Abstract: S102

Title: LUSPATERCEPT VERSUS EPOETIN ALFA FOR TREATMENT (TX) OF ANEMIA IN ESA-NAIVE LOWER-RISK MYELODYSPLASTIC SYNDROMES (LR-MDS) PATIENTS (PTS) REQUIRING RBC TRANSFUSIONS: DATA FROM THE PHASE 3 COMMANDS STUDY

Abstract Type: Oral Presentation

Session Title: Plenary Abstracts Session

Background:

LR-MDS pts who require RBC transfusions experience chronic anemia, increased morbidity, iron overload, and poor overall survival. The current standard tx, erythropoiesis-stimulating agents (ESAs), is suboptimal as many pts are ineligible or have limited and/or transient responses. There is an unmet need for effective tx of anemia due to LR-MDS. Luspatercept is approved in the US and EU to treat anemia in LR-MDS following ESA failure and until now has not been directly compared with ESAs in ESA-naive pts.

Aims:

To report interim efficacy and safety data from the phase 3, open-label, randomized COMMANDS trial (NCT03682536) comparing luspatercept with epoetin alfa in ESA-naive LR-MDS pts.

Methods:

Eligible pts were ≥18 y old, had serum erythropoietin (sEPO) <500 U/L, and required RBC transfusions. Pts received subcutaneous luspatercept (1.0–1.75 mg/kg; once every 3 wk) or epoetin alfa (450–1050 IU/kg; weekly) for ≥24 wk. Pts were stratified by baseline (BL) RBC transfusion burden (<4 vs ≥4 RBC U/8 wk), BL sEPO (≤200 vs >200 U/L), and RS status (RS+, RS−). The primary endpoint was the proportion of pts who were RBC transfusion independent (RBC-TI) ≥12 wk with a concurrent mean hemoglobin increase ≥1.5 g/dL during wk 1–24. Secondary endpoints included hematologic improvement-erythroid (HI-E) ≥8 wk, RBC TI 24 wk, and ≥12 wk in wk 1–24, as well as subgroup analyses, impact of MDS-associated gene mutations on response, and safety.

Results:

178 pts were randomized to luspatercept and 178 to epoetin alfa (31Aug2022); median tx durations were 41.6 and 27.0 wk, respectively. BL characteristics were balanced between arms. The primary endpoint was achieved by 86/147 (58.5%) luspatercept and 48/154 (31.2%) epoetin alfa pts ($P<0.0001$; Fig. A); primary endpoint achievement favored luspatercept or was similar to epoetin alfa for all subgroups (Fig. B).

Luspatercept tx also favored achievement of HI-E ≥8 wk, RBC-TI 24 wk, and RBC-TI ≥12 wk in wk 1–24 (Fig. A). Median duration of RBC-TI ≥12 wk (wk 1 to end of tx) was longer with luspatercept vs epoetin alfa tx overall (126.6 and 77.0 weeks, respectively), and for clinically relevant subgroups, including RS+ and RS−.

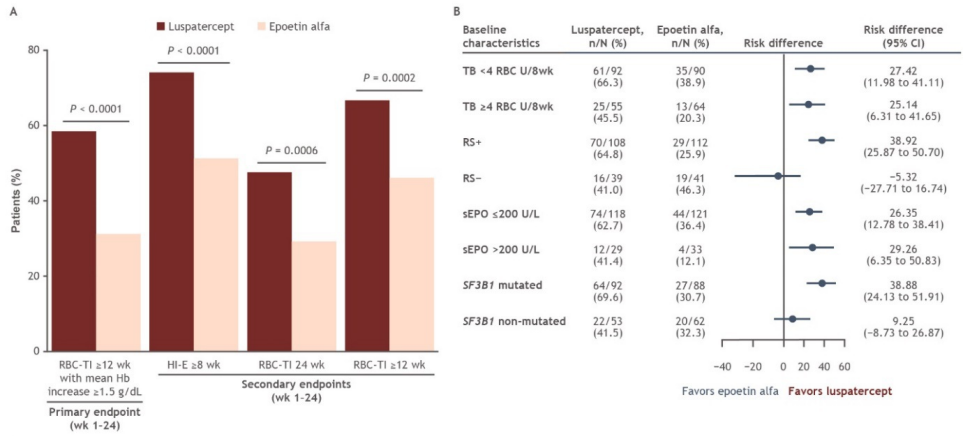
Pts with *SF3B1*, *SF3B1α*, *ASXL1*, *TET2*, *DNMT3A*, *EZH2*, *IDH2*, and *U2AF1* mutations also demonstrated favorable luspatercept response vs epoetin alfa (Fig. C). Luspatercept pts had a higher probability of achieving clinical benefit, regardless of overall mutational burden.

