RECOMBINANT HUMAN ACID α -GLUCOSIDASE: MAJOR CLINICAL BENEFITS IN INFANTILE-ONSET POMPE DISEASE

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Background: Pompe disease is a progressive metabolic neuromuscular disorder resulting from deficiency of lysosomal acid α -glucosidase (GAA). Infantile-onset Pompe disease is characterized by cardiomyopathy, respiratory and skeletal muscle weakness, and early death. The safety and efficacy of recombinant human (rh) GAA were evaluated in 18 patients with rapidly progressing infantile-onset Pompe disease.

Methods: Patients were diagnosed at 6 months of age and younger and exhibited severe GAA deficiency and cardiomyopathy. Patients received IV infusions of rhGAA at 20 mg/kg (n = 9) or 40 mg/kg (n = 9) every other week. Analyses were performed 52 weeks after the last patient was randomized to treatment.

Results: All patients (100%) survived to 18 months of age. A Cox proportional hazards analysis demonstrated that treatment reduced the risk of death by 99%, reduced the risk of death or invasive ventilation by 92%, and reduced the risk of death or any type of ventilation by 88%, as compared to an untreated historical control group. There was no clear advantage of the 40-mg/kg dose with regard to efficacy. Eleven of the 18 patients experienced 164 infusion-associated reactions; all were mild or moderate in intensity.

Conclusions: Recombinant human acid α -glucosidase is safe and effective for treatment of infantile-onset Pompe disease. Eleven patients experienced adverse events related to treatment, but none discontinued. The young age at which these patients initiated therapy may have contributed to their improved response compared to previous trials with recombinant human acid α -glucosidase in which patients were older.

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Comment from Andrew G. Engel, MD, FAAN Associate Editor: This well-designed cooperative study of 18 patients vs untreated historical controls evaluated the safety and efficacy of replacement therapy over 52 weeks. The therapy reduced the risk of death or invasive ventilation by 92%.

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Recombinant human acid α -glucosidase: Major clinical benefits in infantile-onset Pompe disease

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