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ORAL ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Long-Term Evaluation of Luspatercept in Erythropoiesis-Stimulating Agent (ESA)-Intolerant/Refractory Patients (pts) with Lower-Risk Myelodysplastic Syndromes (LR-MDS) in the Phase 3 MEDALIST Study

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Background: Pts with LR-MDS receiving luspatercept in the phase 3 MEDALIST trial previously reported durable, long-term red blood cell (RBC) transfusion independence (RBC-TI) (Fenaux P, et al. *J Clin Oncol* 2022;40[suppl 16]. Abstract 7056). MEDALIST pts were eligible to enroll in a follow-up study to evaluate long-term efficacy and safety.
Aims: To report long-term efficacy and safety outcomes in ESA-refractory/intolerant pts with LR-MDS treated with luspatercept in the MEDALIST trial with an additional 26 mo of follow-up from the final MEDALIST data cutoff.
Methods: Eligible pts were ≥ 18 y of age; IPSS-R-defined Very low-, Low-, or Intermediate-risk MDS with ring sideroblasts; were refractory, intolerant, or unlikely to respond to ESAs, and required regular RBC transfusions. Pts were randomized 2:1 to luspatercept (starting dose 1.0 mg/kg, with titration up to 1.75 mg/kg) or placebo. Efficacy outcomes include RBC-TI ≥ 8 wk and ≥ 16 wk. Cumulative duration of response was determined by Kaplan-Meier (KM) analysis. Rates of longest single and cumulative duration of RBC-TI ≥ 1 y and exposure-adjusted incidence rates (EAIR) of treatment-emergent adverse events (TEAEs) and AEs of special interest (AESIs) were calculated. Rates of high-risk (HR)-MDS and acute myeloid leukemia (AML) progression were calculated from LR-MDS diagnosis to HR-MDS/AML diagnosis, or to last HR-MDS/AML follow-up date for pts who did not progress.
Results: As of January 2, 2023, 11 pts remained on luspatercept treatment; 8 pts randomized to luspatercept and none from placebo continued in post-treatment follow-up. The median (range) follow-up time was 39.9 (2.8-76.0) mo for luspatercept arm pts and 38.7 (1.7-68.6) mo for placebo arm pts. The median (range) duration of treatment was 50.9 (5.9-332.9) wk for luspatercept pts and 24.0 (9.0-103.0) wk for placebo pts. Seventy-five of 153 (49.0%) luspatercept pts achieved RBC-TI ≥ 8 wk during the entire treatment period and 53/75 (70.7%) had ≥ 2 response periods with a median cumulative duration of 110.14 wk (95% confidence interval [CI], 53.71-154.14; Figure A). Overall, 31/75 (41.3%) luspatercept pts had the longest RBC-TI duration ≥ 1 y, and 44/75 (58.7%) had a cumulative RBC-TI duration ≥ 1 y. In total, of the 48/153 (31.4%) pts receiving luspatercept who achieved RBC-TI ≥ 16 wk during the entire treatment period, 32/48 (66.7%) had ≥ 2 response periods with a median cumulative duration of 129.29 wk (95% CI, 79.86-240.43). Grade 3/4 treatment-related TEAEs were reported in 14/153 (9.2%; EAIR, 5.3 per 100 pt-y [PYs]) and 3/76 (3.9%; EAIR, 6.6 per 100 PYs) luspatercept and placebo pts, respectively; TEAEs of any grade leading to permanent treatment discontinuation were reported in 24/153 (15.7%; EAIR, 8.6 per 100 PYs) luspatercept and 6/76 placebo pts (7.9%; EAIR, 13.0 per 100 PYs). The most common TEAEs of any grade reported in > 5% of luspatercept pts were fatigue (47/153 [30.7%]; EAIR, 22.1 per 100 PYs; vs placebo, 11/76 [14.5%]; EAIR, 27.1 per 100 PYs), diarrhea (47/153 [30.7%]; EAIR, 23.5 per 100 PYs; vs placebo, 8/76 [10.5%]; EAIR, 18.4 per 100 PYs), asthenia (41/153 [26.8%]; EAIR, 18.8 per 100 PYs; vs placebo, 9/76 [11.8%]; EAIR, 21.5 per 100 PYs), peripheral edema (40/153 [26.1%], EAIR, 17.6 per 100 PYs; vs placebo, 13/76 [17.1%]; EAIR, 32.0 per 100 PYs), and back pain (38/154 [24.7%]; EAIR, 16.8 per 100 PYs; vs placebo, 5/76 [6.6%]; EAIR, 11.7

