EP915 BENEFIT OF CONTINUING LUSPATERCEPT THERAPY IN PATIENTS WITH LOWER-RISK MYELODYSPLASTIC SYNDROMES WHO DID NOT ACHIEVE RED BLOOD CELL TRANSFUSION INDEPENDENCE BY WEEK 25 IN THE MEDALIST STUDY

Author(s): Ulrich Germing, Pierre Fenaux, Uwe Platzbecker, Rena Buckstein, Valeria Santini, María Díez-Campelo, Derek Tang, Rodrigo Ito, Shannon Fabre, Emily Mantovani, George Zhang, Xianwei Ha, Dimana Miteva, Christina Hughes, Wasiulla Khan, Rami S. Komrokji, Guillermo Garcia-Manero

EHA Library. Germing U. 06/09/21; 325673; EP915

Type: E-Poster Presentation

Session title: Myelodysplastic syndromes - Clinical

Background:

MEDALIST (NCT02631070) is an ongoing, randomized, placebo-controlled phase 3 trial evaluating the efficacy and safety of luspatercept, the first and only erythroid maturation agent, in patients with anemia due to lower-risk myelodysplastic syndromes (LR-MDS) with ring sideroblasts. A greater proportion of patients receiving luspatercept than placebo achieved the primary endpoint of red blood cell transfusion independence (RBC-TI) for ≥8 weeks during Weeks 1–24 (Fenaux P, et al. N Engl J Med 2020;382:140-151). However, for patients not achieving the primary endpoint during the first 24 weeks, the value of continuing luspatercept treatment is not yet well understood.

Aims:

To evaluate the clinical benefit of continuing luspatercept treatment beyond 24 weeks in patients not achieving the RBC-TI primary endpoint during the first 24 weeks of the MEDALIST study.

Methods:

Eligible patients were aged ≥18 years; were refractory, intolerant, or unlikely to respond to erythropoiesis-stimulating agents; and required regular RBC transfusions (≥2 units/8 weeks) in the 16 weeks prior to randomization. Overall, 229 patients were randomized 2:1 to receive either luspatercept (n=153) or placebo (n=76) every 3 weeks through the clinical assessment visit at Week 25, defined as 24 calendar weeks after the first dose, regardless of dose delays. Patients who did not achieve RBC-TI for ≥8 weeks on luspatercept by Week 25 but continued treatment were included in this analysis; the data cutoff was July 1, 2019. For this analysis, transfusion burden, serum ferritin (SF) levels, and hematologic improvement-erythroid (HI-E) response were assessed every 24 weeks. HI-E response was defined as a reduction in RBC transfusions of ≥4 units/8 weeks (for patients with baseline RBC transfusion burden of ≥4

units/8 weeks) or as an increase in hemoglobin level of ≥1.5 g/dL over 8 weeks (for patients with baseline RBC transfusion burden of <4 units/8 weeks).

Results:

Of the patients receiving luspatercept, 68 did not meet the primary endpoint during the first 24 weeks and continued treatment. During Weeks 25–48, 16.2% (n=11/68) of these patients achieved RBC-TI for ≥8 weeks for the first time, and a mean change from baseline of −1.3 RBC units transfused was achieved in 36 pts. 44.1% (n=30/68) of patients who did not meet the primary endpoint achieved any degree of reduction in SF levels from baseline during Weeks 25–48, while 17.9% (n=7/39) shifted from a SF level ≥1,000 µg/L at baseline to <1,000 µg/L. During Weeks 1–48, 60.3% (n=41/68) of patients who did not meet the primary endpoint achieved ≥50% reduction in RBC transfusion burden for ≥8 weeks from baseline and 47.1% (n=32/68) achieved HI-E response. Over the entire treatment period up to the data cutoff, 60.3% (n=41/68) achieved ≥50% reduction in transfusion burden for ≥8 weeks from baseline, 22.1% (n=15/68) achieved RBC-TI for ≥8 weeks, and 48.5% (n=33/68) achieved HI-E response.

Conclusion:

A considerable proportion of patients with LR-MDS in the MEDALIST study who did not achieve the primary endpoint, but continued to receive luspatercept beyond 24 weeks of treatment, experienced a broad range of clinical improvements, including reduced transfusion burden, reduced SF levels, and even TI.

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