Abstract: S183

Title: DURABLE CLINICAL BENEFIT WITH ELRITERCEPT (KER-050) TREATMENT: FINDINGS FROM AN ONGOING PHASE 2 TRIAL IN PARTICIPANTS WITH LOWER-RISK MDS

Abstract Type: Oral Presentation

Session Title: Immune and targeted therapies in MDS

Background:

Ineffective hematopoiesis in myelodysplastic neoplasms (MDS) leads to cytopenia, red blood cell (RBC) transfusion dependence, and reduced quality of life (QoL). Imbalanced signaling by TGF-β superfamily ligands, particularly activin A, plays a key role in MDS pathogenesis. Elritercept is an investigational, modified activin receptor type IIA ligand trap designed to inhibit activin A and other select TGF-β superfamily ligands (activin B, GDF 8 and 11) to address ineffective hematopoiesis. The potential for elritercept to address the underlying pathophysiology of MDS and provide durable hematologic improvement in lower-risk (LR) MDS, including in patients with high transfusion burden (HTB; ≥4 RBC U/8 weeks) or non-ring sideroblast (RS) MDS, is being investigated in an ongoing Phase 2 trial.

Aims:

To present updated findings from the ongoing KER050-MD-201 trial (NCT04419649) evaluating safety, tolerability and response profile of elritercept in participants with LR-MDS and anemia.

Methods:

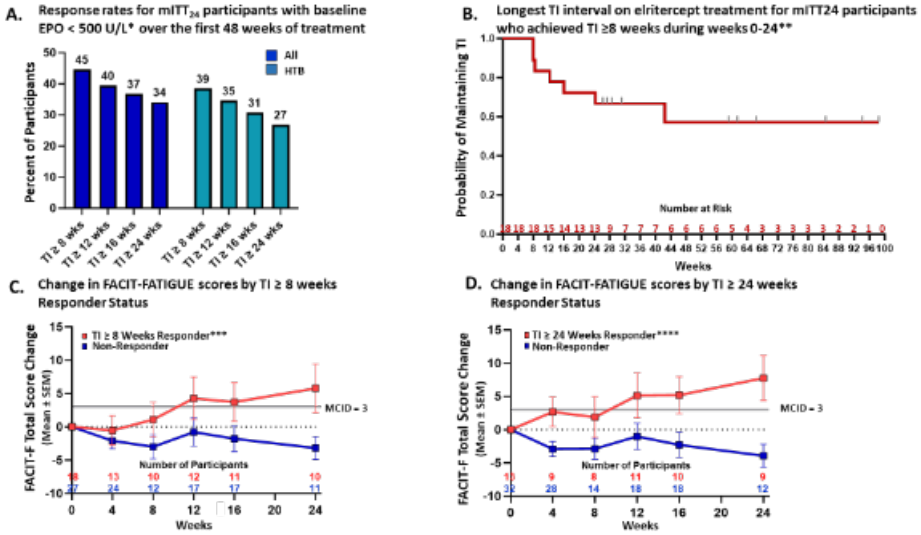
Data from this ongoing Phase 2 trial are presented as of a cutoff date of 1Sep2023. Baseline and safety data are from participants receiving the recommended Part 2 dose (RP2D, N=79). Because this trial has several ongoing participants early in treatment with limited data, response was evaluated in a modified intent-to-treat-24 (mITT24) population that included participants who received ≥24 weeks of treatment or discontinued (N=60). Modified IWG 2006 Hematological Improvement-Erythroid (HI-E), transfusion independence (TI), duration of response (DOR), and changes in QoL scores are presented.

Results:

Of RP2D participants, 56% had HTB and 32% received ≥6 RBC U/8 weeks at baseline. Disease was mostly low-/intermediate-risk per IPSS-R and 7.9% of cases were reclassified as high- or very high-risk by IPSS-M. Median treatment duration was 29 weeks with 63% ongoing at the data cutoff. Overall, 93.7% of participants experienced a treatment-emergent adverse event (TEAE), most of which were mild-to-moderate in severity. TEAEs leading to treatment discontinuation were infrequent (13.8%). The most frequently observed TEAEs were dyspnea and diarrhea (22.8% each), fatigue (20.3%), nausea (19.0%), and headache (15.2%). Half of all mITT24 participants achieved a HI-E and/or TI response over the first 24 weeks of treatment, including 45.5% of participants with HTB. Nine (15%) mITT24 participants had baseline erythropoietin (EPO) levels ≥ 500 U/L, a factor predicting low likelihood of response for multiple treatments. When responses were evaluated in mITT24 participants with baseline EPO < 500 U/L, overall response rates were higher (56% vs. 50%) and rates of TI ≥8 weeks were notably higher in participants with non-RS MDS (33% vs. 21%), especially in those with HTB (50% vs. 30%). Among mITT24 participants who achieved TI ≥8 weeks, 72% maintained TI ≥24 weeks, reflecting durability (FigA). The median DOR had not been reached at the cutoff date (FigB) and 11/18 TI responders had ongoing TI, including 6 with TI >52 weeks, 5 of whom had HTB at baseline. Observed mean improvements in FACIT-Fatigue scores for TI responders exceeded a clinically meaningful threshold within 24 weeks, especially for those with TI ≥24 weeks (FigC,D).

Summary/Conclusion

As of the cutoff date, data support that elritercept was generally well tolerated in the RP2D population and has the potential to address the underlying pathophysiology of LR-MDS to bring about durable hematologic improvement. Further updates will be provided at presentation and will include longer-term data for the RP2D population and more participants in the mITT24 efficacy population.



MCID = minimal clinically important difference.*Excludes 1 participant with del5q MDS. **Participants with ongoing response censored at time of data cutoff (denoted by vertical lines). ***Includes data for mITT$_{24}$ participants with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 8 weeks Responder, assessed from Weeks 0 to 24; **** Includes data for mITT$_{24}$ participants with baseline FACIT-Fatigue scores (n = 1 missing) for TI ≥ 24 weeks Responder, assessed from Weeks 0 to 48.

Keywords: Quality of life, Myelodysplastic syndrome, Hematopoiesis, Fatigue