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

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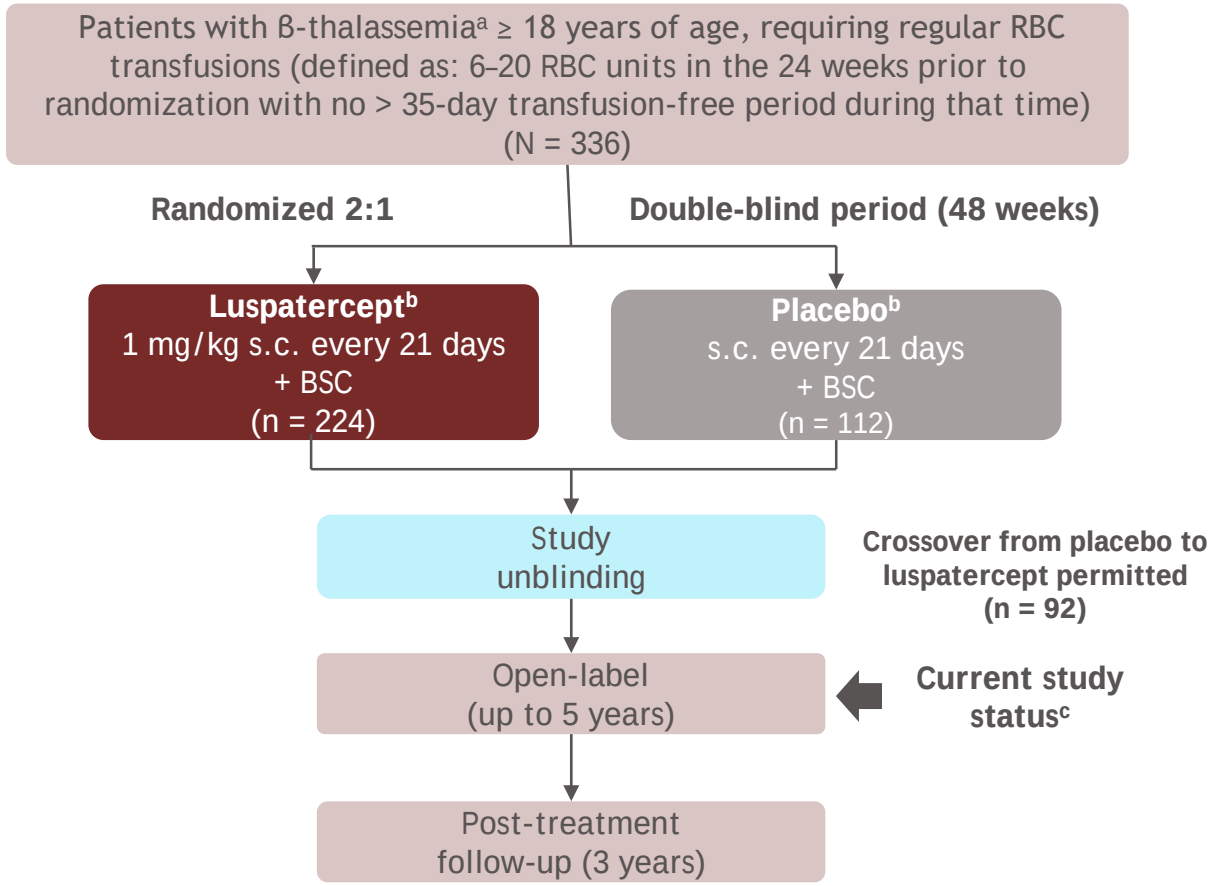
Introduction

- ß-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 ß-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 ß-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]

Figure 1. BELIEVE study trial design



[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 to maintain their baseline Hb level and ICT. [c]The trial is fully enrolled and patients continue to receive treatment or follow-up.
BSC, best supportive care; Hb, hemoglobin; ICT, iron chelation therapy; RBC, red blood cell; s.c., subcutaneously.

1. Taher AT, et al. *Lancet* 2018;391:155-167. 2. Taher AT, Cappellini MD. *Blood* 2018;132:1781-1791. 3. Suragani RNVS, et al. *Blood* 2014;123:3864-3872. 4. Attie KM, et al. *Am J Hematol* 2014;89:766-770. 5. Piga A, et al. *Blood* 2019;133:1279-1289. 6. Reblozyl (luspatercept-aamt) [package insert]. Summit, NJ: Celgene Corporation; April 2020. 7. Cappellini MD, et al. *N Engl J Med* 2020;382:1219–1231.

