P778 LONG-TERM UTILIZATION AND BENEFIT OF LUSPATERCEPT IN PATIENTS (PTS) WITH LOWER-RISK MYELODYSPLASTIC SYNDROMES (LR-MDS) FROM THE MEDALIST TRIAL

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Background:
Luspatercept has been shown to improve anemia in the phase 3 MEDALIST trial of pts with LR-MDS ineligible/intolerant or refractory to erythropoiesis-stimulating agents (ESAs).

Aims:
To report the long-term clinical value of luspatercept treatment (Tx) in pts from the MEDALIST study including dosing, duration of Tx (DOT) and response, baseline characteristics of pts receiving luspatercept in a long-term follow-up (LTFU) study, and rates of progression to acute myeloid leukemia (AML) and high-risk MDS (HR-MDS).

Methods:
Eligible pts were ≥18 y of age, had LR-MDS requiring regular red blood cell (RBC) transfusions, and were ineligible/intolerant or refractory to ESAs. Pts were randomized 2:1 to subcutaneous luspatercept or placebo every 3 wk for 24 wk. The primary endpoint was RBC transfusion independence (RBC-TI) ≥8 wk during wk 1–24. MEDALIST pts who continued to receive luspatercept due to ongoing clinical benefit were eligible for enrollment into the LTFU study, a phase 3b rollover study to evaluate the long-term safety of luspatercept in pts who participated in other luspatercept studies. DOT was calculated as (Tx end date − date of first dose) + 1) / 7. Duration of response was determined by Kaplan–Meier analysis. Total person-years for pts at risk of HR-MDS/AML progression was 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 Jan 15, 2021, the median (95% confidence interval [CI]) DOT was 11.70 (8.97–16.33) mo for luspatercept pts and 5.52 (5.52–5.59) mo for placebo pts. Median (interquartile range [IQR]) DOT for placebo pts who transitioned to LTFU was 24.0 (24.0–25.3) wk and 24.0 (24.0–

39.0) wk for placebo pts who discontinued prior to LTFU. The median (IQR) DOT for luspatercept pts who transitioned to LTFU was longer than for those pts who discontinued (190.0 [86.0–211.0] wk vs 31.0 [24.0–64.1] wk). Baseline characteristics more frequently observed in luspatercept pts who transitioned to LTFU than in pts who discontinued include younger age, female sex, and lower Eastern Cooperative Oncology Group performance status score, transfusion burden, erythropoietin, and serum ferritin levels (Table A). In MEDALIST, 106/153 (69.3%) pts receiving luspatercept and 64/76 (84.2%) receiving placebo escalated to the maximum dose of 1.75 mg/kg. During the entire Tx phase, RBC-TI ≥8 wk was observed in 74/153 (48.4%) and 12/76 (15.8%) luspatercept and placebo pts, respectively, with a median (95% CI) cumulative duration of response of 80.7 (53.71–154.14) wk and 21.0 (10.86–NE) wk, respectively. During the entire Tx period, RBC-TI ≥16 wk was observed in 48/153 (31.4%) and 6/76 (7.9%) luspatercept and placebo pts, respectively (Table B). Among luspatercept pts, 13/153 (8.5%) progressed to HR-MDS/AML during the entire Tx period, compared with 5/76 (6.6%) placebo pts. The total person-years for pts randomized to luspatercept at risk of progressing to HR-MDS/AML was 401.7 y vs 190.9 y for placebo.

Table. Baseline characteristics associated with transitioning to the LTFU study (A). Achievement of RBC-TI ≥16 wk during the entire treatment period (B).

A

	Patients who transitioned to LTFU		Patients who discontinued prior to LTFU	
	Luspatercept (n=52)	Placebo (n=21)	Luspatercept (n=101)	Placebo (n=55)
Duration of treatment, median (IQR), wk	190.0 (86.0–211.0)	24.0 (24.0–25.3)	31.0 (24.0–64.1)	24.0 (24.0–39.0)
Baseline characteristics				
Age, mean (SD), y	68.0 (9.4)	63.2 (13.7)	71.8 (8.0)	73.6 (8.0)
Age category, n (%), y				
≤64	15 (28.8)	8 (38.1)	14 (13.9)	8 (14.5)
65–74	24 (46.2)	9 (42.9)	48 (47.5)	20 (36.4)
≥75	13 (25.0)	4 (19.0)	39 (38.6)	27 (49.1)
Sex, n (%)				
Female	24 (46.2)	8 (38.1)	35 (34.7)	18 (32.7)
Baseline TB, mean (SD), RBC transfusion/ last 8 weeks	4.9 (2.7)	5.7 (2.9)	6.3 (3.0)	6.4 (3.0)
ECOG PS, n (%)				
0	21 (40.4)	11 (52.4)	33 (32.7)	22 (40.0)
1	29 (55.8)	7 (33.3)	62 (61.4)	25 (45.5)
2	2 (3.8)	3 (14.3)	6 (5.9)	8 (14.5)
SF, mean (SD), ug/L	971.23 (705.36)	1209.40 (1027.06)	1542.02 (1033.56)	1616.26 (1307.07)
Serum EPO, mean (SD), U/L	184.92 (170.26)	318.67 (303.00)	327.43 (419.24)	271.48 (476.21)

B

	Luspatercept (N=153)	Placebo (N=76)
Achieved RBC-TI ≥16 wk, n (%)	48 (31.4)	6 (7.9)
95% CI	24.12–39.39	2.95–16.40
Common risk difference in response rate, % (95% CI)	23.37 (14.05–32.69)	
Odds ratio (95% CI)	5.90 (2.34–14.90)	
P value	<0.0001	

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EPO, erythropoietin; LTFU, long-term follow-up; RBC, red blood cell; RBC-TI, RBC transfusion independence; SD, standard deviation; SF, serum ferritin; TB, transfusion burden.

Conclusion:

Pts receiving luspatercept had an extended period of clinical benefit and >50% of pts continued to receive luspatercept for >1 y, the majority of whom underwent dose escalations to achieve an optimal response. Pts experienced durable responses with luspatercept, with a median cumulative duration of RBC-TI response of approximately 20 mo. Pts receiving luspatercept also remained on Tx longer than placebo regardless of participation in the LTFU study, suggestive of luspatercept's clinical benefit with significant durability.

Keyword(s):

Anemia, Clinical trial, Long-term follow-up, Myelodysplastic syndrome