M301. Treatment Related Effects of Anti-GAA Antibodies in Late Onset Pompe Disease

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Late onset Pompe disease (LOPD), a lysosomal storage disorder characterized by deficiency of the enzyme acid alpha-glucosidase (GAA), presents with diaphragm and skeletal muscle weakness with little or no cardiac involvement. The disease is progressive, and if left untreated, may result in significant motor disability and respiratory failure. Pompe disease is now considered treatable, with FDA-approved enzyme replacement therapy (ERT) Lumizyme®. Initial published data in LOPD showed improvement in forced vital capacity (FVC) and endurance, measured by 6-minute walk. However, subsequent publications have shown plateauing of this benefit and worsening of FVC may occur with time. In infantile cases of Pompe disease, development of IgG antibodies against GAA results in reduced treatment efficacy, especially in cross-reactive immunologic material negative (CRIM-) individuals. The role of these antibodies in neutralizing effects of treatment in LOPD is not clear since most individuals at this stage are CRIM+. We plan to present a retrospective analysis of our 9 patients who regularly follow with us, have been on uninterrupted enzyme replacement therapy and have been checked for these antibodies on a routine basis. We intend to correlate their treatment related adverse events, their treatment response, as measured by muscle function tests (manual muscle strength, 6-minute walk test), respiratory function trends (serial FVC, maximal inspiratory pressures (MIP) and sniff nasal inspiratory pressures (SNIP)), and quality of life data with the antibody titers. Furthermore we will correlate these data with their genotype results, and when available, pre-treatment GAA enzyme levels and urinary Hex4 results. Our hypothesis is that development of anti-GAA antibody titers has no effects on treatment efficacy in LOPD.

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