Results

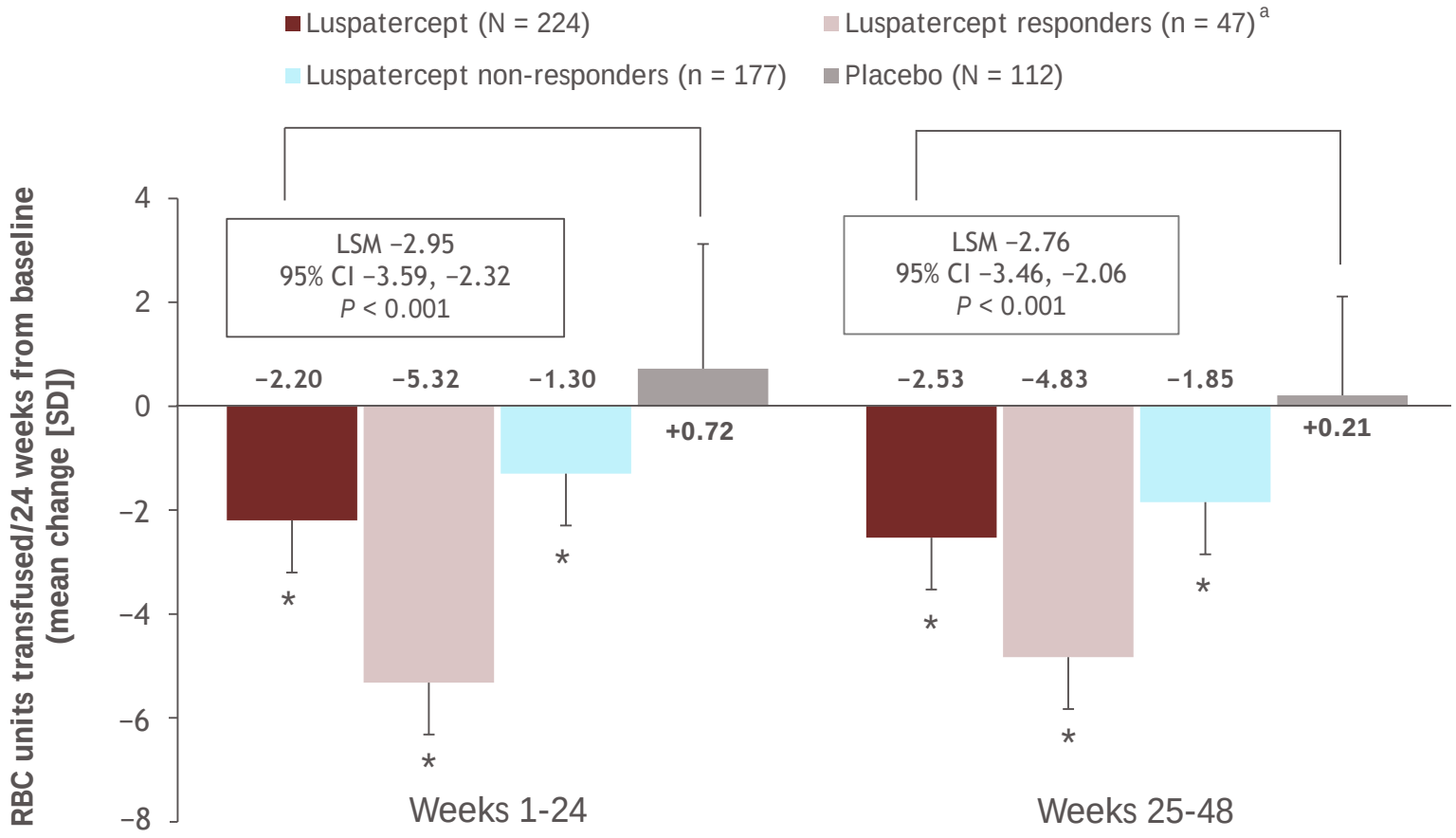
Table 1. Patient baseline characteristics

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

[a]Defined 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.

