic targets for lysosomal diseases