Home-infusion experience in patients with Pompe disease receiving avalglucosidase alfa during three clinical trials (COMET, NEO-EXT, and Mini-COMET)

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INTRODUCTION

• Avalglucosidase alfa is a recombinant human acid alpha-glucosidase enzyme replacement therapy with increased mannose-6-phosphate content for improved cellular uptake compared with alglucosidase alfa
• Avalglucosidase alfa is approved in the United States for patients with late-onset Pompe disease (LOPD) aged ≥1 year and in Japan for all patients with Pompe disease

METHODS

• During three clinical trials (COMET [NCT02782741], NEO-EXT [NCT02032524], Mini-COMET [NCT03019406]), * 16 patients with Pompe disease received avalglucosidase alfa via home infusion under healthcare professional supervision
• Home infusion was possible if no infusion-associated reactions (IAR) of moderate or severe intensity had occurred during the 12 months prior to home infusion implementation

*COMET: Study to Compare the Efficacy and Safety of Enzyme Replacement Therapies Avalglucosidase Alfa and Alglucosidase Alfa Administered Every Other Week in Patients With Late-onset Pompe Disease Who Have Not Been Previously Treated for Pompe Disease. NEO-EXT: NeogAAG Extension Study. Mini-COMET: A Study to Assess Safety and Efficacy of Avalglucosidase Alfa Administered Every Other Week in Pediatric Patients With Infantile-onset Pompe Disease Previously Treated With Alglucosidase Alfa
RESULTS

• As of September 2, 2021, 16 patients received a total of 279 home infusions (Table)
  ▪ 12 patients with late-onset Pompe disease (LOPD) in COMET received between 2 and 36 infusions
  ▪ 2 patients with LOPD in NEO-EXT received 13 and 32 infusions, respectively
  ▪ 2 patients with infantile-onset Pompe disease (IOPD) in Mini-COMET received 6 and 8 infusions, respectively

• History of IAR prior to the home setting: 4 patients had experienced IARs in the period ≥12 months prior to home infusion, but not in the period <12 months prior to home infusion

Table: Distribution of home infusions and reported adverse events

<table>
<thead>
<tr>
<th>Patient</th>
<th>Study</th>
<th>Number of home infusions</th>
<th>IARs during home infusion</th>
<th>Non-IAR AEs on day of home infusion</th>
<th>County</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOPD-1</td>
<td>NEO-EXT</td>
<td>13</td>
<td>No</td>
<td>None</td>
<td>Netherlands</td>
</tr>
<tr>
<td>LOPD-2</td>
<td>NEO-EXT</td>
<td>32</td>
<td>No</td>
<td>1 (unrelated, non-serious)</td>
<td>France</td>
</tr>
<tr>
<td>LOPD-3</td>
<td>COMET</td>
<td>6</td>
<td>No</td>
<td>None</td>
<td>France</td>
</tr>
<tr>
<td>LOPD-4</td>
<td>COMET</td>
<td>35</td>
<td>No</td>
<td>None</td>
<td>France</td>
</tr>
<tr>
<td>LOPD-5</td>
<td>COMET</td>
<td>34</td>
<td>No</td>
<td>None</td>
<td>France</td>
</tr>
<tr>
<td>LOPD-6</td>
<td>COMET</td>
<td>19</td>
<td>No</td>
<td>None</td>
<td>Netherlands</td>
</tr>
<tr>
<td>LOPD-7</td>
<td>COMET</td>
<td>10</td>
<td>No</td>
<td>None</td>
<td>Netherlands</td>
</tr>
<tr>
<td>LOPD-8</td>
<td>COMET</td>
<td>11</td>
<td>No</td>
<td>2 (unrelated, non-serious)</td>
<td>Netherlands</td>
</tr>
<tr>
<td>LOPD-9</td>
<td>COMET</td>
<td>19</td>
<td>Yes</td>
<td>None</td>
<td>Spain</td>
</tr>
<tr>
<td>LOPD-10</td>
<td>COMET</td>
<td>17</td>
<td>No</td>
<td>None</td>
<td>Turkey</td>
</tr>
<tr>
<td>LOPD-11</td>
<td>COMET</td>
<td>24</td>
<td>No</td>
<td>None</td>
<td>Turkey</td>
</tr>
<tr>
<td>LOPD-12</td>
<td>COMET</td>
<td>36</td>
<td>No</td>
<td>4 (unrelated, non-serious)</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>LOPD-13</td>
<td>COMET</td>
<td>7</td>
<td>No</td>
<td>1 (unrelated, non-serious)</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>LOPD-14</td>
<td>COMET</td>
<td>2</td>
<td>No</td>
<td>2 (unrelated, non-serious)</td>
<td>United States</td>
</tr>
<tr>
<td>IOPD-1</td>
<td>Mini-COMET</td>
<td>8</td>
<td>No</td>
<td>None</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>IOPD-2</td>
<td>Mini-COMET</td>
<td>6</td>
<td>No</td>
<td>None</td>
<td>United States</td>
</tr>
</tbody>
</table>