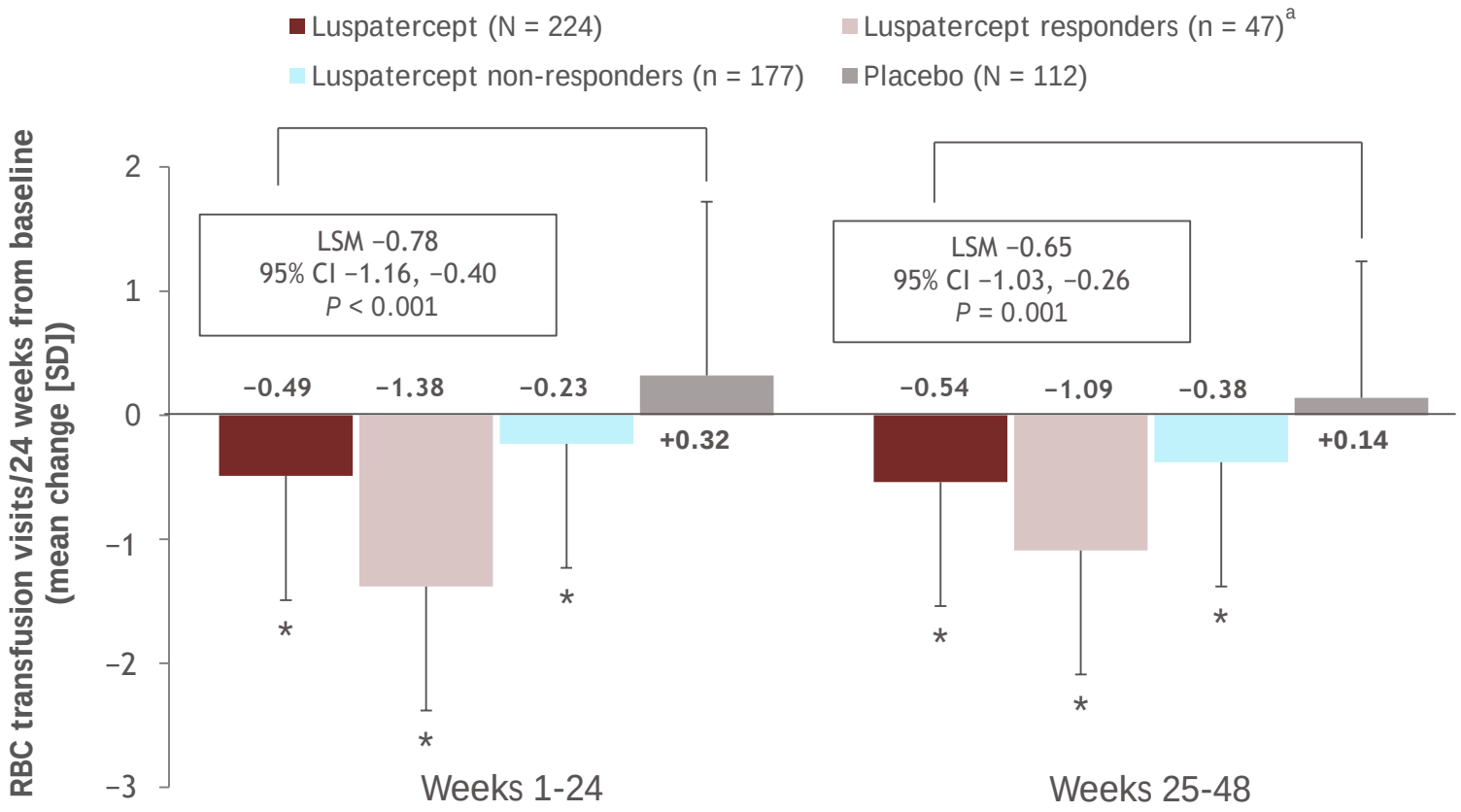
[a]Defined as patients achieving ≥ 33% reduction in RBC transfusions during Weeks 13–24, with a reduction of ≥ 2 RBC units, versus baseline.

*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



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[a]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

	Luspatercept at baseline (N = 224)	Weeks 1-24 (n = 210)	Weeks 25-48 (n = 201)	Weeks 49-72 (n = 177)	Weeks 73-96 (n = 155)	Weeks 97-120 (n = 104)	Weeks 121-144 (n = 4)
RBC units transfused/24 weeks							
Mean (SD)	14.53 (3.6)	12.27 (4.4)	11.85 (4.7)	11.71 (4.5)	11.38 (4.6)	10.93 (4.6)	11.27 (4.1)
Mean change from baseline (SD)		−2.20 (2.8)	−2.53 (3.3)	−2.67 (3.1)	−2.83 (3.2)	−3.36 (3.0)	−4.16 (3.4)
P value[a]		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.092
Number of transfusion visits							
Mean (SD)	7.65 (1.9)	7.13 (2.0)	7.01 (2.0)	7.02 (2.0)	7.01 (2.1)	6.88 (2.3)	7.25 (0.5)
Mean change from baseline (SD)		−0.49 (1.9)	−0.54 (2.0)	−0.53 (2.0)	−0.40 (2.2)	−0.54 (2.2)	−0.50 (1.3)
P value[a]		< 0.001	< 0.001	0.001	0.025	0.014	0.495

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

Data cutoff: July 1, 2019.
[a]ANCOVA was used to compare differences between luspatercept (overall) at baseline versus post-baseline.

Summary

- 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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