Evaluating the impact of an electronic medical record alert on appropriate dosing of luspatercept in patients with lower-risk myelodysplastic syndromes in a community oncology network

MDS-238

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Introduction

- Myelodysplastic syndromes (MDS) are diagnosed in approximately 10,000 people each year in the United States (US)[1]
- Erythropoiesis-stimulating agents (ESAs) are an established treatment for chronic anemia in patients with lower-risk MDS (LR-MDS) who have serum erythropoietin levels ≤ 500 U/L and who may require transfusion[2]
- Approximately 1 in 3 patients respond to ESAs, with a median duration of response of 6-18 months[3,4]
- Luspatercept is a first-in-class erythroid maturation agent[5]
  - In the phase 3 MEDALIST study (NCT02631070), a significantly greater proportion of patients receiving luspatercept compared with placebo achieved red blood cell transfusion independence (RBC-TI) for ≥ 8 weeks in weeks 1-24 and RBC-TI ≥ 12 weeks in weeks 1-24 and weeks 1-48[6]
  - Based on these results, luspatercept was approved by the US Food and Drug Administration (FDA) in April 2020 for the treatment of anemia in adult patients with very low- to intermediate-risk MDS with ring sideroblasts (MDS-RS) or with MDS/myeloproliferative neoplasm with RS and thrombocytosis after failing to respond to treatment with an ESA and requiring ≥ 2 RBC units over 8 weeks[5]
  - In the phase 3 COMMANDS study (NCT03682536) comparing efficacy in patients treated with luspatercept versus ESA, full analysis results revealed significantly more patients treated with luspatercept compared with ESA achieved RBC-TI (60.4% vs 34.8% respectively; $P < 0.0001$) for ≥ 12 weeks and a median hemoglobin (Hb) increase of 1.5 g/dL[7]
  - In August 2023, the US FDA approved luspatercept as first-line therapy for transfusion-dependent (TD) patients with very low- to intermediate-risk MDS following the results from the COMMANDS study
- Despite evidence supporting dose escalation of luspatercept to achieve better outcomes, recent observational studies indicate that dose escalation is infrequent in clinical practice, and > 50% of patients stop therapy at the starting dose of 1.0 mg/kg[8]

Objective

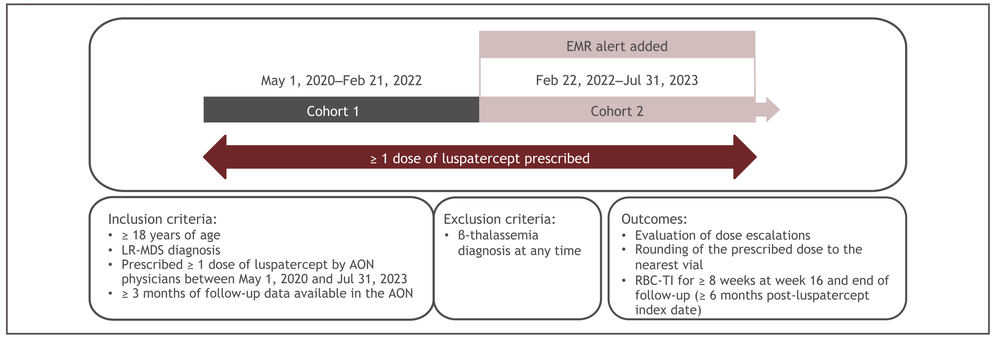
- To investigate the impact of an electronic medical record (EMR) alert on luspatercept dosing patterns, including the suitability of the dose prescribed, dose rounding, and time to reach therapeutic dose

Methods

Study design

- This was a multicenter, retrospective, observational cohort study evaluating patients within the American Oncology Network (AON), which includes > 250 providers across > 40 practices in 21 states
- Data were abstracted from medical charts from the AON EMR database
- Study design and key eligibility criteria are shown in **Figure 1**

