Fewer red blood cell transfusion units and visits across baseline transfusion burden levels in patients with ß-thalassemia treated with luspatercept in the phase 3 BELIEVE trial

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Introduction

- ß-thalassemia is a genetic blood disorder marked by ineffective erythropoiesis and anemia[1]
  - Although red blood cell (RBC) transfusions are a key supportive treatment, they may be associated with life-threatening complications, including iron overload[2]
- The first-in-class erythroid maturation agent, luspatercept, enhances late-stage erythropoiesis[3]
- Luspatercept was shown to be effective in reducing RBC transfusion burden (TB) in adult patients with ß-thalassemia requiring regular RBC transfusions in the phase 3, double-blind, randomized, placebo-controlled BELIEVE trial (NCT02604433)[4]
- The effectiveness of luspatercept in reducing RBC TB based on pretreatment burden levels remains unknown

Objective

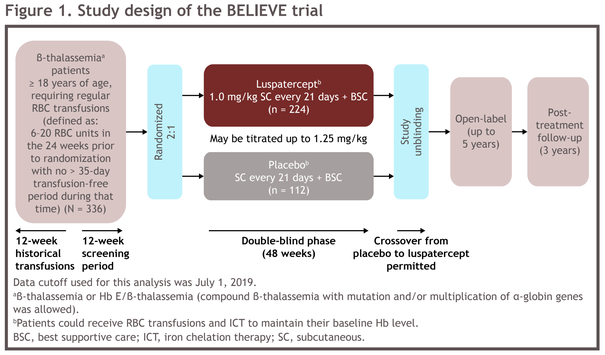
- To evaluate the mean cumulative number of RBC transfusion units and visits among patients with low, medium, or high baseline RBC TB levels in the BELIEVE trial

Methods

Study design

- The BELIEVE trial study design is shown in **Figure 1**

Figure 1. Study design of the BELIEVE trial



Data cutoff used for this analysis was July 1, 2019.
[a]ß-thalassemia or Hb E/ß-thalassemia (compound ß-thalassemia with mutation and/or multiplication of α-globin genes was allowed).
[b]Patients could receive RBC transfusions and ICT to maintain their baseline Hb level.
BSC, best supportive care; ICT, iron chelation therapy; SC, subcutaneous.

- Patients with ß-thalassemia were randomized 2:1 to luspatercept 1.0 mg/kg or placebo every 3 weeks for 48 weeks during the double-blind phase
- The primary endpoint was ≥ 33% reduction from baseline in RBC TB during weeks 13-24 (≥ 2 RBC units)
- After study unblinding, patients randomized to placebo were eligible to cross over to receive luspatercept in an open-label phase

Luspatercept responders

- In this analysis, luspatercept responders were defined as patients who achieved a reduction in RBC TB of ≥ 33% from baseline during weeks 13-24 (≥ 2 RBC units)

RBC TB, units, and visits

- Baseline low, medium, and high TB was defined as receipt of ≤ 10, > 10 to ≤ 15, and > 15 RBC units/24 weeks, respectively
- RBC transfusion units and visits were assessed among luspatercept responders and placebo-treated patients up to week 48 and in luspatercept responders and non-responders up to week 120, excluding patients who crossed over from placebo
- Mean cumulative number of RBC transfusion units and visits were estimated using the Nelson-Aalen nonparametric estimators with robust variance estimates
- Data cutoff for this analysis was July 1, 2019

Results

Patients

- The intent-to-treat population comprised 336 patients; 224 patients were randomized to luspatercept and 112 to placebo
  - Median age was 30 years in both groups
  - In the luspatercept group, 132 (58.9%) patients were female versus 63 (56.3%) in the placebo group
  - Both groups had similar proportions of patients from North America and Europe, Asia-Pacific, and the Middle East and North Africa
- Of the 224 patients randomized to luspatercept, 47 (21.0%) achieved an RBC transfusion reduction of ≥ 33% from baseline during weeks 13-24 (≥ 2 RBC units) and were defined as luspatercept responders for this analysis
  - The 177 patients who did not achieve an RBC transfusion reduction of ≥ 33% during weeks 13-24 were defined as luspatercept non-responders
- The number of patients with low, medium, and high TB at baseline is shown in **Table 1**

Table 1. Patients with low, medium, and high baseline TB

Baseline TB, n	Luspatercept responders (n = 47)	Luspatercept non-responders (n = 177)	Placebo (n = 122)
Low	9	22	14
Medium	22	70	40
High	16	71	48

