LONGER-TERM RED BLOOD CELL (RBC) TRANSFUSION REDUCTION IN THE PHASE 3 MEDALIST STUDY OF LUSPATERCEPT IN PATIENTS WITH LOWER-RISK MYELODYSPLASTIC SYNDROMES (LR-MDS) WITH RING SIDEROBLASTS (RS)

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Background

MEDALIST (NCT02631070) is an ongoing randomized, placebo-controlled, phase 3 trial evaluating the efficacy and safety of luspatercept, a first-in-class erythroid maturation agent, in patients with anemia due to LR-MDS with RS (Fenaux P & Platzbecker U, et al. N Engl J Med. 2020;382:140-51).

Aims

This analysis evaluated long-term transfusion burden reduction with luspatercept in all patients in the MEDALIST trial.

Methods

Eligible patients were aged ≥18 years; had Revised International Prognostic Scoring System-defined Very low-, Low-, or Intermediate-risk MDS with RS; were refractory, intolerant, or unlikely to respond to erythropoiesis-stimulating agents; and required RBC transfusions (≥2 units/8 weeks in the 16 weeks prior to randomization). All patients provided informed written consent. Overall, 229 patients were randomized 2:1 to luspatercept (1.0 mg/kg, titration to 1.75 mg/kg) or placebo subcutaneously every 3 weeks.

Results

As of July 1, 2019, 77/153 (50.3%) and 11/76 (14.5%) patients in the luspatercept and placebo arms, respectively, achieved ≥50% RBC transfusion burden reduction for ≥24 weeks ($P<0.0001$). The median longest single response episode was 131.6 weeks with luspatercept, and not estimable with placebo due to patients stopping treatment. In Weeks 9–24, mean change from baseline in RBC units transfused was −3.0 (95% confidence interval [CI] −3.9, −2.1) vs +0.4 (95% CI −0.6, 1.4) in the luspatercept vs placebo arms. In Weeks 33–48, mean change in RBC units transfused in the luspatercept arm was −4.9 (95% CI −5.9, −3.9). In Weeks 1–24, the mean number of transfusion visits was 5.9 vs 9.5 in the luspatercept vs placebo arms. Risk of recurrent transfusion visits in Weeks 1–24 for luspatercept vs placebo was 0.699 (95% CI 0.597, 0.819; $P<0.0001$).

Mean number (least squares [LS] mean) of RBC units transfused/48 weeks during Weeks 1–48 was 22.89 (23.28) vs 35.98 (35.20) in the luspatercept vs placebo arms (LS mean difference −11.92 [95% CI −15.55, −8.28]; $P<0.0001$). The mean number (LS mean) of RBC transfusion events over 48 weeks was 12.95 (13.14) vs 19.54 (19.15) in the luspatercept vs placebo arms (LS mean difference −6.00 [95% CI −8.16, −3.85]; $P<0.0001$).

LS mean change from baseline in serum ferritin was −2.7 vs +226.5 µg/L with luspatercept vs placebo (LS mean difference −229.1 µg/L; $P=0.0024$) in Weeks 9–24; and −72.0 vs +247.4 µg/L in Weeks 33–48 (LS mean difference −319.5 µg/L; $P=0.0294$).

In Weeks 1–24, 38/127 (29.9%) vs 5/65 (7.7%) patients ($P=0.0005$) achieved major hematologic improvement-erythroid (HI-E) response per International Working Group 2018 criteria in the luspatercept vs placebo arms, respectively.

Conclusion

Luspatercept demonstrated clinically meaningful responses in patients with LR-MDS with RS and was associated with statistically significant reductions in RBC transfusions (≥50%; $P<0.0001$) and serum ferritin ($P=0.0024$ in Weeks 9–24; $P=0.0294$ in Weeks 33–48).

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Keyword(s): Clinical trial, MDS, Phase III