Sustained reductions in red blood cell transfusion burden and events in β-thalassemia with luspatercept: longitudinal results of the BELIEVE trial


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Presenting author disclosures

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Introduction

- **β-thalassemia** is a genetic blood disorder characterized by ineffective erythropoiesis and anemia\(^1\)
  - RBC transfusions, a key supportive treatment, may be associated with life-threatening complications including iron overload\(^2\)

- Thus, there is a clinical need to reduce transfusions and iron burden in patients with anemia due to **β-thalassemia**

- Luspatercept, a first-in-class erythroid maturation agent, is approved by the US Food and Drug Administration for the treatment of anemia in adult patients with **β-thalassemia** requiring regular RBC transfusions\(^3-6\)

- This analysis presents a longitudinal analysis of the benefits of luspatercept on RBC transfusion burden in the phase 3 BELIEVE trial (NCT02604433)\(^7\)

\(^a\)β-thalassemia or Hb E/β-thalassemia (compound β-thalassemia with mutation and/or multiplication of α-globin genes was allowed). \(^b\)Patients could receive RBC transfusions to maintain their baseline Hb level and ICT. \(^c\)The trial is fully enrolled and patients continue to receive treatment or follow-up.

**Figure 1. BELIEVE study trial design**

Patients with **β-thalassemia** \(\geq 18\) years of age, requiring regular RBC transfusions (defined as: 6-20 RBC units in the 24 weeks prior to randomization with no > 35-day transfusion-free period during that time) \((N = 336)\)

**Randomized 2:1**
- **Luspatercept**
  - 1 mg/kg s.c. every 21 days + BSC
  - \((n = 224)\)
- **Placebo**
  - s.c. every 21 days + BSC
  - \((n = 112)\)

**Double-blind period (48 weeks)**
- Crossover from placebo to luspatercept permitted \((n = 92)\)

**Current study status**
- Open-label (up to 5 years)
- Post-treatment follow-up (3 years)

Results

Table 1. Patient baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Luspatercept (N = 224)</th>
<th>Placebo (N = 112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>30 (18-66)</td>
<td>30 (18-59)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>132 (58.9)</td>
<td>63 (56.3)</td>
</tr>
<tr>
<td>Hb (24 weeks),a median (range), g/dL</td>
<td>9.31 (4.5-11.4)</td>
<td>9.15 (5.8-11.7)</td>
</tr>
<tr>
<td>RBC transfusion burden, median (range), units/12 weeks</td>
<td>6.1 (3-14)</td>
<td>6.3 (3-12)</td>
</tr>
<tr>
<td>RBC transfusion burden, median (range), units/24 weeks</td>
<td>14 (6-24)</td>
<td>15 (6-26)</td>
</tr>
<tr>
<td>Splenectomy, n (%)</td>
<td>129 (57.6)</td>
<td>65 (58.0)</td>
</tr>
<tr>
<td>Serum ferritin, mean (SD), μg/L</td>
<td>2,097 (1,757)</td>
<td>1,845 (1,669)</td>
</tr>
<tr>
<td>LIC, mean (SD), mg/g dw</td>
<td>12.0 (14.8)</td>
<td>10.1 (11.5)</td>
</tr>
<tr>
<td>&gt; 7 mg/g dw, n (%)</td>
<td>103 (46.0)</td>
<td>45 (40.2)</td>
</tr>
<tr>
<td>Myocardial iron by T2* MRI, mean (SD), ms</td>
<td>33.5 (16.2)</td>
<td>34.8 (10.7)</td>
</tr>
</tbody>
</table>

aDefined as the mean of all documented pre-transfusion Hb values during the 24 weeks prior to first dose for each patient.
dw, dry weight; LIC, liver iron concentration; SD, standard deviation; T2* MRI, T2-weighted magnetic resonance imaging.
Results (cont.)

Figure 2. Mean change in RBC units transfused by primary endpoint responders during Weeks 1-24 and Weeks 25-48

Data cutoff: July 1, 2019.

*Defined as patients achieving ≥ 33% reduction in RBC transfusions during Weeks 13-24, with a reduction of ≥ 2 RBC units, versus baseline.

*Indicates a statistically significant difference between luspatercept (overall, responder, non-responder) with placebo using ANCOVA. ANCOVA, analysis of covariance; CI, confidence interval; LSM, least squares mean.
Results (cont.)

Figure 3. Mean change in RBC transfusion visits by primary endpoint responders during Weeks 1-24 and Weeks 25-48

Data cutoff: July 1, 2019.
*Defined as patients achieving ≥ 33% reduction in RBC TB during Weeks 13-24, with a reduction of ≥ 2 RBC units, versus baseline.
*Indicates a statistically significant difference between luspatercept (overall, responder, non-responder) with placebo using ANCOVA.
Results (cont.)

Table 2. Sustained reductions in RBC transfusions and transfusion visits in all patients randomized to the luspatercept arm

<table>
<thead>
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<tbody>
<tr>
<td>RBC units transfused/24 weeks</td>
<td></td>
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<tr>
<td>Mean (SD)</td>
<td>14.53 (3.6)</td>
<td>12.27 (4.4)</td>
<td>11.85 (4.7)</td>
<td>11.71 (4.5)</td>
<td>11.38 (4.6)</td>
<td>10.93 (4.6)</td>
<td>11.27 (4.1)</td>
</tr>
<tr>
<td>Mean change from baseline (SD)</td>
<td>-2.20 (2.8)</td>
<td>-2.53 (3.3)</td>
<td>-2.67 (3.1)</td>
<td>-2.83 (3.2)</td>
<td>-3.36 (3.0)</td>
<td>-3.36 (3.0)</td>
<td>-4.16 (3.4)</td>
</tr>
<tr>
<td>P valuea</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.092</td>
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<tr>
<td>Number of transfusion visits</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Mean (SD)</td>
<td>7.65 (1.9)</td>
<td>7.13 (2.0)</td>
<td>7.01 (2.0)</td>
<td>7.02 (2.0)</td>
<td>7.01 (2.1)</td>
<td>6.88 (2.3)</td>
<td>7.25 (0.5)</td>
</tr>
<tr>
<td>Mean change from baseline (SD)</td>
<td>-0.49 (1.9)</td>
<td>-0.54 (2.0)</td>
<td>-0.53 (2.0)</td>
<td>-0.40 (2.2)</td>
<td>-0.54 (2.2)</td>
<td>0.025</td>
<td>-0.50 (1.3)</td>
</tr>
<tr>
<td>P valuea</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>0.014</td>
<td>0.495</td>
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</tbody>
</table>

- Sustained reductions in RBC units transfused and transfusion visits persisted for over 2 years

Data cutoff: July 1, 2019.

*ANCOVA was used to compare differences between luspatercept (overall) at baseline versus post-baseline.
Luspatercept was associated with sustained reductions in RBC transfusion units in responders and non-responders during the first 48 weeks versus placebo.

Patients receiving luspatercept continued to experience reductions in RBC transfusion burden and transfusion visits over 2 years.

The BEYOND study is an ongoing phase 2 trial to determine the efficacy and safety of luspatercept in patients with non-transfusion-dependent β-thalassemia (NCT03342404).

A phase 2a study is evaluating the safety and pharmacokinetics of luspatercept in pediatric patients with transfusion-dependent β-thalassemia (NCT04143724).
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