AE, adverse event; IAR, infusion-associated reaction; IOPD, infantile-onset Pompe disease; LOPD late-onset Pompe disease

Safety events

• Safety events occurred in 6 patients

Infusion-associated reactions (IARs)

• COMET: 1 patient receiving avalglucosidase alfa in the home setting experienced an IAR
  ▪ 32-year-old female who began treatment with avalglucosidase alfa in March 2019, started to receive home infusions in April 2020 (1st home infusion given at Week 59 in the open-label period of COMET)
  ▪ During the 1st home infusion and 2 hours after the start of infusion, the patient had eyelid edema and flushing. Both events were assessed as non-serious adverse events of special interest and IARs of mild intensity
  ▪ Therapy with avalglucosidase alfa was interrupted and the patient received methylprednisolone and dexchlorpheniramine as corrective treatments
  ▪ Patient recovered from both events the same day
  ▪ After this dose interruption, the patient returned to the study site to receive a further 4 infusions, all with no IAR recurrence (12 were missed due to COVID-19 restrictions). She then returned to the home-setting and received 18 home infusions before the data cut-off, with no further IARs observed
RESULTS (continued)

Non-treatment related, non-serious adverse events (AEs)

- **NEO-EXT**: 1 patient had 1 non-treatment related, non-serious AE
  - Patient had a medical history of prostate adenoma and experienced an event of urinary retention, which started on the day of a home infusion. No treatment was given and the event resolved 11 days after starting

- **COMET**: 4 patients had a total of 9 non-treatment related, non-serious AEs
  - 1 patient had 4 AEs:
    - 1 episode of a red, sore, inflamed right eye, starting on a day of home infusion. No corrective treatment was given and the event resolved 2 days after starting
    - 1 episode of nasopharyngitis and 1 of headache, both starting on the same day of a home infusion. Corrective treatment with paracetamol was given for both events, which resolved 4 days after starting
    - 1 episode of headache, starting on the day of a home infusion. Corrective treatment with ibuprofen was given and the event resolved the same day
  - 1 patient had 2 AEs:
    - 2 episodes of headache, each starting on 2 home infusion days. On both occasions, corrective treatment with paracetamol was given and both events resolved the next day
  - 1 patient had 1 AE:
    - 1 episode of vaginal discharge, starting on the day of a home infusion. No corrective treatment was given and event is reported as ongoing
  - 1 patient had 2 AEs:
    - 1 episode of injection site extravasation, starting on the day of a home infusion. No corrective treatment was given and the infusion was temporarily stopped leading to the end of the event. The event recurred after the infusion was resumed and a second episode of injection site extravasation was reported. The infusion was stopped without resumption, leading to the end of the event

- **Mini-COMET**: No AEs reported during the day of infusion

- No medication error occurred in the setting of home infusion

**CONCLUSIONS**

- Safety events occurred in 6 out of 16 patients, for 5 of the patients these events were all considered non-serious and unrelated to treatment
- Out of a total 279 home infusions, 1 IAR event was experienced by 1 patient
  - After the event, the patient continued infusions in the clinical setting for 4 visits (12 missed due to COVID-19 restrictions) without IAR recurrence, thereafter, the patient received 18 home infusions before data cut-off, again without IAR recurrence
- Overall, no unmanageable safety concerns and no medication errors were observed during home infusion of avalglucosidase alfa across the clinical trials in LOPD and IOPD
- These preliminary data suggest that avalglucosidase alfa can be safely administered at home, similar to the experience seen with alglucosidase alfa

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