Real-world treatment patterns and outcomes of luspatercept in treatment-naive patients with lower-risk myelodysplastic syndromes in a large US community oncology practice

MDS-1233

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Introduction

- Myelodysplastic syndromes (MDS) are a group of heterogeneous bone marrow failure disorders that manifest as ineffective function of hematopoietic cells, such as cytopenias, which leads to anemia, the need for frequent blood transfusions, and increased risk of infections[1]
- Treatment goals for patients with lower-risk MDS (LR-MDS) include managing anemia; reducing or eliminating transfusion dependency and thereby reducing or eliminating management of related complications, such as iron overload; and improving patient quality of life[2]
- Erythropoiesis-stimulating agents (ESAs) have historically been a mainstay of anemia treatment for patients with LR-MDS; however, up to two-thirds of patients experience primary ESA failure[3,4]
- Luspatercept was approved by the FDA in 2020 for the treatment of anemia in patients with transfusion-dependent LR-MDS after ESA failure, intolerance, or ineligibility
  - In August 2023, the luspatercept label was updated to include the FDA approval of anemia treatment for patients with LR-MDS without previous ESA treatment who may require regular red blood cell transfusion based on the phase 3 COMMANDS trial

Objective

- To describe patient demographics, clinical characteristics, and outcomes of ESA-naive patients with LR-MDS treated with luspatercept

Methods

Study design

- This was a non-interventional, retrospective review of clinical data from electronic medical records of patients treated at the Florida Cancer Specialists & Research Institute, across nearly 100 community oncology sites; data were originally collected during routine care
- Inclusion criteria
  - Diagnosis of LR-MDS at or before luspatercept initiation
    - LR-MDS was defined as an International Prognostic Scoring System (IPSS) score of low or intermediate, or an IPSS-Revised score of very low, low, or intermediate
  - ≥ 18 years of age at diagnosis
  - Received luspatercept treatment as first-line therapy (ie, treatment-naive prior to luspatercept initiation) from June 1, 2023 (corresponding to initial disclosure of the COMMANDS trial[5]) to 12 weeks prior to data extraction
  - Had ≥ 12 weeks of follow-up data available from luspatercept initiation
  - Had ≥ 6 months of data prior to diagnosis
- Exclusion criteria included participation in a clinical trial at any time during the study
- Patients were followed for ≥ 12 weeks from luspatercept initiation until lost to follow-up or death from any cause

Outcomes

- Outcomes of interest were demographic and clinical characteristics as well as clinical outcomes (such as hematologic improvement and transfusion burden)

Data analysis

- Data were analyzed descriptively in the overall population and in the following subgroups:
  - Ring sideroblast (RS) status at diagnosis: RS < 5%, 5% to < 15%, or ≥ 15%
  - Erythropoietin (EPO) level at diagnosis: < 200, 200 to 500, or > 500 IU/L
  - Transfusion occurrence during the 8 weeks prior to luspatercept initiation: 0, 1 to 2, or ≥ 3
  - Mutation burden at diagnosis: 0, 1 to 2, ≥ 3, or unknown

Results

Patient characteristics

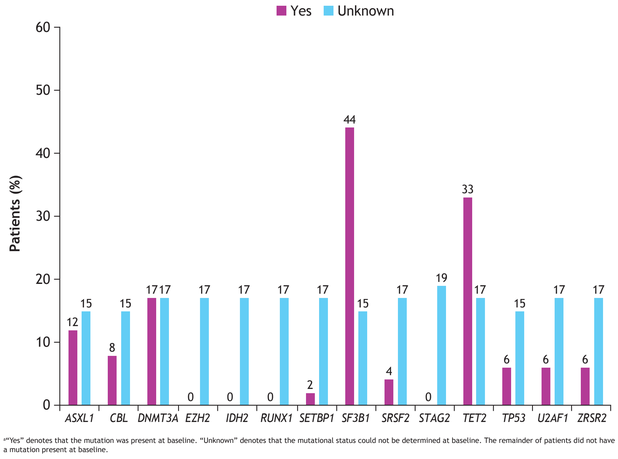
- As of July 2025, 52 patients met the inclusion criteria and were included in analysis
- Baseline demographic and clinical characteristics are shown in **Table 1**
  - Median age at diagnosis was 79 years, 65% of patients were male, and 94% were White
  - 22 patients (42%) had EPO < 200 U/L, although 27 (52%) had unknown EPO status
  - 24 patients (46%) had RS < 5%, 13 (25%) had RS ≥ 15%, and 10 (19%) had unknown or unavailable RS status
    - 9 of the 24 patients with RS < 5% also had EPO < 200 U/L
  - 40 patients (77%) had no red blood cell transfusions in the 8 weeks prior to luspatercept initiation
- 0, 1, 2, or ≥ 3 mutations were identified in 4%, 35%, 36%, and 10% of patients, respectively, and 15% of patients had an unknown mutation burden
  - Details on frequency by mutation can be seen in **Figure 1**
- 15% of patients had no symptoms at baseline; 33% each had 1 or 2 baseline symptoms
- The most common symptoms at baseline were fatigue (79%), shortness of breath (31%), and weakness (25%)

