**Luspatercept Increases Hemoglobin and Reduces Transfusion Burden in Patients with Low-Intermediate Risk Myelodysplastic Syndromes (MDS): Long-Term Results from Phase 2 PACE-MDS Study**

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**Introduction**

Anemia, a hallmark of MDS, is a significant clinical challenge to treat, particularly after failure of ESAs. Defects in maturation of erythroid precursors (ineffective erythropoiesis) lead to erythropoietin hyperplasia and anemia. Ineffective erythropoiesis leading to erythropoietin hyperplasia and RBC apoptosis in the bone marrow is associated with increased Smad2/3 signaling.1,2

Luspatercept, a modified activin receptor type IIB (ActRIIB) fusion protein, acts as a ligand trap for GDF-11 and other TGF-β family ligands to suppress Smad2/3 signaling, promotes late-stage RBC maturation, and increases hemoglobin levels in MDS mice and healthy human volunteers.3-4

**Study Design**

A phase 2, multicenter, open-label, 3-month dose-escalation study in adults with lower-risk MDS followed by a 5-year extension study (ESA refractory/inefficacious or ESA ≤ 0.75 mg/kg; no prior ESA; no current ESA, G-CSF, GM-CSF)

**Efficacy endpoints (extension study)**

- **LTB: Low transfusion burden (≤200 U in 8 wk)**
- **WGS Hb: Hb increase ≥ 1.5 g/dL for all values over 8 weeks**
- **HTB: High transfusion burden (≥ 4 U in 8 wk)**

**Other efficacy endpoints: RBC transfusion independence (TI), time to/duration of Hb ≥ 8 g/dL**

**Safety**

- **Majority of adverse events (AEs) were grades 1 or 2**
- **Four possibly/probably related grade 3 serious AE of 28 Nov 2016: blast cell count increase, myelagia, worsening of general condition, progression to AML**

**Baseline Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Study N=73</th>
<th>Extension Study N=42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, median (range)</td>
<td>57 (39-78)</td>
<td>54 (37-72)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>44 (60)</td>
<td>25 (60)</td>
</tr>
<tr>
<td>Time since diagnosis, yr, median (range)</td>
<td>3.1 (1-10)</td>
<td>2.0 (1-9)</td>
</tr>
<tr>
<td>Prior ESA treatment, n (%)</td>
<td>10 (14)</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Prior ESA treatment, n (%)</td>
<td>13 (19)</td>
<td>8 (19)</td>
</tr>
<tr>
<td>Baseline ESA, n (%)</td>
<td>12 (17)</td>
<td>8 (19)</td>
</tr>
<tr>
<td>Baseline Hb, g/dL, median (range)</td>
<td>9.8 (6.4-10.1)</td>
<td>8.6 (6.4-10.1)</td>
</tr>
</tbody>
</table>

**Erythroid Response**

**Summary/Conclusions**

- Lower-risk MDS patients treated with luspatercept demonstrated robust and sustained increases in hemoglobin and decreases in transfusion burden (per IWG HI-E) and a high rate of RBC transfusion independence

- In patients with ESA levels ≤200, response rates were similar in both RS+ and RS- patients

- In patients with ESA levels ≤200 to ≤500, response rates were higher in RS+ compared to RS- patients

- These data support the initiation of Phase 3 studies of luspatercept in lower-risk MDS (NCT 02631070)

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**Acknowledgments/References**

**German MDS Study Group (D-MDS)**


References:
4. Attie, K et al. Hematologica 2014;99:766

**Disclosure**: