Abstract: S223

Title: ELRITERCEPT (KER-050) DEMONSTRATED POTENTIAL TO TREAT MYELOFIBROSIS AND MITIGATE RUXOLITINIB-ASSOCIATED CYTOPENIAS IN THE PHASE 2 RESTORE TRIAL

Abstract Type: Oral Presentation

Session Title: Clinical advances in myelofibrosis and mastocytosis

Background:

Myelofibrosis (MF) is characterized by abnormal JAK and TGF-b signaling, ineffective hematopoiesis, and splenomegaly. JAK inhibitors improve spleen size and symptoms but are associated with dose-limiting cytopenias. Elritercept is an investigational modified activin receptor type IIA ligand trap designed to inhibit select TGF-β superfamily ligands (activins A&B, GDFs 8&11) to address ineffective hematopoiesis. Potential for elritercept to treat MF and ruxolitinib-associated cytopenias is being studied in the Phase 2 RESTORE trial.

Aims:

RESTORE (NCT05037760) is evaluating safety, tolerability, PK/PD, and efficacy of elritercept with or without ruxolitinib in participants with MF and anemia, either hemoglobin (Hgb) <10 g/dL or transfusion-dependent (TD; ≥6U/12W and ≥1 transfusion within 4W prior to elritercept start). Part 1 involved escalation over 4 elritercept doses (0.75-4.5 mg/kg) given subcutaneously every (Q)4W as monotherapy (Arm A) or in combination with ruxolitinib (Arm B). Part 1 aimed to identify the recommended Part 2 dose (RP2D) and evaluate preliminary data.

Methods:

Data are as of 14Sep2023. Baseline and safety data are presented for participants who received ≥1 dose of elritercept. PD and efficacy data are presented for 0.75-3.0 mg/kg, as data were limited for 4.5 mg/kg. For 12W endpoints, data are presented for evaluable participants (consecutive 12W post-baseline data) only. Analyses include data from both arms unless otherwise noted.

Results:

In Part 1 (N=41), 15 participants (37%) were TD. Baseline splenomegaly (spleen volume ≥450 cm3) and symptoms (total symptom score [TSS] ≥10) were present in 23 (70%) and 29 (71%) participants, respectively.

Treatment-emergent adverse events observed in ≥15% were diarrhea (22%), thrombocytopenia (17%), and fatigue, asthenia and pyrexia (15% each). One participant had an asymptomatic Hgb increase that required dose reduction and was therefore a dose-limiting toxicity (DLT). No other DLTs were observed and the RP2D selected for both arms was 3.75 mg/kg with option to up-titrate to 5.0 mg/kg Q4W, consistent with the RP2D in an ongoing myelodysplastic neoplasms trial.

Erythropoiesis was assessed in non-TD participants (n=19) to reduce confounding by transfusions. Sustained increases in Hgb (Fig A) and generally dose-dependent increases in soluble transferrin receptor (sTfR; marker of erythropoiesis), reticulocytes, and Hgb (Fig B) were observed. Mean 12W Hgb increased by ≥1 g/dL in 7 of 13 (54%) evaluable participants.

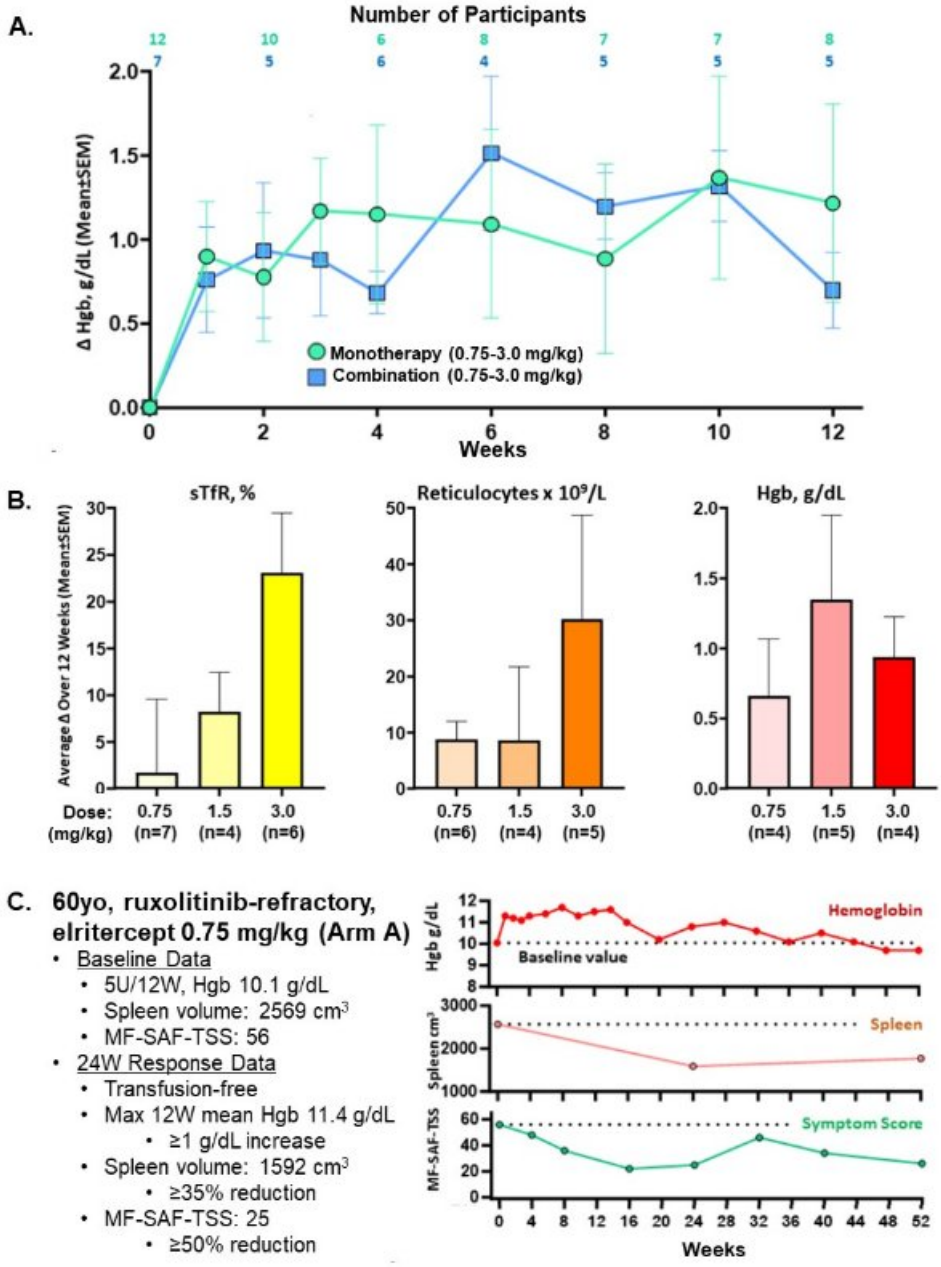
Among 13 evaluable TD participants, 12W transfusion burden was reduced by ≥50% in 5 (38%, baseline 6-15U/12W). In broader evaluation of 21 with baseline transfusion burden ≥3U/12W (13 TD, 8 non-TD), reduction was observed in 15 (71%), including 2 non-TD participants (baseline 5-9U/12W) who were transfusion-free for ≥12W.

Platelets were generally stable or increased.

W24 spleen and TSS reduction were evaluable in 7 and 12 participants, respectively. Four (57%) had reduced spleen size (-48% to -11%), 8 (67%) had reduced TSS (-56% to -7%), and 1 had a trifactor response (anemia, spleen, TSS; Fig C).

Summary/Conclusion:

These data from RESTORE suggest that elritercept was generally well tolerated and has potential to treat several aspects of MF. Improvements in Hgb and transfusion burden with maintenance of platelets demonstrate potential to address ineffective hematopoiesis and treat cytopenias associated with MF and ruxolitinib. Data also support potential for elritercept to reduce spleen size and improve symptoms. An updated analysis including data from the 4.5 mg/kg cohorts and those receiving elritercept at the RP2D will be presented.



Keywords: Myelofibrosis, Hematopoiesis, TGF-, Ruxolitinib