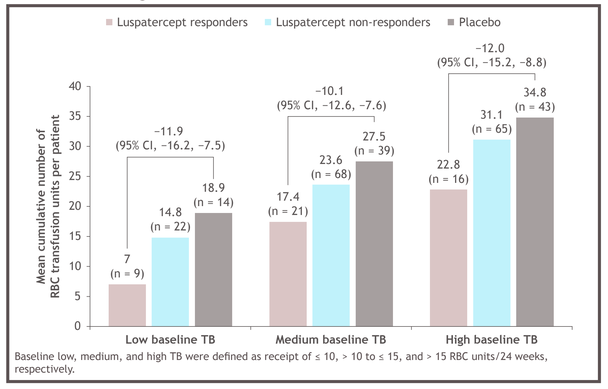
RBC transfusion units

- Overall, luspatercept responders had fewer RBC units transfused than placebo through week 48 across all levels of baseline RBC TB (**Figure 2**)
- A similar trend was observed through week 120, where luspatercept responders had fewer RBC units transfused than luspatercept non-responders across low, medium, and high levels of baseline TB (**Figure 3**)

RBC transfusion visits

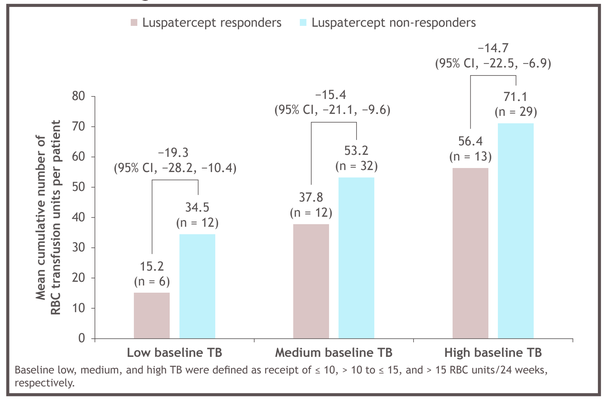
- Luspatercept responders had fewer RBC transfusion visits than placebo through week 48 across baseline TB levels (**Figure 4**)
- Luspatercept responders also had fewer RBC transfusion visits than luspatercept non-responders through week 120, across baseline TB levels (**Figure 5**)
- Findings were particularly favorable for luspatercept responders and for any luspatercept patients with low baseline TB

Figure 2. Mean cumulative number of RBC transfusion units by level of baseline TB through week 48



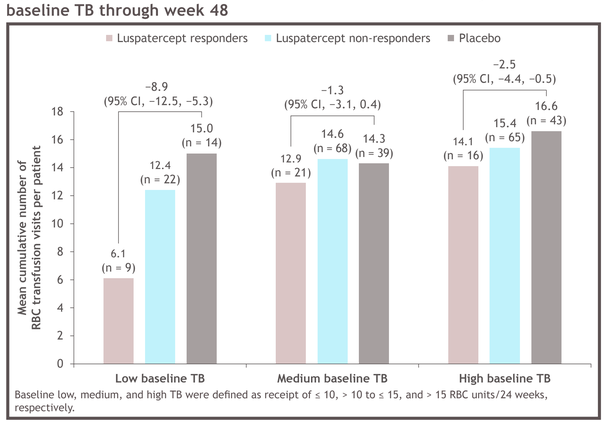
Baseline low, medium, and high TB were defined as receipt of ≤ 10, > 10 to ≤ 15, and > 15 RBC units/24 weeks, respectively.

Figure 3. Mean cumulative number of RBC transfusion units by level of baseline TB through week 120



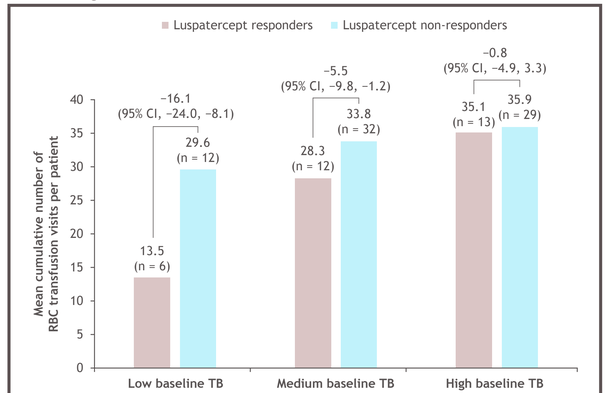
Baseline low, medium, and high TB were defined as receipt of ≤ 10, > 10 to ≤ 15, and > 15 RBC units/24 weeks, respectively.

Figure 4. Mean cumulative number of RBC transfusion visits by level of baseline TB through week 48



Baseline low, medium, and high TB were defined as receipt of ≤ 10, > 10 to ≤ 15, and > 15 RBC units/24 weeks, respectively.

Figure 5. Mean cumulative number of RBC transfusion visits by baseline TB level through week 120



Baseline low, medium, and high TB were defined as receipt of ≤ 10, > 10 to ≤ 15, and > 15 RBC units/24 weeks, respectively.

Conclusions

- Patients receiving luspatercept in the BELIEVE trial had fewer mean cumulative RBC transfusion units and visits through week 48 across all levels of baseline RBC TB
- Luspatercept responders also showed meaningful reductions in RBC transfusion units and visits across all levels of baseline RBC TB through week 120
- These findings may inform clinical and health policy decisions for patients with ß-thalassemia

References

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