(PS1761) UPDATED PHASE 2 RESULTS OF ELRITERCEPT IN PATIENTS (PTS) WITH TRANSFUSION-DEPENDENT (TD) LOWER-RISK MYELODYSPLASTIC NEOPLASMS (LR-MDS)

Topic: 10. Myelodysplastic syndromes - Clinical

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Background

Anemia is common in pts with LR-MDS, and transfusion dependency can be a substantial burden. Over time, all pts may become resistant to first-line erythroid-stimulating agents (ESAs), requiring ongoing red blood cell (RBC) transfusions. Elritercept (TAK-226), an investigational modified activin receptor type IIA ligand trap, rebalances TFG-β superfamily signaling, which may lead to durable transfusion independence (TI) and improve quality of life.

Aims

We report updated safety and efficacy data from a phase 2 trial of elritercept in pts with LR-MDS (NCT04419649).

Methods

TD pts with International Prognostic Scoring System-Revised (IPSS-R) Very Low-, Low-, or Intermediate-risk MDS were enrolled. During dose escalation, 31 pts received treatment every 4 weeks (wks; Q4W) for ≤24 cycles to establish the recommended part 2 dose (RP2D). The expansion phase (n=71) evaluated the RP2D of 3.75 mg/kg Q4W, with potential for up-titration to 5.0 mg/kg. Pts deriving clinical benefit continued in a long-term study. Endpoints included safety (assessed in all pts who received ≥1 RP2D), RBC TI ≥8 wks and hematologic improvement-erythroid (HI-E) per Modified International Working Group 2006 criteria. TI rates (≥8 wks and ≥24 wks) were analysed over the first 24 and 48 wks of treatment, respectively, in a modified intent-to-treat-24 ($mITT_{24}$) population (all pts who received ≥3.75 mg/kg Q4W and had 24 wks of treatment or discontinued before reaching Wk 24 at data cutoff, and received ≥2 RBC units [U] at baseline). Pts in the HI-E analysis were defined similarly but did not require ≥2 RBC U; response was defined as a mean increase in hemoglobin (Hgb) ≥1.5 g/dL (in low transfusion burden [LTB] pts) or reduction in transfusion of ≥4 RBC U/8 wks (high transfusion burden [HTB]) on treatment vs 8-Wk pretreatment period. Overall erythroid response was defined as HI-E or TI over any 8-wk period.

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Results

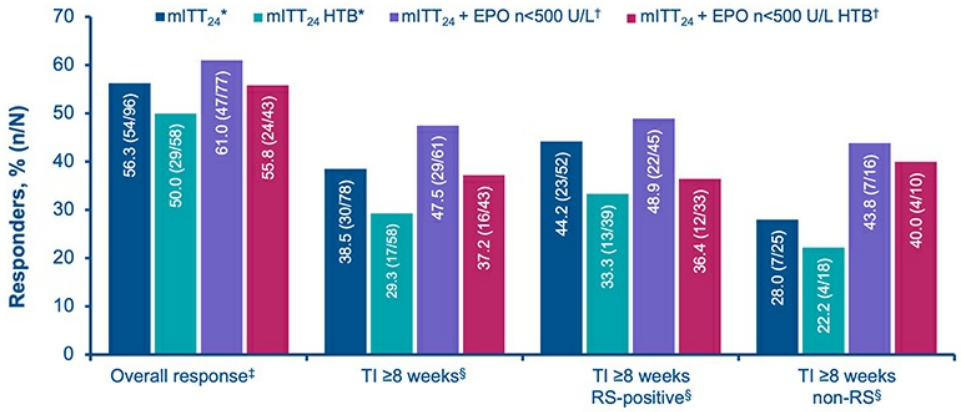
As of April 3, 2025, 96 pts were enrolled and treated with the RP2D. Median treatment exposure was 13.8 months. Drug-related treatment-emergent adverse events (TEAEs) occurred in 44 (45.8%) pts [grade ≥3 in 5 (5.2%)], with nausea (7.3%) and diarrhea (6.3%) reported most commonly. Overall erythroid response and TI rates are shown in Figure 1. By Wk 24, TI ≥8 wks was achieved by 38.5% of all evaluable pts, 29.3% of HTB pts, 44.2% of ring sideroblast (RS)+ pts, 28.0% of non-RS pts, 37.2% of pts with erythropoietin (EPO)<500 U/L HTB, 48.9% of RS+ pts with EPO<500 U/L, and 43.8% of non-RS pts with EPO<500 U/L (Figure 1). By Wk 48, 26.9% of pts achieved TI ≥24 wks (HTB: 15.5%) with a median time to first TI of 0.4 wks (95% confidence interval [CI]: 0.3–5.3). Sustained TI ≥24 wks was seen in 67.3% of pts with TI ≥8 wks. Median TI duration was 110.9 wks (95% CI: 24.3–not estimable) in pts who achieved TI ≥8 wks by Wk 24. In pts with *SF3B1* mutation, TI ≥8 wks occurred in 51.2% pts at Wk 24, 56.1% at Wk 48, and 63.4% overall. By Wk 24, HI-E response was achieved by 49.0% of evaluable pts, 48.3% of HTB pts, 51.9% of pts with EPO<500 U/L, 53.1% of RS+ pts, and 38.7% of non-RS pts, with a median time to response of 3.1 wks (95% CI: 1.1–8.1). Median duration of HI-E was 43.9 wks (95% CI: 24.6–59.1). Sustained increases for ≥8 wks in absolute neutrophil and platelets counts were seen in 31.8% and 33.3% of pts, respectively.

Summary/Conclusion

Elritercept was well tolerated and led to rapid, durable responses in pts with LR-MDS, including non-RS and HTB pts.

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Figure 1: Transfusion independence rates for ≥8 weeks by Week 24 in the miTT$_{24}$ population and across subgroups



*Includes data for Weeks 0–24 for mITT$_{24}$ patients. †Includes data for Weeks 0–24 in mITT$_{24}$ patients with baseline EPO <500 U/L, excluding one patient with del5q MDS. ‡Defined as achieving modified IWG 2006 HI-E and/or TI. §Includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching week 24 at the data cutoff date in addition to having ≥2 units of RBC transfusion at baseline. EPO, erythropoietin; HI-E, hematologic improvement-erythroid; HTB, high transfusion burden; IWG, International Working Group; MDS, myelodysplastic neoplasms; mITT$_{24}$, modified intent-to-treat-24 includes all MDS RP2D patients who have had 24 weeks of treatment or have discontinued before reaching week 24 at the data cutoff date; RP2D, recommended part 2 dose; RS, ring sideroblast; TI, transfusion independence; U/L, units per liter.

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