Revisiting Erythroid Response to Luspatercept in the Phase III BELIEVE Trial Using Real-World Response Criteria

The publication of this infographic was supported by **Bristol Myers Squibb**.
Prescribing information for Reblozyl® (luspatercept) can be found here.
Healthcare professionals are asked to report any suspected adverse reactions.
Details on adverse event reporting are given at the bottom of this infographic.

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INTRODUCTION

Patients with TDT have impaired erythropoiesis and face a chronic treatment burden of **regular transfusions** and iron chelation therapy to treat anaemia.[1]

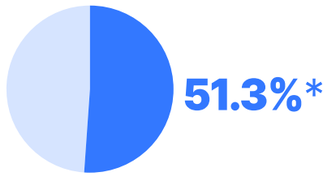
In the Phase III BELIEVE trial, **significantly more luspatercept-treated patients achieved the study primary endpoint of ≥33% reduction in TB** compared with placebo during weeks 13–24 (21.4% vs 4.5%).[2]

REAL-WORLD RESPONSE CRITERIA APPLIED TO THE BELIEVE TRIAL

When recategorised based on the modified response criteria, a **greater proportion of patients in the luspatercept group achieved an excellent or good response compared with placebo** in Weeks 1–24 and Weeks 1–48.[3]

Excellent or good response in luspatercept vs placebo

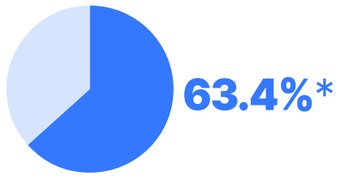
Weeks 1–24



51.3%*

= luspatercept (n=115/224)

Weeks 1–48



63.4%*

= luspatercept (n=142/224)

*p<0.0001

Most 'Excellent' responders met criterion E1 (TB reduction).[3]

Similar portions of 'Good' responders met critierion G1 (TB reduction) and G2 (Hb improvement).[3]

Achievement of 'excellent' or 'good' response increased between Weeks 1–24 and 1–48, and suggests longer treatment with luspatercept could be warranted.[3]

Weeks 1–24 Luspatercept vs placebo	Criteria met for luspatercept	Weeks 1–48 Luspatercept vs placebo	Criteria met for luspatercept
Excellent 21.4% vs 2.7%	**E1** - 19.6% **E2** - 1.8% **E3** - 2.7%	**Excellent** 29.9% vs 7.1%	**E1** - 26.8% **E2** - 3.1% **E3** - 4.0%
Good 29.9% vs 13.4%	**G1** - 20.5% **G2** - 17.4%	**Good** 33.5% vs 15.2%	**G1** - 25.5% **G2** - 18.8%
Satisfactory 17.0% vs 17.9%	N/A	**Satisfactory** 17.0% vs 25.9%	N/A

'Excellent', 'good', and 'satisfactory' responses to luspatercept (n=224) compared with placebo (n=112) when modified response criteria are applied to BELIEVE data. Response categories were defined considering changes from baseline in RBC, TB, and pre-transfusion Hb level over rolling 12-week periods during Weeks 1–24 and Weeks 1–48 of BELIEVE; patients could achieve more than one criterion per response category.

REAL-WORLD RESPONSE FRAMEWORK

Real-world experience and reported clinical benefits of luspatercept[2,4,5] informed the development of a more practical treatment response evaluation framework:[1]

- Evaluation over a period of 6 months
- Stratification by depth of response
- Inclusion of improvement in pre-transfusion Hb level and quality of life in addition to reduction in TB

Retrospective evaluation of this framework in a large cohort of patients in Italy has highlighted its utility in the real world.[6]

The published framework was modified to support its application to the BELIEVE dataset, as outlined below:

Excellent	Good	Satisfactory
E1: ≥50% TB reduction, reduction of ≥2 RBC units, and same/better Hb level over the same period E2: ≥2 g/dL increase in Hb level, same TB E3: RBC-TI for ≥12 weeks	G1: ≥33% TB, reduction of ≥2 RBC units, and same/better Hb level over the same period G2: ≥1 g/dL increase in Hb level, and same or lower TB over the same period	Any TB reduction with same or better Hb level over the same period

THE REAL-WORLD RESPONSE FRAMEWORK MAY:

- ✓ Be a practical approach for evaluating response in clinical practice
- ✓ Be useful in regions where pre-transfusion Hb levels are suboptimal
- ✓ Have potential to better reflect spectrum of response and increased understanding of patient benefit

References:

1. Musallam KM et al. Ther Adv Hematol. 2023;14:20406207231195594.
2. Cappellini MD et al. N Engl J Med. 2020;382(13):1219-31.
3. Musallam K et al. Abstract 1139. ASH Annual Meeting, 6-9 December, 2025.
4. Piga A et al. Abstract EP1306. EHA Congress, 9-17 June, 2021.
5. Kuo KHM et al. HemaSphere. 2024;8(Suppl 1):2816-7.
6. Origa R et al. Am J Hematol. 2025;100(9):1651-5.

Abbreviations:

Hb: haemoglobin; RBC: red blood cell; RBC-TI: red blood cell-transfusion independence; TB: transfusion burden; TDT: transfusion-dependent β-thalassaemia; vs: versus.