Impact of elosulfase alfa treatment on patient-reported outcomes in Morquio A Syndrome: results from the first year of an English managed access agreement

Background

- Morquio A syndrome is an ultra-rare, inherited, multi-systemic disease which, if untreated, results in impaired functioning, mobility, and quality of life (QoL), and early death.
- Enzyme replacement therapy with elosulfase alfa is the only approved treatment.
- In England, access to elosulfase alfa is granted to all patients on a conditional basis through a managed access agreement (MAA) (Figure 1).
- Patients must fulfill four out of five response criteria to continue receiving treatment; one of the five criteria covers patient-reported outcomes (PROs).
- PROs support continuing treatment if stabilization or improvement are reported in two of the following three domains: QoL, depression, and pain.
- PROs for those patients completing the first year of the program are reported herein.

Results

- As of March 2017, 25 children and 10 adults had completed one year of treatment under the MAA.
- Ten patients entered the program treatment-naïve, the remainder came from clinical trials (mean years on treatment=6.08 [SD 1.36], n=25).
- The assessment of PROs versus the agreed clinically meaningful changes are summarised in Figure 2.

- Overall, PROs provided evidence supporting continued treatment for 33 of 35 patients.
- Results for the individual measures are presented below, results for patients who took part in the MOR 002 study are presented separately as these patients have received elosulfase alfa for the longest period prior to the start of the MAA.
- Mean QoL scores for the caregiver burden domain of the MPS HAQ are shown in Figure 3.
- MPS HAQ mobility and self care domains were also collected but are not part of the MAA criteria. Changes in mean scores are shown in Figure 3.

Methods

- All patients completed PRO assessments on entry to the MAA, and at 4, 8 and 12 months (Table 1).
- PRO questionnaires were completed by either the patient or their parent/carer depending on the age of the patient.
- Patients or their parent/carer completed the questionnaires either over the telephone or during a face to face interview with a patient organisation representative.
- QoL was measured using the EQ-5D-5L tool and the caregiver assessment domain of the MPS Health Assessment Questionnaire (MPS HAQ).
- The Beck Depression Inventory (BDI) is only applicable for patients aged 13 years or over.
- Pain was measured using the Adolescent and Paediatric Pain Tool (APPT) for patients under 18 years of age or the Brief Pain Inventory (BPI) for patients aged 18 years and over.
- Thresholds for clinically meaningful changes versus inherent assessment variability were established post-hoc by the MAA stakeholders (Table 2).

Conclusions

- Assessment of multiple domains was a critical component of the program due to patient heterogeneity and the importance of individualized patient management in Morquio A syndrome.
- BDI is a new tool for use in this patient cohort and the exact meaning of changes in this measure will have to be further explored in the future. The current changes seen in the naïve patients may be linked to the initial improvement in fatigue which is widely reported and to which patients may adapt over time.
- Based on PROs, the majority of patients met or exceeded the necessary level of treatment benefit established by the MAA stakeholders.

Acknowledgments

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- This research was funded by BioMarin Europe Ltd. under the requirements of the MAA.

References


Table 1. PRO assessment schedule

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline</th>
<th>Month 4</th>
<th>Month 5</th>
<th>Month 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPS HAQ</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D-5L</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPI/APPT</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BDI</td>
<td>X</td>
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</table>

*Day before and day after infusion

Table 2. Thresholds for PRO measurements

<table>
<thead>
<tr>
<th>MPS HAQ Caregiver Domain</th>
<th>EQ-5D-5L</th>
<th>APPT / BPI</th>
<th>BDI</th>
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</thead>
<tbody>
<tr>
<td>Clinically meaningful change</td>
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<td>Change in point score of 13 or more</td>
<td>Change in point score of 13 or more</td>
</tr>
<tr>
<td>Change in mean score</td>
<td>0.2 or more*</td>
<td>0.2 or more</td>
<td>0.2 or more*</td>
</tr>
</tbody>
</table>

*The EQ-5D-5L threshold for the MAA is still under review, a 0.2 change in value was used for illustration.

Figure 1. The Managed Access Agreement criteria*

Figure 2. Patient reported outcomes at one year

Figure 3. Change in MPS HAQ over 1 year by patient origin

Figure 4. Change in EQ-5D-5L, over 1 year by patient origin

Figure 5. Change in pain severity over 1 year by patient origin

Figure 6. Mean change in BDI over 1 year by patient origin

SD: standard deviation; Tx: treatment

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References