Treatment patterns and transfusion outcomes among erythropoietin-stimulating agent-naïve patients with lower-risk myelodysplastic syndromes receiving luspatercept in routine clinical practice in the United States

MDS-065

Sudipto Mukherjee,[1] Cherrishe Brown-Bickerstaff,[2] David Huggar,[3] Angelica Falkenstein,[2] Adeola Y. Makinde,[3] Emily Bland,[2] JaLyna Laney,[2] Marné Garretson,[2] Ali McBride[3]

[1]Cleveland Clinic, Cleveland, OH; [2]Cardinal Health Specialty Solutions, Dublin, OH; [3]Bristol Myers Squibb, Princeton, NJ; USA

Introduction

- Lower-risk myelodysplastic syndromes (LR-MDS) are stem cell disorders characterized by ineffective hematopoiesis, progressive cytopenias, and variable risk of progression to acute myeloid leukemia[1-3]
- Erythropoietin-stimulating agents (ESAs) are the standard of care for most patients with LR-MDS[4]
  - However, 50% of patients will not respond and 33% will experience failure within 8 weeks[4-6]
- Luspatercept is a first-in-class erythroid maturation agent approved by the US Food and Drug Administration for the management of anemia following inadequate response to ESAs and requiring ≥ 2 red blood cell (RBC) units over 8 weeks in patients with LR-MDS with ring sideroblasts (RS) or with MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T)[7]
- More than half of ESA-naïve patients treated with luspatercept in the interim efficacy analysis of the phase 3 COMMANDS trial (NCT03682536) achieved transfusion independence (TI) for ≥ 12 weeks and a mean hemoglobin increase of ≥ 1.5 g/dL during weeks 1-24 of luspatercept treatment[8]
- Data on real-world treatment patterns and outcomes of luspatercept among ESA-naïve patients with LR-MDS are currently lacking

Objective

- To examine patient characteristics, treatment patterns, and transfusion outcomes among adults with LR-MDS or MDS/MPN-RS-T who received luspatercept in clinical practice, and who were not treated with ESAs prior to luspatercept treatment in the US

Methods

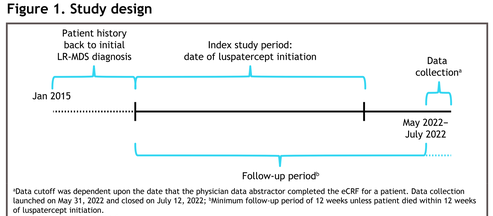
Study design

- This was a retrospective, observational, US cohort study of patients with LR-MDS treated with luspatercept

Patient inclusion criteria

- Diagnosed with LR-MDS, LR-MDS with RS, or MDS/MPN-RS-T on or after January 1, 2015 (**Figure 1**)
- Had an International Prognostic Scoring System (IPSS) score of Low- or Intermediate-1-risk or a Revised IPSS score of Very low, Low, or Intermediate at the time of diagnosis[3]
- Received luspatercept for the treatment of LR-MDS for ≥ 12 weeks (unless < 12 weeks due to patient death)
- Were ≥ 18 years of age at initiation of luspatercept
- Managed by the abstracting physician or by another physician in the same practice for ≥ 1 year before initiation of luspatercept

Figure 1. Study design



[a]Data cutoff was dependent upon the date that the physician data abstractor completed the eCRF for a patient. Data collection launched on May 31, 2022 and closed on July 12, 2022; [b]Minimum follow-up period of 12 weeks unless patient died within 12 weeks of luspatercept initiation.
eCRF, electronic case report form.

Patient exclusion criteria

- Received luspatercept as part of a clinical trial
- Received any treatment for MDS as part of a clinical trial prior to luspatercept initiation
- Received prior treatment with luspatercept for the treatment of ß-thalassemia

Data collection

- De-identified patient data (patient demographics, treatment-related clinical characteristics, treatment patterns, and transfusion outcomes) for eligible patients were abstracted from patient medical records by 24 participating physicians from the Cardinal Health Oncology Provider Extended Network (OPEN) and captured via an eCRF
  - OPEN is a community of > 800 private practice and hospital-based oncologists/hematologists across the US
- Data collection occurred from May 31, 2022 to July 12, 2022 (**Figure 1**)