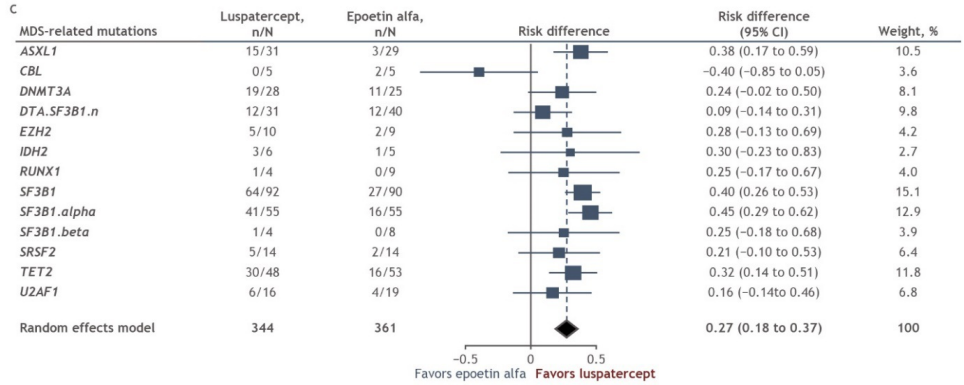
164 (92.1%) luspatercept and 150 (85.2%) epoetin alfa pts reported tx-emergent adverse events (TEAEs) of any grade; 8 (4.5%) and 4 (2.3%) pts discontinued tx due to TEAEs. The most common TEAEs (any grade) with luspatercept were fatigue (14.6%), diarrhea (14.6%), and hypertension (12.9%), and with epoetin alfa were asthenia (14.2%), diarrhea (11.4%), and anemia (9.7%). The most common TEAEs in luspatercept pts were mild to moderate, non-serious, and generally did not lead to discontinuation. 4 (2.2%) luspatercept and 5 (2.8%) epoetin alfa pts progressed to AML; overall death rates were similar between arms (32 [18.0%] vs 32 [18.2%], respectively).

Summary/Conclusion:

Luspatercept demonstrated superiority over epoetin alfa with clinically meaningful improvements in RBC-TI and HI-E rates in ESA-naive LR-MDS pts who require transfusions. Luspatercept showed more favorable outcomes compared to epoetin alfa across a spectrum of known MDS mutations. Luspatercept safety profile was comparable with previous reports; no new safety events were identified. Luspatercept may transform the current landscape by establishing a new standard of tx for ESA-naive pts with transfusion dependent LR-MDS.

Figure. (A) Proportion of patients who achieved the primary and secondary study endpoints. (B) Association of baseline characteristics with achievement of the primary endpoint. (C) Association of MDS-related mutations with the achievement of the primary endpoint.





CI, confidence interval; Hb, hemoglobin; HI-E, hematologic improvement-erythroid; MDS; myelodysplastic syndromes; RBC-TI, RBC transfusion independent; RS, ring sideroblasts; sEPO, serum erythropoietin; TB, transfusion burden.

Keywords: Mutation analysis, Myelodysplastic syndrome, Erythropoieisis, Clinical trial