Introduction

− Lower-risk myelodysplastic syndromes (LR MDS) are characterized by ineffective erythropoiesis, leading to anemia, reduced bone marrow cellularity, and transfusion dependence, and reduced quality of life.

− There is a need for effective treatments for anemia in transfusion-dependent patients with LR MDS.

− Luspatercept is the first-in-class erythroid maturation agent that blocks select transforming growth factor β (TGF-β) signaling and enhances late-stage erythroblasts.

− Luspatercept is indicated for the treatment of anemia in adult patients with LR MDS with ring sideroblasts (RS) who require regular RBC transfusions.

Methods

− Study design: Randomized, double-blind, placebo-controlled phase 3 study.

− Setting: 165 centers in 11 countries.

− Patients were randomized 2:1 to receive luspatercept (starting dose 1.0 mg/kg, with titration to a maximum of 1.75 mg/kg) or placebo (s.c.) every 21 days.

− Inclusion criteria: Adult patients with LR MDS with RS ≥15%.

− Exclusion criteria: Patients with active hematopoietic malignancy or hematopoietic stem cell transplantation within the previous 5 years.

− Key secondary endpoint: RBC transfusion independence (RBC-TI).

− Primary endpoint: RBC transfusion burden at baseline and weeks 1–24.

− Secondary endpoints: Average RBC transfusion burden, RBC transfusion burden ≥1.5 g/dL from baseline, and risk of recurrent transfusion visits during Weeks 9–24.

− Disease and response assessment: Transfusion burden ≥3.5 units RBCs from baseline, sustained for ≥8 weeks (Weeks 1–24) was achieved by 58 of 153 (37.9%) patients in the luspatercept arm and 12 of 76 (15.8%) patients in the placebo arm (p < 0.0001).

− The mean (standard deviation) transfusion burden at baseline was 5.5 (2.76) and 5.8 (2.95) RBC units per week in the luspatercept and placebo arms, respectively.

− The median (interquartile range) treatment duration was 55.2 (26.1–84.7) weeks in the luspatercept arm and 56.6 (27.6–83.1) weeks in the placebo arm.

− The mean (standard deviation) transfusion burden reduction ≥75% was 131.6 weeks in the luspatercept arm and 41.8 weeks in the placebo arm (p < 0.0001).

− The mean (standard deviation) relative change in RBC transfusion burden was 52.7% (51.9%) in the luspatercept arm and 27.7% (27.7%) in the placebo arm (p < 0.0001).

− The mean (standard deviation) change in serum ferritin was −229.1 (74.43) μg/L in the luspatercept arm and −319.5 (144.57) μg/L in the placebo arm (p < 0.0001).

− The mean (standard deviation) change in transfoglobin was +0.4 (−0.6, +1.4) g/dL in the luspatercept arm and −1.5 (−1.8, −1.2) g/dL in the placebo arm (p = 0.0004).

− Adverse events: The most common adverse events were pyrexia, reactor syndrome rash, injection-site reactions, and pruritus.

− Achievements:

  − Luspatercept produced clinically meaningful and durable reductions in RBC transfusions in patients with LR MDS with RS.

  − Luspatercept also resulted in statistically significant reductions in serum ferritin in patients with LR MDS with RS.

Conclusions

− Luspatercept produced clinically meaningful and durable reductions in RBC transfusions in patients with LR MDS with RS.

− Luspatercept also resulted in statistically significant reductions in serum ferritin in patients with LR MDS with RS.

References