Data analysis

- A subgroup analysis of patients who did not receive ESA therapy prior to luspatercept treatment was conducted
- Baseline (the 8-week period prior to luspatercept initiation) transfusion burden (TB) was defined based on the lowest number of transfusion sessions (any units of RBCs and/or platelets received in a single day):
  - Non-transfusion dependent (NTD), 0 sessions; low TB, 1-3 sessions; moderate TB, 4-5 sessions; and high TB, ≥ 6 sessions
- Luspatercept duration of treatment was assessed using the Kaplan-Meier method; all other results were summarized using descriptive statistics

Results

Patient demographic and treatment-related characteristics

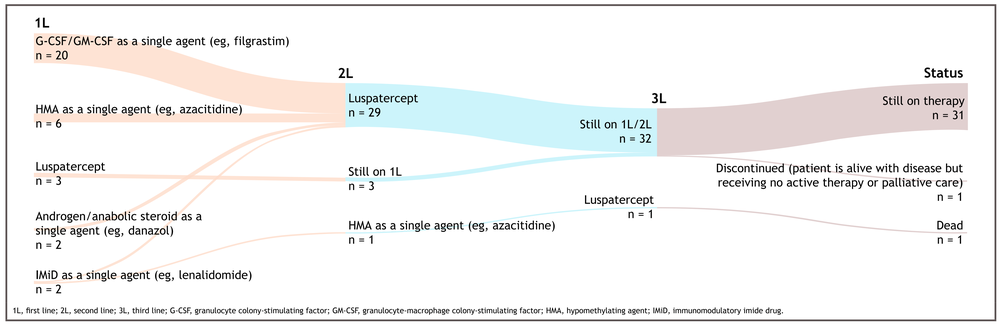
- Data from 33 ESA-naïve patients were included in this analysis (**Table 1**)
- Mean age at luspatercept initiation was 70.1 years (**Table 1**)
- Most patients were male (51.5%), White (78.8%), non-Hispanic/Latino (87.9%), had Medicare coverage (60.6%), and were alive at the time of data collection (97.0%) (Table 1)

Table 1. Patient demographic and treatment-related characteristics[a]

Characteristic	ESA-naïve patients (N = 33)
Age, mean (SD), years	
At diagnosis	68.8 (8.3)
At luspatercept initiation	70.1 (8.2)
Male, n (%)	17 (51.5)
Race, n (%)	
White	26 (78.8)
Black	3 (9.1)
Asian	4 (12.1)
Ethnicity, n (%)	
Hispanic/Latino	4 (12.1)
Non-Hispanic/Latino	29 (87.9)
US region, n (%)	
West	1 (3.0)
South	28 (84.9)
Northeast	1 (3.0)
Midwest	3 (9.1)
Duration of follow-up, median (range), months	4.1 (2.1-13.4)
Baseline TB[b] (8 weeks prior), n (%)	
NTD	1 (3.0)
Low TB	27 (81.8)
Moderate TB	5 (15.2)
High TB	0
Patient status at data collection, n (%)	
Alive	32 (97.0)
Deceased	1 (3.0)
Insurance type, n (%)	
Medicare	20 (60.6)
Commercial	12 (36.4)
Unknown	1 (3.0)

[a]Percentages may not total 100% due to rounding; [b]TB based on transfusion sessions (any units of RBCs and/or platelets in a single day) where NTD = 0 transfusion sessions; low TB = 1-3 transfusion sessions; moderate TB = 4-5 transfusion sessions; high TB = ≥ 6 transfusion sessions. SD, standard deviation.

Figure 2. Treatment sequencing of ESA-naïve patients treated with luspatercept (N = 33)



1L, first line; 2L, second line; 3L, third line; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; HMA, hypomethylating agent; IMiD, immunomodulatory imide drug.

- At baseline, 3.0% of patients were NTD, 81.8% had low TB, and 15.2% had moderate TB (**Table 1**)
- Median duration of follow-up was 4.1 months (**Table 1**)

Treatment patterns

- Treatment sequencing of all ESA-naïve patients is shown in **Figure 2**
- Three patients (9.1%) patients received luspatercept as first-line (1L) therapy, and 30 (90.9%) received ≥ 1 line of therapy prior to luspatercept initiation (**Table 2**), with the most frequent being G-CSF/GM-CSF (n = 20)

Table 2. Treatment patterns[a]