Table 1. Baseline demographic and clinical characteristics

Characteristic	N = 52
Age at MDS diagnosis	
Median (IQR), years	79 (74-84)
Sex, n (%)	
Female	18 (35)
Male	34 (65)
Race, n (%)	
White	49 (94)
Black or African American	1 (2)
Other	2 (4)
Ethnicity, n (%)	
Hispanic or Latino	1 (2)
Not Hispanic or Latino	40 (77)
Unknown	11 (21)
EPO levels at diagnosis, n (%)	
< 200 U/L	22 (42)
200 to 500 U/L	2 (4)
> 500 U/L	1 (2)
Unknown	27 (52)
RS status at diagnosis, n (%)	
< 5%	24 (46)
5 to < 15%	5 (10)
≥ 15%	13 (25)
Unknown	6 (12)
Unavailable	4 (8)
Hemoglobin value ≤ 8 weeks prior to luspatercept initiation[a]	
Median (IQR), g/dL	9.2 (8-10)
RBC transfusion occurrence ≤ 8 weeks prior to luspatercept initiation, n (%)	
0	40 (77)
1 to 2	10 (19)
≥ 3	2 (4)
Time from diagnosis to luspatercept initiation	
Median (IQR), days	20 (8-62)
Duration of follow-up from luspatercept initiation to patient status date	
Median, days	347

[a]Excludes hemoglobin values within 3 days following a transfusion.
EPO, erythropoietin; MDS, myelodysplastic syndromes; RBC, red blood cell; RS, ring sideroblast; U, units.

Figure 1. Mutation burden[a]



[a]"Yes" denotes that the mutation was present at baseline. "Unknown" denotes that the mutational status could not be determined at baseline. The remainder of patients did not have a mutation present at baseline.

Treatment patterns

- All patients received a starting dose of luspatercept of 1 mg/kg
  - Aligning with the luspatercept prescribing information,[6] median time between doses was 3 weeks, but the IQR ranged from 3 to 6 weeks
  - 13 patients (25%) received ≥ 1 dose escalation, 9 patients (17%) received ≥ 1 dose reduction, 3 patients (6%) received both a dose escalation and a dose reduction, and 27 patients (52%) received neither a dose escalation nor a dose reduction
- Most patients (94%) received luspatercept as monotherapy, with the remaining 3 patients (6%) receiving luspatercept in combination with epoetin alfa (n = 2) or azacitidine (n = 1)
- Treatment is ongoing for 35 patients (67%), with a median treatment duration of 57.1 weeks (IQR, 40.1-67.4)
  - 12 patients discontinued treatment, and 3 were lost to follow-up; the median treatment duration of those who discontinued was 18.1 weeks (IQR, 10.8-26.5)
- 10 patients went on to receive second-line treatment (epoetin alfa [n = 5]; azacitidine [n = 2]; and cedazuridine plus decitabine, imetelstat, or lenalidomide [n = 1 each])

Clinical outcomes

- Red blood cell transfusion burden was decreased in 9 of 12 patients (75%) who had red blood cell transfusions prior to starting luspatercept
  - Among patients who received ≥ 1 red blood cell transfusion ≤ 8 weeks prior to treatment initiation, mean change in transfusion burden decreased by 1.25 packed red blood cells within 12 weeks of luspatercept initiation
- 43 patients (83%) achieved a ≥ 1.5 g/dL increase in hemoglobin within 12 weeks of luspatercept initiation, and results were consistent across subgroups (**Table 2**)
- Among all patients, 46 patients (88%) achieved or maintained a ≥ 12-week transfusion-independent period following luspatercept treatment, with consistent results across subgroups (**Table 2**)

Table 2. Clinical outcomes across subgroups

	Hb increase ≥ 1.5 g/dL from baseline within 12 weeks of luspatercept initiation[a,b]	RBC-TI ≥ 12 weeks
Total population (N = 52), n (%)	43 (83)	46 (88)
RS status at diagnosis, n (%)		
< 5% (n = 24)	19 (79)	22 (92)
5% to < 15% (n = 5)	3 (60)	4 (80)
≥ 15% (n = 13)	12 (92)	12 (92)
Unknown or unavailable (n = 10)	9 (90)	8 (80)
EPO level at diagnosis, n (%)		
< 200 U/L (n = 22)	18 (82)	18 (82)
200 to 500 U/L (n = 2)	2 (100)	2 (100)
> 500 U/L (n = 1)	0	0
Unknown (n = 27)	23 (85)	26 (96)
RBC transfusion occurrence ≤ 8 weeks prior to luspatercept initiation, n (%)		
0 (n = 40)	34 (85)	37 (93)
1 to 2 (n = 10)	7 (70)	8 (80)
≥ 3 (n = 2)	2 (100)	1 (50)
Mutation burden at diagnosis, n (%)		
0 (n = 10)	7 (70)	8 (80)
1 to 2 (n = 37)	32 (86)	33 (89)
≥ 3 (n = 5)	4 (80)	5 (100)
Mutation present at diagnosis, n (%)		
SF3B1 (n = 23)	21 (91)	22 (96)
TET2 (n = 17)	16 (94)	16 (94)
SF3B1 and *TET2* (n = 5)	5 (100)	5 (100)

[a]Median (range) time to Hb increase ≥ 1.5 g/dL was 25 days (9-91).
[b]Excludes hemoglobin values within 3 days following a transfusion.
EPO, erythropoietin; Hb, hemoglobin; RBC, red blood cell; RBC-TI, red blood cell-transfusion independent; RS, ring sideroblast; U, units.

Conclusions

- In patients with LR-MDS treated at the Florida Cancer Specialists & Research Institute community oncology sites, luspatercept demonstrated clinical effectiveness of hemoglobin improvement and transfusion independence, with 83% of patients achieving a hemoglobin increase of ≥ 1.5 g/dL within 12 weeks of treatment initiation and 75% of patients with prior red blood cell transfusions demonstrating reduced red blood cell transfusion burden
- Clinical effectiveness of luspatercept was maintained regardless of subgroups categorized by RS status, EPO level, transfusion burden, or mutation burden
- These findings highlight the clinical benefit luspatercept has on treating real-world ESA-naive patients with LR-MDS

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