Pompe Disease: Current Landscape and Promising Developments

Pompe disease, a rare and progressive neuromuscular disorder, is gaining new visibility as clinicians and researchers push for better treatment strategies and long-term outcomes. To gain a clear understanding of where Pompe disease developments currently stand, we asked Tahseen Mozaffar, MD, Professor of Neurology and Pathology at the University of California, Irvine, and Co-Director of the MDA ALS Neuromuscular Center, what patients and providers need to know.

An inherited muscle disorder, Pompe can manifest in two primary forms: infantile and late-onset.

“The infantile version is a severe disease,” Dr. Mozaffar says, noting that without treatment, affected children typically do not survive past two years. In contrast, late-onset Pompe, which presents after age 1, is more common and is characterized by slowly progressing skeletal muscle weakness and diaphragm involvement, which can lead to respiratory complications.

Currently, Pompe is managed through a multidisciplinary approach, involving neurologists, geneticists, pulmonologists, physical therapists, and respiratory therapists. Enzyme replacement therapy (ERT) is the primary treatment. There are now three FDA-approved options: alglucosidase alfa (Lumizyme, 2006), avalglucosidase alfa (Nexviazyme, 2021), and cipaglucosidase alfa (Pombiliti, 2023). However, “none of these drugs has a superiority claim,” Dr. Mozaffar says.

While current treatments offer stability, new strategies under clinical investigation offer the hope of transformative outcomes. These fall into three categories:

1. **Next-generation ERTs** using alternative delivery pathways, such as targeting transferrin receptors, for improved muscle and potential central nervous system targeting
2. **Substrate reduction therapies**, such as a gene silencing and small molecule approach that aims to prevent glycogen buildup
3. **Gene therapy**, which may enable the body to produce its own enzyme and potentially offer a one-time treatment

While new approaches are still in preclinical stages, Dr. Mozaffar notes that Denali Therapeutics and Regeneron will soon start clinical trials for next-generation ERTs. In addition, the New England Journal of Medicine published a promising case study on starting ERT in utero for a fetus known to have infantile-onset Pompe (“In Utero Enzyme-Replacement Therapy for Infantile-Onset Pompe’s Disease”).

Resources

- "Pompe Disease: a Clinical, Diagnostic, and Therapeutic Overview," co-authored by Dr. Mozaffar
- MDA's Pompe Disease information page
- MDA's Pompe Disease Fact Sheet
- MDA's Pompe Disease Treatment Fact Sheet
- The Acid Maltase Deficiency Association (AMDA) Research page.