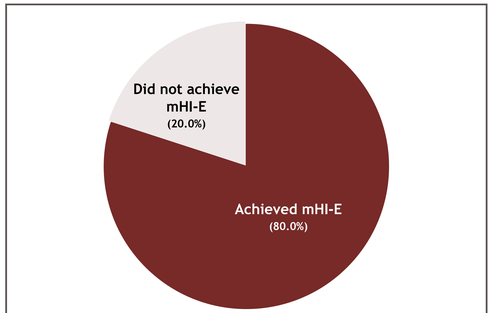
	ESA-naïve patients (N = 33)
No. of treatments received before luspatercept, n (%)	
0	3 (9.1)
1	29 (87.9)
2	1 (3.0)
3	0
Luspatercept treatment therapy status, n (%)	
Still on luspatercept	31 (93.9)
Discontinued luspatercept	2 (6.1)
Primary rationale for discontinuation	
Lack of hematologic improvement (based on hemoglobin levels)	1 (3.0)
Normalization of hemoglobin	1 (3.0)
Luspatercept dose/frequency modifications	
Dose reductions, n (%)	
0	23 (69.7)
1	10 (30.3)
Dose increases, n (%)	
0	31 (93.9)
1	2 (6.1)
Dose holds/interruptions, n (%)	
0	32 (97.0)
1	0
2	0
≥ 3	1 (3.0)

- Most patients had no dose escalations (93.9%), reductions (69.7%), or holds/interruptions (97.0%) (**Table 2**)
- Most patients (93.9%) were still receiving treatment with luspatercept at data collection; however, 2 patients (6.1%) discontinued luspatercept during study follow-up, 1 due to lack of hematologic improvement and 1 due to normalization of hemoglobin (**Table 2**)
  - Data maturity was insufficient to reliably estimate median duration of luspatercept therapy because 93.9% of patients did not experience treatment discontinuation/were censored during study follow-up (**Table 2**)

Transfusion outcomes

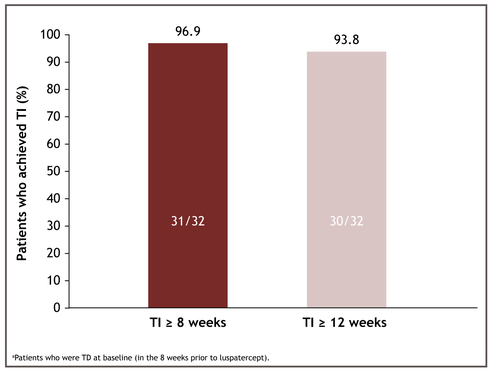
- Among all ESA-naïve patients with a known physician-reported modified hematologic response-erythroid (mHI-E) status (n = 10), 80.0% achieved physician-reported mHI-E and 20.0% did not achieve physician-reported mHI-E (**Figure 3**)
- Among the 32 TD ESA-naïve patients at baseline, 31 (96.9%) achieved TI ≥ 8 weeks, and 30 (93.8%) achieved TI ≥ 12 weeks during luspatercept treatment (**Figure 4**)
- One (3.0%) patient was NTD at baseline and maintained NTD status for TI ≥ 12 weeks during luspatercept treatment

Figure 3. Physician-reported achievement of mHI-E during luspatercept treatment (n = 10[a])



[a]Patients who were TD at baseline (in the 8 weeks prior to luspatercept initiation) with a known mHI-E reported during luspatercept treatment. TD, transfusion dependent.

Figure 4. Achievement of TI during luspatercept treatment (n = 32[a])



[a]Patients who were TD at baseline (in the 8 weeks prior to luspatercept).

Limitations

- This study utilized purposive sampling that selected physicians and patients based on prespecified selection criteria, and thus, findings may not be representative of all patients with ESA-naïve LR-MDS treated with luspatercept in routine clinical practice
- This was an exploratory subgroup analysis with a small sample size and a censoring rate for luspatercept discontinuation of more than 90%
  - Further studies using a larger patient sample of ESA-naïve LR-MDS patients treated with luspatercept with longer follow-up are warranted to estimate treatment pattern outcomes, such as duration of therapy, and confirm generalizability of study findings overall

Conclusions

- This real-world study showed nearly all ESA-naïve patients who were TD at baseline achieved TI for ≥ 8 weeks (96.9%) and for ≥ 12 weeks (93.8%) after initiating luspatercept treatment
- These findings from routine clinical practice provide additional evidence supporting interim results from the COMMANDS trial,[8] which found that luspatercept significantly promoted TI achievement among ESA-naïve patients with LR-MDS

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