Figure 1. Study design



Outcomes

- Evaluation of luspatercept dose escalations, including inappropriate dose escalations (those outside of 1.0, 1.33, or 1.75 mg/kg) measured and compared between cohorts
- Rounding of the prescribed dose to the nearest vial
- RBC-TI for ≥ 8 weeks at week 16 and end of follow-up (≥ 6 months post-luspatercept index date)
  - RBC-TI was defined as having 0 RBC units in the previous 8 weeks and RBC-TD as having ≥ 1 RBC unit in the previous 8 weeks

Statistical analysis

- Comparisons were made between Cohort 1 and Cohort 2 to evaluate the impact of implementing the dosing alert
- Continuous variables (eg, age and Hb level at index date) were described with means and medians, and compared with Wilcoxon rank-sum tests
- Categorical variables (eg, TD and RS status) were described with frequencies and proportions, and compared using chi-square tests or Fisher's exact t-test

Results

Patient characteristics

- A total of 93 patients (Cohort 1, n = 54; Cohort 2, n = 39) who received luspatercept were included in the analysis
- Demographic and clinical characteristics are shown in **Table 1** and were comparable between the cohorts
  - Median age in Cohort 1 vs Cohort 2 was 81.0 vs 76.0 years and 53.7% vs 56.4% were male, respectively
  - Both cohorts had median Hb levels of 8.4 g/dL; TD status (≥ 1 RBC unit in the previous 8 weeks) was 66.7% in Cohort 1 vs 53.8% in Cohort 2, and the proportion of patients with RS presence was 77.8% in Cohort 1 vs 71.8% in Cohort 2
  - The proportion of patients having previously received ESAs was similar (Cohort 1, 81.5%; Cohort 2, 74.4%)

Table 1. Baseline patient demographic and clinical characteristics

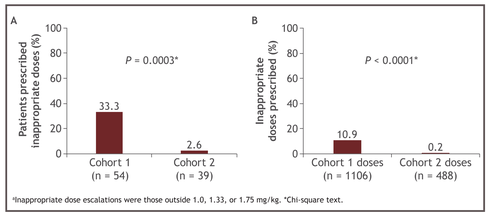
	Cohort 1 (n = 54)	Cohort 2 (n = 39)	*P* value
Age, median (IQR), years	81.0 (75.0-88.0)	76.0 (73.0-83.0)	0.0491[a]
Sex, n (%)			
Male	29 (53.7)	22 (56.4)	0.7958[b]
Female	25 (46.3)	17 (43.6)	
Hb level at index, median (IQR), g/dL	8.4 (7.7-9.3)	8.4 (7.5-9.5)	0.7971[a]
TD[c] at index, n (%)			
Yes	36 (66.7)	21 (53.8)	0.2104[b]
No	18 (33.3)	18 (46.2)	
RS status, n (%)			
Positive	42 (77.8)	28 (71.8)	0.5093[b]
Unknown	12 (22.2)	11 (28.2)	
Previous ESA, n (%)			
Yes	44 (81.5)	29 (74.4)	0.4094[b]
No	10 (18.5)	10 (25.6)	

[a]Wilcoxon rank-sum test; [b]Chi-square test; [c]Defined as ≥ 1 RBC unit in the previous 8 weeks. IQR, interquartile range.

Treatment patterns

- The proportion of patients experiencing inappropriate dosing was significantly higher in Cohort 1 (33.3%) than in Cohort 2 (2.6%); $P = 0.0003$ (**Figure 2A**)
- The proportion of inappropriately prescribed doses in terms of the overall number of doses was higher in Cohort 1 than in Cohort 2 (10.9% vs 0.2%; $P < 0.0001$) (**Figure 2B**)
- Among patients requiring dose escalation (Cohort 1, n = 30; Cohort 2, n = 16), the median time to highest dose in the first 24 weeks was numerically greater in Cohort 1 than in Cohort 2 (15.1 weeks vs 12.1 weeks; $P = 0.5329$) (**Table 2**)
- Dose rounding (**Figure 3**) occurred in more patients in Cohort 1 compared with Cohort 2 (75.9% vs 53.8%; $P = 0.0258$)
- Median drug waste (**Table 2**) was similar between Cohorts 1 and 2 (7.5 mg vs 6.9 mg respectively; $P = 0.9008$)

