Introduction

- Lower-risk myelodysplastic syndromes (LR-MDS) are characterized by ineffective erythropoiesis, leading to anemia, red blood cell (RBC) transfusion dependence, and reduced quality of life.
- There is a need for effective treatments for anemia in transfusion-dependent patients with LR-MDS who require regular RBC transfusions.

Luspatercept is a first-in-class erythroid maturation agent that binds to and blocks transforming growth factor β (TGF-β) signaling and enhances late-stage erythropoiesis.
- Luspatercept is indicated for the treatment of anemia in adult patients with LR-MDS with ring sideroblasts (RS) who require regular RBC transfusions.

Methods

Study design

- Patients were randomized at 65 sites between March 2016 and June 2017.
- Eligible patients were aged 18 years and had active disease due to transfusion-dependent anemia; no history of serious bleeding complications, intolerance of, or inability to respond to (serum erythropoietin > 200 U/L) erythropoiesis-stimulating agents, and required RBC transfusion support.
- Patients were randomized 2:1 to receive luspatercept (starting dose 1.0 mg/kg, with titration to a maintenance dose of 0.5 mg/kg) or placebo.

Study endpoints

- Primary endpoint: RBC transfusion burden.
- Key secondary endpoints: erythropoiesis, RS; were refractory to, intolerant of, or unlikely to respond to (serum erythropoietin > 200 U/L) erythropoiesis-stimulating agents, and required RBC transfusion support.

Additional endpoints

- Reduction in RBC units transfused from baseline
- Achievement of modified hematopoietic improvement-erythroid (HI-E) (per International Working Group [IWG] 2006 criteria)
- Defined as a reduction of ≥ 4 units of RBCs from baseline, sustained for 8 weeks (for patients with baseline RBC transfusion burden of ≥ 4 units/8 weeks) or ≥ a hematocrit increase of ≥ 1.5 g/dL from baseline, sustained for 8 weeks (for patients with baseline RBC transfusion burden of ≥ 1.5 g/dL).
- Longest duration of primary response

Data and change in parameters

- Baseline RBC transfusion burden: ≥ 4 units/8 weeks
- Baseline transfusion burden: ≥ 1.5 g/dL
- Baseline serum ferritin: ≥ 500 μg/L
- Baseline IPSS-R, n (%)a
- Low risk: 148 (96.7%)
- Intermediate risk: 70 (92.1%)
- Very low risk: 5 (65.8%)

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luspatercept</td>
<td>9.7 (2.6)</td>
<td>9.2 (2.7)</td>
</tr>
<tr>
<td>Placebo</td>
<td>11.0 (3.4)</td>
<td>10.4 (3.5)</td>
</tr>
</tbody>
</table>

Results

- 229 patients were randomized; 153 to receive luspatercept and 76 to receive placebo.
- The median (range) transfusion burden at baseline was 5.5 (1.2–25.9) RBC units over 8 weeks in the luspatercept and placebo arms.

Objective

- To evaluate long-term transfusion burden reduction in patients treated with luspatercept in the MEDALIST trial.

Conclusions

- Luspatercept produced clinically meaningful and durable reductions in RBC transfusions in patients with LR-MDS with RS.
- Luspatercept also resulted in statistically significant reductions in serum ferritin in patients with LR-MDS with RS.

Acknowledgments

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References


Figure 2. Mean change from baseline in RBC units transfused

Table 3. Mean change from baseline in serum ferritin

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (SD)</th>
</tr>
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<tbody>
<tr>
<td>Luspatercept</td>
<td>−7.6 (5–10)</td>
</tr>
<tr>
<td>Placebo</td>
<td>6.8 (5–9)</td>
</tr>
</tbody>
</table>

Figure 3. Mean number of transfusion visits in Weeks 1-24