



Position Paper

PATIENT REPORTED OUTCOMES

NOVEMBER 2021

BACKGROUND

Pompe disease is a progressive neuromuscular disorder. It is a spectrum disease, with infantile-onset at the most severe end of the spectrum. Without treatment, infantile-onset patients rarely survive past their first birthday. Late-onset patients may present at any time from birth to their seventies or later. These patients are very heterogenous in terms of age of onset and rate of progression. However, the natural history of the disease shows that patients will ultimately progress to the point that they die of respiratory failure or other serious complications of the condition.

In 2006, the first treatment for Pompe disease was approved. This treatment dramatically changed the trajectory of natural history of Pompe disease in that it slowed or stopped progression for most patients. Infantile onset patients began to survive their infancy. Late-onset patients also showed improvements in survival and quality of life. A generation of patients are now living longer and more productive lives.

However, this treatment was only a first step. Not all patients experience equal benefit from current treatment options, and unfortunately too many Pompe patients are still dying from this progressive disease. But there is hope because today there are multiple new treatments under development for Pompe. They range from second generation enzyme replacement therapies to gene therapies and patients need the potential options that this offers.

One common challenge that all potential future therapies will face is how to best design trials in an ultra-rare disease with a heterogenous late-onset population. On behalf of the international Pompe community, the IPA would like to take this opportunity to advocate for an increased value to be placed on Patient Reported Outcomes in clinical trial design, as well as in regulatory review of future treatment option.

IPA POSITION STATEMENT

Due to the rare nature of Pompe, which leads to the necessity of small trial sizes and the heterogenous nature of Pompe disease, patients in trials are likely to be at different stage in the development of their disease. Furthermore, just as there is a great degree of heterogeneity in Pompe disease progression for patients, over the last twenty years we have seen that there is also a large degree of heterogeneity in patient response to treatment. Therefore, we believe the broadest range of evaluation is necessary to ensure that all the benefits of treatment are seen. And with a progressive disease like Pompe, we must not forget that stabilization of symptoms is a benefit for patients.

While clinical outcomes such as the Six-Minute-Walk-Test (6MWT) and Forced Vital Capacity (FVC) are important outcomes to consider, we believe that equal consideration should be given to Patient Reported Outcomes. Ultimately, the patient is the end-user of these treatments, and are in the best position at times to report on small but very significant improvements or stabilization to their quality of life that may not be reflected as quickly in clinical outcomes.

For example, a patient's ability to have less pain during the day, or to more easily complete activities of daily living, may not necessarily be reflected in their ability to walk significantly further during six minutes. However, if you were to ask that same patient which is more important to them, they would invariably say that it was the small improvement in their daily life that mattered most. The ability to more easily rise from a chair (as perceived by them), or to more easily make lunch, or socialize with friends and family are things that have a direct impact on a patient's quality of life than their ability to walk an additional 10 or 20 meters in 6 minutes.

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For other patients, who have spent years experiencing decline in their abilities, having their condition stabilize would be a benefit to their quality of life.

Every patient is different with different interests and challenges. We believe that evaluating a comprehensive range of Patient Reported Outcomes to measure the effectiveness of new treatments is critical to understanding the true potential benefits these treatments possess for patients. In a degenerative disease such as Pompe, every gain is momentous; even those that may not be reflected on a 6MWT or FVC test.

As we continue down a bright path filled with multiple potential new treatments and interventions, we strongly encourage all regulatory agencies around the world to look closely and critically at all outcome measures.

Additionally, we strongly believe that Patient Reported Outcomes should receive an equal value as clinical outcome measures. The patient is ultimately in the best position to report on the improvements. Stabilization, or declines that they experience in their daily lives. They are the ones who have the disease. They are the ones that live with its effects on a daily basis.