POMPE SUPPORT NETWORK

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Notes from SSIEM 2019

Rotterdam, 3-5 September 2019

Allan Muir, Pompe Support Network

Allan Muir attended the 2019 symposium of the Society for Study of Inborn Errors of Metabolism (SSIEM) on behalf of the UK LSD Collaborative. It was a fantastic networking event with many specialists in metabolic medicine and industry representatives present. The programme featured many oral and poster presentations concerning Lysosomal Diseases, including Pompe diseases and featured current therapies in the clinic and under development.

A few interesting take-away messages (for me) from the SSIEM presentations included:

- The side-effects of drugs are the 4th most common cause of death
- Animal models are poor predictors of human response to drugs
- The traditional view of the Lysosome as the last step in the catabolic pathway is being replaced – it is now considered to be regulating processes by acting as a signalling hub. Talk of mTOR, TFEB, Ca_2, were a little over my head, but it was interesting to hear that the significance of TFEB, as an inhibitor of protein synthesis, is being better understood.
- RNA drugs are coming of age. They will lead to many drugs in the future, very specific and mostly targeted to liver and kidney. Dosing perhaps every 3 to 6 months.
- As drug efficiencies increase, so doses may be reduced.
- Interesting presentation on the Virtual Metabolic Human – see www.vmh.life for more information. Creating metabolic computer models to test drugs.
- Understanding of muscle pathology is improving
- Poor-responders to Myozyme/Lumizyme are more likely to suffer lysosomal rupture
- Baseline glycogen in cytoplasm is much higher in Pompe infants
- LOPD lose 1.6 to 4% lung function each year, leading to frequent chest infections.
- Some patients can be clinically silent (few symptoms) for many years
- 10 to 15% of patients are non-responders to ERT. Prediction not possible.
- Improvements can continue 3 years after cessation of ERT.
- Dr Chen (Salford Royal Hospital) asked the question “Are we failing to support cognitive and mental health of adults with IMDs”
    - Learning & cognitive difficulties, anxiety, depression, chronic stress
    - IMD service now linking more with neuropsychology
    - Building new protocols, training and collaborations
    - Mental health training

    - Using telemedicine and other technologies
- Simon Jones (Manchester Children's Hospital): Future Therapies – Lessons from the Past
    - The lysosome is most treatable of the organelles
    - We are *hurtling* towards a bright future
    - Early diagnosis is the key
    - Awareness strategies have failed – after 10 years diagnostic rates remain poor
    - New-born screening is the only way for dramatic change
    - Decades have passed from available treatment to NBS
    - Dosing requires flexibility
    - Problems won't go away with Gene therapies
    - SSIEM shouldn't discuss reimbursement – but primary issue is drug cost.

Below is a list of oral and poster presentations given at SSIEM2019 concerning Pompe disease. The Abstracts are copyright and cannot be reproduced here; they are published in JIMD, the Journal of Inherited Metabolic Disease, V42, Suppl 1, September 2019. Jimd.org.

- Engineered human iPSC-derived skeletal muscles to model Pompe disease
- Benefits of higher and more frequent dosing and immunomodulation on long-term outcome in classic infantile Pompe disease
- Central nervous system involvement in late-onset Pompe disease: a role for brief cognitive assessment?
- Urinary tetrasaccharide is a biomarker for Pompe disease
- Stem cell mediated lentiviral gene therapy corrects central nervous system pathology in a murine model of Pompe disease
- Ex-vivo expanded muscle regenerative cells for the treatment of Pompe disease
- Combined proteomic and lipidomic studies in Pompe disease
- Chest MRI to diagnose early diaphragmatic weakness in adult patients with Pompe disease
- The application of target next-generation sequencing for the diagnosis of metabolic myopathies
- Severe distal muscle weakness in enzyme-treated classic infantile Pompe patients
- Cross-European validity of the Rasch-built Pompe-specific Activity (R-PAct) scale
- Discontinuation of enzyme replacement therapy in adults with Pompe disease: evaluating motives and clinical course
- A Challenge for Pediatricians: The Floppy Infants
- Airway anomalies in infantile-onset pompe disease: a large-scale survey by flexible bronchoscopy

- Screening of twelve lysosomal storage diseases with LCMS/MS in Gazi university hospital in Turkey: The first results of validation
- Review of lysosomal storage disorder clinical and homecare services in the UK
- Mini-COMET: Safety/immunogenicity of avalglucosidase alfa in IOPD patients with clinical decline on alglucosidase alfa
- Efficacy of hyperproteic diet combined with exercise in patients with late-onset Pompe disease
- Long term follow-up of patients diagnosed by Pompe Disease newborn screening
- A genetic modifier of symptom onset in Pompe disease
- Variable effects of enzyme replacement therapy in adults with Pompe disease: 10 years' follow-up
- Urinary Glucose Tetrasaccharide: a useful Prognostic Biomarker for Pompe Disease ?
- Preclinical development of SPK-3006, an investigational liver-directed AAV gene therapy for the treatment of Pompe disease
- Extension of the Pompe mutation database by linking disease-associated variants to clinical severity
- Characteristics of Pompe disease patients with and without the c.-32-13T>G (IVS1) variant: data from the Pompe Registry
- Evidence of increased oxidative stress in Pompe disease. A new therapeutic target?
- Satellite cells fail to contribute to muscle repair but are functional in Pompe disease
- Clinical characteristics and molecular genetic analysis of Moroccan patients in infantile-onset Pompe disease