per 100 PYs; Figure B). During the entire treatment period, 26/44 (59.1%), 9/23 (39.1%), and 12/86 (14.0%) pts who received ≤ 1 mg/kg, 1.33 mg/kg, and 1.75 mg/kg luspatercept, respectively, reported fatigue of any grade. No new progression to HR-MDS or AML events have been reported since the last data cutoff (Santini V et al. *Blood* 2022;140[suppl 1]:4079-4081). *Conclusions:* Pts with LR-MDS who received luspatercept for > 2 years longer than in the original MEDALIST study, continued to experience sustained periods of RBC-TI with more than half of pts experiencing cumulative RBC-TI for ≥ 1 year. The long-term safety profile of luspatercept is consistent with previous shorter-term reports, and AEs were mostly lower grade with rates of fatigue decreasing with increasing luspatercept dose. These data demonstrate the long-term efficacy and safety of luspatercept in pts with LR-MDS intolerant/ineligible for ESA treatment.

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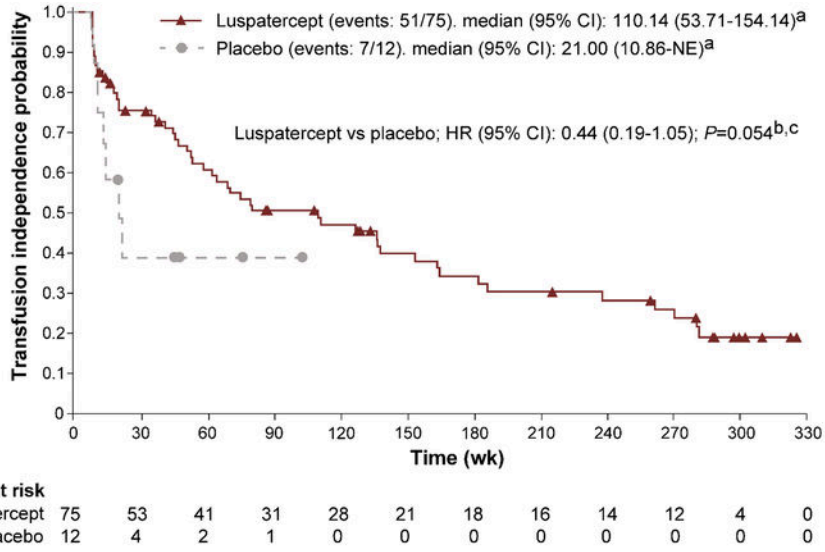
A



B

	Luspatercept (N = 153)		Placebo (N = 76)	
TEAE	n (%)	EAIR per 100 pt y	n (%)	EAIR per 100 pt y
Treatment-related grade 3/4	14 (9.2)	5.3	3 (3.9)	6.6
Treatment-related grade 5	0	0	0	0
TEAE leading to permanent treatment discontinuation	24 (15.7)	8.6	6 (7.9)	13
TEAE				
Preferred Term	n (%)	EAIR per 100 PY	n (%)	EAIR per 100 PY
Fatigue	47 (30.7)	22.1	11 (14.5)	27.1
Diarrhea	47 (30.7)	23.5	8 (10.5)	18.4
Asthenia	41 (26.8)	18.8	9 (11.8)	21.5
Peripheral edema	40 (26.1)	17.6	13 (17.1)	32.0
Back pain	38 (24.8)	16.8	5 (6.6)	11.7
AESI				
Preferred Term	n (%)	EAIR per 100 PY	n (%)	EAIR per 100 PY
Cardiac-related events	54 (35.3)	26.9	11 (14.5)	25.7
Tachycardia	11 (7.2)	4.1	0	0
Hypertension	20 (13.1)	8.0	7 (9.2)	16.9
Thromboembolic events	7 (4.6)	2.6	3 (3.9)	6.6
Malignancies	19 (12.4)	6.8	6 (7.9)	10.4
Basal cell carcinoma	5 (3.3)	1.8	0	0

Cumulative duration of RBC-TI is defined as the sum of all respective durations for responders over the entire treatment period. [a]Medians and associated two-sided 95% CIs were calculated using the KM method. [b]*P*-values were calculated using the log-rank test to compare luspatercept and placebo, stratified by average baseline RBC transfusion requirement (≥ 6 units vs. < 6 units of RBC per 8 wks) and baseline IPSS-R score (Very low or Low vs. Intermediate). [c]HRs were calculated using the Cox proportional hazards model with RBC transfusion requirement (≥ 6 units vs. < 6 units of RBC per 8 weeks) and baseline IPSS-R score (Very low or Low vs. Intermediate) as covariates. CI, confidence interval; HR, hazard ratio; IPSS-R, Revised International Prognostic Scoring System; KM, Kaplan–Meier; NE, not estimable; RBC, red blood cell; RBC-TI, RBC transfusion independence; wk, week.

Figure 1

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