Highlights of the Late-Onset Treatment Study (LOTS)[1]

Introduction

New information regarding the use of enzyme replacement therapy (alglucosidase alfa) in children and adults with Pompe disease is now available following the completion of the Late-Onset Treatment Study (LOTS).[1] Earlier studies have shown that, if left untreated, the symptoms of Pompe disease, including problems with walking and breathing, gradually worsen over time.[2, 3] The purpose of this study was to assess the safety and efficacy (overall ability to produce a therapeutic effect) of alglucosidase alfa in children and adults with Pompe disease.

LOTS Study Background

With 90 patients participating in the study, LOTS was the largest clinical trial of children and adults with Pompe disease.

To participate in the study, patients

- Had to be at least 8 years of age
- Had to be able to walk on their own (use of walking aids allowed)
- Did not require a breathing tube at any time or need any type of non-invasive breathing assistance while awake

Patients received either alglucosidase alfa or placebo (a medication with no active ingredients) every 2 weeks for 18 months. The groups were then compared to see whether there were differences in walking distance and lung function between patients who received alglucosidase alfa and patients who received the placebo.

- Patients' ability to walk and functional capacity were assessed using the 6-minute walk test (6MWT); this test measures the distance that a patient is able to walk in 6 minutes
- Lung function was assessed by measuring the maximum amount of air that a patient can exhale from his/her lungs after taking a deep breath. This measurement is known as forced vital capacity (FVC)

Key Study Results

The LOTS study showed that alglucosidase alfa treatment improved walking distance and stabilized lung function in children and adults with Pompe disease. Patients on placebo demonstrated a deterioration of walking distance and lung function over the course of the study.

- In the 6MWT, the average distance walked increased by 25.1 meters in patients treated with alglucosidase alfa but decreased by 3.0 meters in those on placebo (Figure 1)

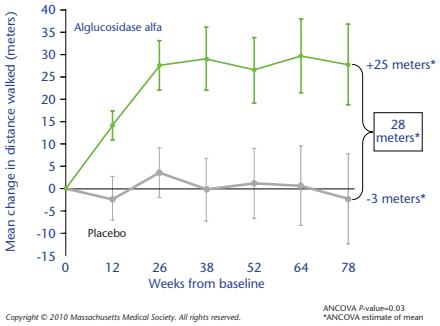

Figure 1

- Patients treated with alglucosidase alfa had an average increase in lung function (FVC) of 1.2%, whereas the placebo group had an average decrease in lung function of 2.2% (Figure 2)

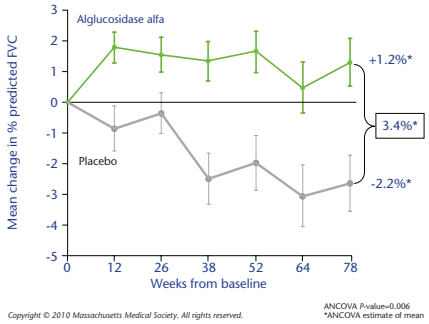

Figure 2

Alglucosidase alfa was generally well tolerated and side effects were similar to those observed with placebo. Most side effects were mild or moderate in severity and were not considered to be related to treatment. Anaphylactic, allergic, and infusion-associated reactions that involved urticaria, flushing, hyperhidrosis, chest discomfort, vomiting, and increased blood pressure occurred in 5% to 8% of the patients treated with alglucosidase alfa but were not reported in the placebo group.

Conclusions

- LOTS was the first large-scale study to demonstrate efficacy of alglucosidase alfa in children and adults with Pompe disease
- Treatment with alglucosidase alfa was associated with longer walking distance and stabilization of lung function over the 18-month duration of the study
- Patients receiving placebo experienced deterioration of muscle strength and function

Further Information

If you would like more information or have any questions, please contact your physician.

References

1. van der Ploeg AT, Clemens PR, Corzo D, et al. A randomized study of alglucosidase alfa in late-onset Pompe's disease. N Engl J Med. 2010;362(15):1396–1406.
2. Hagemans ML, Winkel LP, Van Doorn PA, et al. Clinical manifestation and natural course of late-onset Pompe's disease in 54 Dutch patients. Brain. 2005;128(Pt 3):671–677.
3. Wokke J, Escolar D, Pestronk A, et al. Clinical features of late-onset Pompe disease: a prospective cohort study. Muscle Nerve. 2008;38(4):1236–1245.

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