Figure 2. Inappropriate doses[a] by number of patients (A) total number of doses (B)



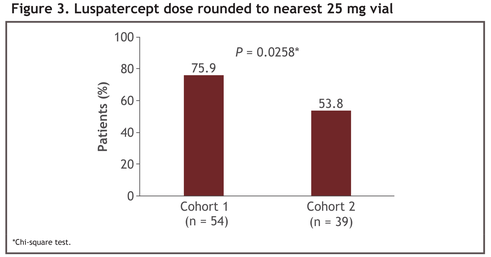
[a]Inappropriate dose escalations were those outside 1.0, 1.33, or 1.75 mg/kg. *Chi-square test.

Table 2. Luspatercept dosing

	Cohort 1 (n = 54)	Cohort 2 (n = 39)	*P* value
Time to reach highest dose administered in the first 24 weeks in patients with any dose escalations,[a] median (min, max), weeks	n = 30[b] 15.1 (3.1, 25.6)	n = 16[b] 12.1 (6.1, 24.1)	0.5329[c]
Maximum dose of 1.75 mg/kg reached, n (%)			
Yes	22 (40.7)	9 (23.1)	0.0746[d]
No	32 (59.3)	30 (76.9)	
Highest dose administered in those not reaching 1.75 mg/kg, n (%)			
1.0	16 (29.6)	20 (51.3)	0.0046[e]
1.25	8 (14.8)	0	
1.33	7 (13.0)	10 (25.6)	
1.5	1 (1.9)	0	
Drug waste, median (min, max), mg	7.5 (0, 23)	6.9 (0, 15.8)	0.9008[c]

[a]Patients with highest luspatercept dose > 1.0 mg/kg; [b]n indicates number of patients requiring dose escalation; [c]Wilcoxon rank-sum test; [d]Chi-square test; [e]Fisher's exact t-test.

Figure 3. Luspatercept dose rounded to nearest 25 mg vial



*Chi-square test.

Treatment outcomes

- The proportion of patients receiving maximum luspatercept dose or achieving RBC-TI at week 16 was lower in Cohort 1 than in Cohort 2 (66.7% vs 82.1%; $P = 0.0987$) (**Table 3**)
- At end of follow-up (≥ 6 months post-luspatercept index date), fewer patients in Cohort 1 achieved/maintained RBC-TI than in Cohort 2 (53.7% vs 61.5%; $P = 0.4514$) (**Table 3**)

Table 3. Treatment outcomes

	Cohort 1 (n = 54)	Cohort 2 (n = 39)	*P* value
Maximum luspatercept dose or RBC-TI at week 16/dose 5, n (%)			
Yes	36 (66.7)	32 (82.1)	0.0987[a]
No	18 (33.3)	7 (17.9)	
RBC-TI at end of follow-up, n (%)			
Yes	29 (53.7)	24 (61.5)	0.4514[a]
No	25 (46.3)	15 (38.5)	

[a]Chi-square test.

Conclusions

- The addition of an EMR alert resulted in a higher proportion of patients being appropriately dosed with luspatercept and enabled > 80% to reach maximum dose/achieve RBC-TI in a real-world setting
- Dose rounding occurred less frequently in patients with an alert on their EMR, indicating more accurate weight-based dosing
- Drug waste was similar between cohorts, suggesting that dose rounding is not associated with reduced drug waste
- EMR interventions may enhance use of an appropriate dose of luspatercept, potentially improving patient outcomes

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