To report long-term BELIEVE trial safety data and compare them with safety data from the primary data cut (May 11, 2018).

Methods: Eligible pts were ≥18 y of age; had β-thalassemia or hemoglobin E/β-thalassemia diagnosis; required regular red blood cell transfusions (RBCT) (6–20 RBC units/24 wk before randomization; no RBCT-free period >35 d). Pts were randomized 2:1 to luspatercept or placebo, 1 mg/kg (up to 1.25 mg/kg allowed) subcutaneously every 3 wk. Pts (N=92) crossed over from placebo to luspatercept after study unblinding. Safety analyses were performed on the safety population (N=332) and summarized using descriptive statistics. TEAEs of special interest were thromboembolic events (TEEs), premalignancies and malignancies, bone pain, and hypertension. Combined luspatercept and crossover arms (N=315) from herein will be referred to as the luspatercept arm.

Results: As of Jan 5, 2021, median (range) duration of treatment was 103.0 (1.7–215.0) vs 74.7 (8.9–104.0) wk for luspatercept vs placebo arms (Table). At least 50% of pts in each treatment group received the maximum dose of study drug (1.25 mg/kg). Treatment-related TEAEs were reported in 175 (55.6%) pts receiving luspatercept vs 31 (28.4%) receiving placebo; 23 (7.3%) pts in luspatercept vs 1 (0.9%) in placebo arm discontinued treatment due to TEAEs. Rate of discontinuation was comparable to the primary data cut. Three of 5 pts died during the study due to TEAEs; no deaths were study drug-related. TEAEs more frequent with luspatercept included headache, vertigo, and hepatocellular carcinoma) were unrelated to the study drug. Median (range) time to TEE was 474.0 (75–1184) vs 238.0 (238–238) d with luspatercept vs placebo, respectively. TEEs occurred in 13 (4.1%) vs 1 (0.9%) pts in the
luspatercept vs placebo arms, respectively; all pts were splenectomized and had ≥1 other TEE risk factor. Similar rates of TEEs with luspatercept were reported in the primary data cut (8 pts [3.6%]). Bone pain was more frequent with luspatercept vs placebo (21.6% vs 8.3%), comparable with the primary data cut (19.7%). Bone pain was mild and occurred more commonly in wk 1–24. Median (range) time to first bone pain event was 24.5 (1–947) vs 16.0 (1–342) d in the luspatercept and placebo arms, respectively. Hypertension was reported in 8.9% vs 2.8% of pts in the luspatercept and placebo arms, respectively; median (range) time to first hypertension event was 209.5 (2–1136) vs 176.0 (148–464) d. Rates of hypertension with luspatercept were comparable between the 2 data cutoffs.

Summary/Conclusion: In this long-term analysis, treatment discontinuations due to TEAEs were more common in the luspatercept arm compared with placebo, as expected due to longer treatment exposure, and similar to the discontinuation rate reported in the primary data cut. No new safety concerns were reported and occurrence of TEAEs of special interest (bone pain, hypertension, and TEE) was comparable with previous reports. Overall, long-term safety analysis showed results consistent with the safety profile of luspatercept.