

WORLD Symposium 2021

Virtual symposium 7th to 11th February 2021

Pompe summary by Allan Muir,
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Introduction

The WORLD symposium is held every year, usually alternating between conference centres in San Diego and Orlando every two or three years, however, due to Covid-19, in 2021 it was a virtual event, held over a similar timeframe. 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 also presented and available to delegates for a limited time after the event.

The day before the official symposium opens, there is always an “Emerging Trends” to educate people new to the field of Lysosomal Disease about the diseases and their treatments. This year, being virtual, entry was free to patients, their family and representatives, and so I and other patient representatives joined the event.

The five days following “Emerging Trends” are filled with oral presentations and satellite symposia organised by industry; there were presentations organised by Audentes, Amicus Therapeutics, AvroBio and Sanofi-Genzyme, each of which had Pompe content.

Emerging Trends

This was a day of varied presentations discussing various topics:

- Function of the Lysosome
- Therapies
- Clinical features
- FDA Regulatory Review
- Newborn Screening
- Case studies
- Patient Advocate’s Perspective
- Covid-19 Clinical impact and management

A few things I took away from the day include:

The lysosome was described as a “nutrient sensor for cells” and LSDs are routinely characterised as “compromised autophagy” which leads to lysosomal membrane damage and permeability which influences the function of other organelles within the cell.

A change in the gene (mutation) is not sufficient to make a diagnosis.

We can’t expect LSD kids to be “typical” and need to assess the level of risk of treatments that give moderate benefit. We should prioritise pain-relief above the gaining of skills.

Oral Presentations

There were eleven oral presentations directly related to Pompe disease, and several others of relevance to all LSDs, on topics such as newborn screening and future therapies.

One very impressive, though slightly troubling presentation, was by Keynote speaker, Michael Osterholm who spoke on the evolving reality of the Covid-19 pandemic.

The Pompe presentations are listed below in List A. All will have abstracts listed in the Poster presentations section (List C), the posters are only available to attendees for a limited time, but many of the published posters and papers may be located by an Internet search.

Satellite Symposia

There were a small number of webinars devoted to Pompe disease and within them there were seven presentations, as listed in Table B. Again, there was a good range of topics by speakers well known to the Pompe patient community; Drs Nina Taben, Priya Kishnani, Benedict Schoser, Pim Pijnappel and others. There was an interesting panel discussion of patient registries where it was suggested that patient representation should be present on registry advisory boards.

Poster Presentations

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

It may be possible to find copies of the papers or posters online through an internet search.

Patient Advocacy Meetings

It is usually the case that industry hosts meetings for patient advocacy leaders and patients at the face-t-face meetings. On this occasion there was only one online meeting that I was invited to. AvroBio held their “2nd Annual Patient Leadership Summit” to inform patient groups about their programme of lenti-viral gene therapies and to answer our questions. There is a hope that their Pompe programme will enter the clinic in 2021.

Next year we might expect WORLD Symposium 2022 to return to San Diego, California, and I would encourage patient groups to send a representative to join others from the international Pompe community, Patient representatives, healthcare professionals, scientists, company representatives and others. It is a unique annual experience, and it would be wonderful to have a significant international representation.

Allan Muir
26 February 2021

List A, Oral Presentations relevant to Pompe Disease

1. VAL-1221: Treating Pompe disease via enhanced glycogen-targeting
2. Engineering α -glucosidase to improve protein stability and cellular uptake for the potential treatment of Pompe disease
3. Immunosuppression with bortezomib and anti-CD20 mAb is effective in reducing neutralizing antibodies to allow repeated AAV administration in mice
4. A phase I/II open-label gene replacement clinical study for late onset Pompe Disease
5. Transforming the clinical outcomes in CRIM-negative infantile Pompe disease identified via newborn screening: The benefits of early treatment with enzyme replacement therapy and immune tolerance induction

6. Efficacy and safety results of the avalglucosidase alfa phase 3 COMET trial in late-onset Pompe disease patients
7. Impact of SARS-CoV-2 on patients with lysosomal diseases in a major NYC hospital system
8. Long-term hematopoietic stem cell gene therapy corrects neuromuscular manifestations in preclinical study of Pompe mice
9. Murine models of lysosomal diseases exhibit differences in brain protein aggregation and neuroinflammation
10. Use of biomarkers to follow up positive lysosomal diseases in newborn screening
11. Top Line Results from the PROPEL Phase 3 Study Comparing AT-GAA (cipaglucosidase alfa/miglustat) versus alglucosidase alfa/placebo in Late Onset Pompe Disease.

