Switching therapy from alglucosidase alfa to avalglucosidase alfa in patients with late-onset Pompe disease (LOPD): Longitudinal assessment of respiratory function from the COMET trial

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INTRODUCTION

• Alglucosidase alfa is a recombinant human α-glucosidase (GAA) enzyme replacement therapy with increased mannose-phosphate content to enhance cellular uptake compared with alglucosidase alfa.

• Avalglucosidase alfa has received marketing authorization in several countries for Pompe disease.

• Alglucosidase alfa was approved in the United States in August 2021 for patients with late-onset Pompe Disease (LOPD) ≥1 year of age, and in the European Union in June 2021 for the treatment of patients with Pompe disease.1

• Approval for PAP was based on the efficacy and safety results of the pivotal Phase 3 COMET trial (NCT02782741).2

• During the 48-week double-blind treatment period, treatment with alglucosidase alfa resulted in greater improvements in forced vital capacity (FVC), 6-minute walk test (6MWT), and other outcomes, and showed a more favorable safety profile compared with alglucosidase alfa in treatment-naïve participants with LOPD.3

OBJECTIVE

The objective of this analysis was to examine respiratory function outcomes in patients who switched from alglucosidase alfa to avalglucosidase alfa at Week 49, based on initial treatment response, in COMET.

METHODS

Study design and participants

• COMET is an ongoing Phase 3, multicenter, multinational, randomized, double-blind trial comparing efficacy and safety of alglucosidase alfa and avalglucosidase alfa.

• The study design is shown in Figure 1.

• Patients aged ≥3 years with a diagnosis of LOPD confirmed by GAA enzyme activity, with at least 1 year of age, and in the PAP, of these 44 were enrolled in the ETP and switched to avalglucosidase alfa.

• The present study focuses on respiratory outcomes in patients who were treated with alglucosidase alfa in the PAP and then switched to avalglucosidase alfa.

RESULTS

Study participants

Overall, 49 patients with LOPD were randomized to receive alglucosidase alfa in the PAP of these 44 were enrolled in the ETP and switched to avalglucosidase alfa and maintained this response after the switch to avalglucosidase alfa (Figure 2).

• Baseline to Week 49 estimated slope: +0.15%/year (SE: 0.73 ± 0.128%/year; p<0.001).

• Week 49 to Week 145 estimated slope: ± 0.14 ± 0.04%/year; p=0.7894.

• Statistical analysis

• Patients who received alglucosidase alfa in the PAP and with at least one observation available at Week 49 were included in the analysis.

• One value at Week 49 was excluded because the change between visits was physiologically implausible.

• The modeling assumed separate pre- and post-switch slopes for the time variable, with random intercept and slope at subject level.

• The trajectories of FVC during the study were assessed according to observed treatment in the PAP.

DISCUSSION

• Our results show that a switch to avalglucosidase alfa stabilizes respiratory function in patients with LOPD, regardless of their response to alglucosidase alfa.

• In the subgroup of patients who on average showed improvement during alglucosidase alfa treatment, respiratory function was maintained following the switch.

• In the subgroup of patients who declined on average during alglucosidase alfa treatment, respiratory function was stabilized following the switch.

• These data suggest there are clinical benefits over 2 years following a switch of therapy to avalglucosidase alfa in patients with LOPD, which can inform patient healthcare provider decisions regarding treatment options for LOPD.

REFERENCES


Table 1. Baseline characteristics of patients treated with alglucosidase alfa in the PAP who switched to avalglucosidase alfa in the ETP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change from baseline to Week 49</th>
<th>ETP slope: +0.15%/year</th>
<th>Overall (N=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>White (≥12)</td>
<td>50.9 (13.5)</td>
<td>48.3 (14.2)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Black or African American</td>
<td>50.8 (24.6)</td>
<td>45.0 (14.7)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Male, n (%</td>
<td>75 (50.8)</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Race, n (%)</td>
<td>7 (50.8)</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Time from disease diagnosis, years, median (range)</td>
<td>1.3 (0-7)</td>
<td>0.7 (0-16)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>FVC percent predicted (FVCpp) in the upright position was calculated as a function of</td>
<td>Mean (SD)</td>
<td>54.6 (2.3)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Male, n (%</td>
<td>50 (46.4)</td>
<td>29 (96.7)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Age, years</td>
<td>52.0 (26.7)</td>
<td>46.5 (19–77)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Height, cm</td>
<td>175.0 (10.0–180.0)</td>
<td>175.0 (10.0–180.0)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>First 48–52 weeks</td>
<td>2.3 (0.7–27)</td>
<td>0.7 (0–18)</td>
</tr>
<tr>
<td>White (≥12)</td>
<td>Change from baseline to Week 49</td>
<td>1.3 (0–29)</td>
<td>9.0 (0–30)</td>
</tr>
</tbody>
</table>

Baseline FVC is reported for this analysis. Table 1. Baseline characteristics of patients treated with alglucosidase alfa in the PAP who switched to avalglucosidase alfa in the ETP

• In the 48-week primary analysis period (PAP), participants were randomized 1:1 to receive 20 mg/kg intravenous alglucosidase alfa or 25 mg/kg intravenous alglucosidase alfa every 2 weeks.

• Thereafter, in the open-label extended treatment period (ETP), participants who received alglucosidase alfa in the PAP continued this treatment and participants who switched from alglucosidase alfa in the PAP to avalglucosidase alfa.

• Two time periods were analyzed: the first from baseline to Week 49 (PAP) and the second from Week 49 to Week 145 (ETP).

• Data cut-off date was 11 March 2022.

FUNDING

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ACKNOWLEDGMENTS

• Avalglucosidase alfa was administered by this author, under the direction of the author, and provided by Amy Amoroso, MS, of Abbott/Pediatrics, and funded by Sanofi in accordance with Abbott/Pediatrics Practice Guidelines.

DISCLOSURES