Management of patients with lower-risk myelodysplastic syndromes in a large US community oncology practice: a focus on patient outcomes post erythropoiesis-stimulating agent treatment

MDS-276

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Introduction

- Anemia adversely impacts health-related quality of life in patients with lower-risk myelodysplastic syndromes (LR-MDS)[1,2]
- Erythropoiesis-stimulating agents (ESAs) are an established treatment for anemia in patients with LR-MDS[3]
- Approximately 1 in 3 patients respond to ESAs, with a median duration of response of 6-18 months[3,4]
- Furthermore, patients with LR-MDS who are transfusion dependent or have serum erythropoietin (EPO) levels > 500 mU/mL may be less likely to respond to ESAs[5]
- The data on response to ESAs mostly originate from clinical trials, which may not always reflect outcomes in routine clinical practice

Objective

- To describe the real-world characteristics, treatment patterns, and clinical outcomes of patients with LR-MDS treated with ESAs

Methods

Study design

- This was a non-interventional, retrospective review of clinical data from electronic medical records of patients treated at Florida Cancer Specialists & Research Institute (FCS), across nearly 100 community oncology sites throughout Florida; data were originally collected during routine care
- Inclusion criteria:
  - Diagnosis of LR-MDS between January 1, 2018 and December 31, 2022 and initiation of ESA treatment
  - ≥ 18 years of age at diagnosis
  - ≥ 6 months of data prior to diagnosis (baseline period)
  - ≥ 1 year of follow-up data from initial diagnosis
  - LR-MDS was defined as an International Prognostic Scoring System (IPSS) risk score of Low or Intermediate-1, or a revised IPSS (IPSS-R) score of Very low, Low, or Intermediate
- Exclusion criteria:
  - Treated with luspatercept (an erythroid maturation agent) prior to ESA initiation
  - Participated in a clinical trial at any time during the study
- Index date was defined as the date of initial LR-MDS diagnosis
- Patients were followed for ≥ 1 year from initial diagnosis date until loss to follow-up or death from any cause

Outcomes

- Outcomes of interest were demographic and clinical characteristics, clinical outcomes (hematologic improvement, transfusion burden), and treatment patterns (ESA failure, time to ESA failure, time on ESA after ESA failure)
- ESA failure was defined as a < 1.5 g/dL increase in hemoglobin (Hb) level or no decrease in red blood cell (RBC) transfusion requirement after 6–8 weeks of treatment, similar to the definition of no response to ESAs by the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[6]
- Hematologic improvement was defined as an increase in mean Hb ≥ 1.5 g/dL (among patients receiving < 4 RBC units/8 weeks at baseline) or as a reduction of ≥ 4 RBC units transfused (among patients receiving ≥ 4 RBC units/8 weeks at baseline), over 56 consecutive days
- Transfusion burden status was defined as: transfusion independence (TI); low transfusion burden (≤ 3 RBC transfusions for Hb level < 9 g/dL within the 16 weeks prior to LR-MDS diagnosis or 8 weeks prior to ESA initiation); or moderate/high transfusion burden (≥ 4 RBC transfusions for Hb level < 9 g/dL within the 16 weeks prior to LR-MDS diagnosis or 8 weeks prior to ESA initiation)
  - TI was calculated from index date throughout ESA treatment (assessed as a rolling 8-, 12-, 16-, and 24-week TI period during the first 6 months of ESA treatment)

Data analysis

- Data were analyzed descriptively in the overall population and in subgroups by ring sideroblast (RS) status (< 5%, ≥ 5% to < 15%, ≥ 15%) and EPO level at ESA initiation (< 200, 200–500, > 500 U/L)

Results

Patient characteristics

- A total of 359 patients with LR-MDS met the eligibility criteria and were included
- Baseline demographic and clinical characteristics are shown in **Table 1**
  - Median age at diagnosis was 79.0 years, 65.2% were male, and 88.0% were White
  - 59.3% of patients had RS < 5% and 22.8% had RS ≥ 15%

Table 1. Baseline demographic and clinical characteristics at diagnosis

Characteristic, n (%)	Patients with LR-MDS (N = 359)
Age, median (Q1, Q3), years	79.0 (74.0, 84.0)
Sex	
Female	125 (34.8)
Male	234 (65.2)
Race	
White	316 (88.0)
Black or African American	3 (0.8)
Asian	1 (0.3)
Other	35 (9.8)
Unknown	4 (1.1)
IPSS risk score	
Low	137 (38.2)
Intermediate-1	120 (33.4)
IPSS-R risk score	
Very low	38 (10.6)
Low	63 (17.6)
Intermediate	1 (0.3)
RS status	
< 5%	213 (59.3)
≥ 5% to < 15%	20 (5.6)
≥ 15%	82 (22.8)
Unknown	44 (12.3)

Q, quartile.