List B, Satellite Symposia relevant to Pompe Disease

1. Pompe disease and GAA processing
2. Pathogenic cascade in Pompe disease
3. Perspectives of a person living with LOPD
4. Pompe disease genetics, clinical presentations, and newborn screening in Taiwan
5. Update of the Pompe variant database for the prediction of clinical phenotypes: a genetic modifier for the IVS1 variant, novel disease-associated variants, common sequence variants, and results from newborn screening
6. Analysis of GAA gene variants in the global Pompe Registry & Perspectives on the U.S. experience with Pompe disease newborn screening
7. Panel Discussion-Rare Disease Registries: Pioneering Real World Evidence and a Continued Commitment to the Rare Disease Community

List C, Poster Presentations relevant to Pompe Disease

1. Impact of SARS-CoV-2 pandemic on the care for patients with lysosomal disorders: The experience of a Mexican pediatric center
2. Miglustat does not enhance alglucosidase alfa or avalglucosidase alfa efficacy in Pompe mice
3. VAL-1221: Treating Pompe disease via enhanced glycogen-targeting
4. Immunosuppression with bortezomib and anti-CD20 mAb is effective in reducing neutralizing antibodies to allow repeated AAV administration in mice
5. A novel nonsense LAMP2 variant associated with Danon disease in a pediatric male: A case report
6. New insights into GI manifestations in late-onset Pompe disease: Lessons from the bench and bedside
7. Glycogen accumulation in smooth muscle in the Pompe disease mouse
8. A perspective on research, diagnosis, and management of lysosomal disorders in Colombia: An update
9. Early diagnosis and treatment of infantile-onset Pompe disease via newborn screen
10. A phase I/II open-label gene replacement clinical study for late onset Pompe Disease
11. Functional analysis and clinical curation of human acid alpha glucosidase (GAA) variants of unknown significance (VUS) screened from infants diagnosed with Pompe disease via newborn screening (NBS)
12. Newborn screening for six lysosomal diseases in Brazil: Pilot study update
13. Analysis of parent perception of newborn screening for lysosomal disorders
14. A meta-analysis of enzyme replacement therapy in late-onset Pompe disease
15. Oregon's experience with newborn screening for Fabry, Gaucher, Pompe and mucopolysaccharidosis type I
16. The impact of the COVID-19 pandemic on patients with inherited metabolic conditions: A survey in Wales

17. Mini-COMET study: Effects of repeat avalglucosidase alfa dosing on ptosis in participants with infantile-onset Pompe disease (IOPD) who were previously treated with alglucosidase alfa
18. NEO1/NEO-EXT studies: Safety and exploratory efficacy of repeat avalglucosidase alfa dosing after up to 6 years in participants with late-onset pompe disease (LOPD)
19. Need leads to change: Transition to home infusion in Pompe disease in Brazil in the COVID-19 pandemic
20. Home treatment for lysosomal diseases during COVID-19: German experience
21. Safety and effectiveness of resistance training in patients with late-onset Pompe disease: A pilot study
22. Mini-COMET study: Individual participant-level responses to treatment in patients with infantile-onset Pompe disease receiving repeated dose regimens of avalglucosidase alfa or alglucosidase alfa who were previously treated with alglucosidase alfa
23. Impact of SARS-CoV-2 on patients with lysosomal diseases in a major NYC hospital system
24. In utero enzyme replacement therapy in fetuses with lysosomal diseases: A phase I clinical trial
25. COVID-19 pandemic impact on Brazilian patients with lysosomal diseases: A patient's perspective
26. Impact of COVID-19 on treatment and follow-up in patients with selected lysosomal diseases in a Brazilian center
27. Patient and family perspective of lysosomal disease clinical care and services in the UK
28. The qualitative development of the Pompe disease symptom scale and Pompe disease impact scale
29. Usefulness of hexose tetrasaccharide as a biomarker for monitoring glycogen accumulation in peripheral tissues and brain in Pompe disease
30. Efficacy and safety results of the avalglucosidase alfa phase 3 COMET trial in late-onset Pompe disease patients
31. Enzyme replacement therapy treatment patterns and patient outcomes in late-onset Pompe disease
32. Aparito's six year journey in lysosomal disorders
33. Long-term hematopoietic stem cell gene therapy corrects neuromuscular manifestations in preclinical study of Pompe mice
34. NEO1/NEO-EXT studies: Muscle MRI results in patients with Pompe disease after long-term avalglucosidase alfa treatment
35. Murine models of lysosomal diseases exhibit differences in brain protein aggregation and neuroinflammation
36. Weekly enzyme replace therapy reverses hypertrophic cardiomyopathy in two Pompe knock-in murine models
37. Use of biomarkers to follow up positive lysosomal diseases in newborn screening