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Plenary Abstract

8 Years of Experience with Alglucosidase Alpha Treatment: Facts and Perspectives

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Pompe disease is a rare multisystemic disease with prominent muscle symptoms caused by the deficiency of acid alpha-glucosidase, which is involved in glycogen degradation. The clinical spectrum ranges from the severe and rapidly progressive infantile form (IOPD) with hypotonia, prominent cardiac and respiratory involvement, to late-onset forms (LOPD) characterised by milder and more heterogeneous phenotypes where the progressive muscle involvement is prominent. Enzyme replacement therapy (ERT), with recombinant human alglucosidase alpha, became available in 2006; in recent years, an increasing number of studies in treated patients have been published, focusing on efficacy, immune tolerance, possible biomarkers and appropriate outcome measures.

For many years, ERT efficacy in IOPD has been widely demonstrated and a number of treated infants are still surviving ventilator-free, standing or walking unaided. Some survivors have reached the age of 16 years. Although ERT has significantly prolonged lifespan and improved motor and respiratory performance, it has also revealed some new aspects of the disease. A new phenotype has emerged in IOPD patients, characterised by prominent bulbar and distal muscle involvement (i.e. facial muscle weakness, speech impairment, swallowing difficulties, distal muscle weakness). Different therapeutic approaches have also been tested in IOPD: it has been demonstrated that early ERT start, higher dosing (40 mg/kg) and more effective immunomodulation strategies in CRIM-negative patients could improve treatment efficacy.

As regards LOPD, ERT has a moderate effect compared to IOPD results. In 2012, a systematic literature review identified 21 studies with ERT efficacy/safety results and showed that at least two-thirds of patients had improved muscular and/or respiratory function. Other studies have later provided evidence that treatment responses seem to be more prominent during the first 2 years of treatment than thereafter, although in some of the largest cohorts studied, the therapeutic effect was maintained up to 36 months. Other authors outlined the characteristics of LOPD responders and they identified as favourable prognostic factors female gender, younger age, better clinical status and early ERT start. Nevertheless, the majority of studies lack long-term ERT results: very few of them report on patients treated over 36 months.

In conclusion, we likely need to reconsider guidelines to start therapy, maybe taking into consideration not only the clinical assessment but even relevant laboratory data (i.e. MRI, enzyme activity, morphological findings) that may help identify early when to start therapy.

In the meantime, new drugs are under development and have shown promising results, suggesting new therapeutic opportunities to improve the quality of life of patients.

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