- At ESA initiation (**Table 2**):
  - Most patients had an Hb level of 8–10 g/dL (61.0%) and an EPO level < 200 U/L (58.8%)
  - 80.8% of patients had been RBC-TI for 8 weeks prior to ESA initiation

Table 2. Clinical characteristics at ESA initiation

Characteristic, n (%)	Patients with LR-MDS (N = 359)
Hb, g/dL	
< 8	45 (12.5)
8–10	219 (61.0)
> 10	85 (23.7)
Unknown	10 (2.8)
EPO, U/L	
< 200	211 (58.8)
200–500	22 (6.1)
> 500	10 (2.8)
Unknown	116 (32.3)
Transfusion burden[a] at ESA initiation	
TI	290 (80.8)
Low	67 (18.7)
Moderate/high	2 (0.6)
Year of ESA initiation[b]	
2017	1 (0.3)
2018	46 (12.8)
2019	65 (18.1)
2020	75 (20.9)
2021	73 (20.3)
2022	84 (23.4)
2023	15 (4.2)

[a]Low transfusion burden was defined as ≤ 3 RBC transfusions for Hb < 9 g/dL within the 8 weeks prior to ESA initiation; moderate/high transfusion burden was defined as ≥ 4 RBC transfusions for Hb < 9 g/dL within the 8 weeks prior to ESA initiation. [b]Patients in the analysis were required to receive a diagnosis of LR-MDS between 2018-2022, with no requirement for the timeframe of receiving ESA treatment.

Clinical outcomes

- Hematologic improvement was observed in 33.7% of patients, and 83.6% of patients achieved RBC-TI for ≥ 8 weeks in the first 6 months following ESA initiation (**Table 3**)

Table 3. Clinical outcomes after ESA initiation

Outcomes, n (%)	Patients with LR-MDS (N = 359)
Hematologic outcomes[a]	
Improvement	121 (33.7)
Reduction in RBC units transfused[b]	37 (10.3)
Increase in mean Hb level ≥ 1.5 g/dL[c]	84 (23.4)
No improvement	238 (66.3)
RBC-TI in first 6 months (rolling weeks)[d]	
8	300 (83.6)
16	284 (79.1)
26	265 (73.8)

[a]Categories are mutually exclusive; no improvement denotes patients who did not experience hematologic improvement during a rolling consecutive 56 days; [b]in patients receiving ≥ 4 RBC units/8 weeks at baseline (regardless of their mean Hb value); [c]in patients receiving < 4 RBC units/8 weeks at baseline and have a mean Hb increase of ≥ 1.5 g/dL over 56 consecutive days; [d]TI was calculated from index date throughout ESA treatment (assessed as a rolling 8-, 12-, 16-, and 24-week TI period during the first 6 months of ESA treatment). Rolling weeks defines a period of consecutive weeks within a specific date range; patients may be included in multiple categories.

Treatment patterns

- A total of 32.0% of patients had an ESA response and 68.0% experienced ESA failure (**Figure 1**)
  - Among those experiencing ESA failure, 91.6% did so within 60 days of ESA initiation
  - Mean time to ESA failure was 58 days
- The proportion of patients experiencing ESA failure was high regardless of RS status and EPO level
  - Median time to ESA failure was similar across subgroup categories (**Table 4**)

Figure 1. Proportion of patients with ESA failure overall and by subgroup

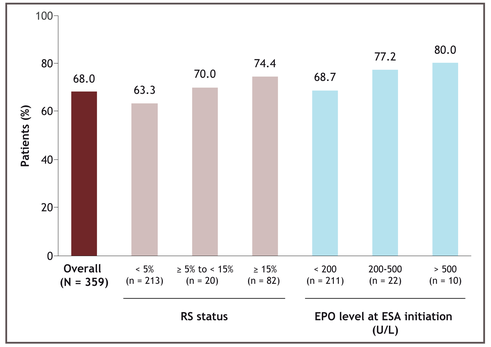
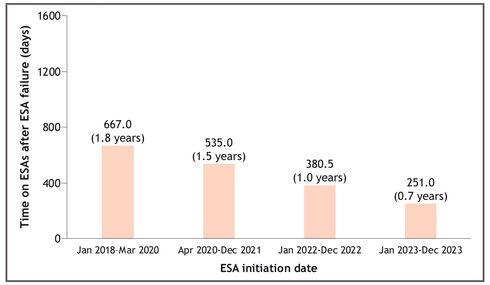


Table 4. Time to ESA failure overall and by subgroup

Time to ESA failure, median (range), days	Patients with ESA failure (n = 244)
Overall	56.0 (42.0-308.0)
RS status at diagnosis	
< 5%	56.0 (42.0-308.0)
≥ 5% to < 15%	56.0 (42.0-218.0)
≥ 15%	56.0 (42.0-203.0)
EPO, U/L	
< 200	56.0 (42.0-308.0)
200–500	56.0 (42.0-56.0)
> 500	54.5 (42.0-56.0)

- The average time that patients remained on ESA treatment after failure was 604 days (1.7 years), and 64.0% of patients remained on ESAs for > 365 days after failure
- Time spent on treatment after ESA failure was shorter in later study periods (**Figure 2**)

Figure 2. Time on ESA after ESA failure by ESA initiation date, median number of days



Conclusions

- In this real-world study, patients with LR-MDS showed a high rate of ESA failure (68.0%), with most patients experiencing failure within 60 days of ESA initiation
  - Rates of ESA failure were also high in key subgroups by RS status and EPO level
- Following ESA failure, 64.0% of patients remained on ESA therapy for > 1 year
  - Patients who experienced ESA failure but remained on ESAs for other health reasons were not accounted for
  - However, patient care may be optimized by switching treatments sooner after identified ESA failure
- Only 33.7% of patients experienced hematologic improvement with ESA treatment and only 10.3% of patients had a reduction in RBC units transfused
  - There was minimal change in TI prior to and during ESA treatment
- This study used retrospective data documented during patient care, which may be incomplete, especially if patients received additional care outside of the FCS
- These findings suggest that ESAs may not be effective at increasing Hb levels in many patients with LR-MDS, and additional treatment options are needed

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