Clinical outcomes and healthcare resource utilization in patients with lower-risk myelodysplastic syndromes reinitiating erythropoiesis-stimulating agents (ESAs) following previous ESA treatment

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Introduction

- Myelodysplastic syndromes (MDS) are a group of stem cell disorders characterized by impaired hematopoiesis, peripheral cytopenias such as anemia, and risk of progression to acute myeloid leukemia (AML)[1]
- Most patients with MDS are diagnosed with lower-risk (LR)-MDS, defined according to the International Prognostic Scoring System (IPSS) or Revised IPSS (IPSS-R) metrics[2]
- LR-MDS-related anemia can lead to red blood cell transfusion dependence, which impacts patient survival (median survival estimated to be 5-10 years[2]) and health-related quality of life[3,4]
- Erythropoiesis-stimulating agents (ESAs) are utilized as first-line treatment for anemia in LR-MDS;[1] however, real-world treatment patterns, clinical outcomes, and healthcare resource utilization (HCRU) for patients with LR-MDS are not well-established

Objective

- To examine real-world treatment patterns, clinical outcomes, including overall survival (OS), and HCRU, in a cohort of LR-MDS patients and in a subgroup of patients with LR-MDS who discontinued and reinitiated ESA therapy

Methods

Data source

- A retrospective cohort study of patients with LR-MDS receiving ESA treatment in the Syapse Learning Health Network, which includes records of patients with cancer who receive care in the US community health system setting
- This study utilized secondary data manually curated from patient electronic medical records (EMRs) by certified tumor registrars

Inclusion criteria

- Patients diagnosed with LR-MDS who received ≥ 1 ESA treatment (as first-line therapy) between January 1, 2016 and June 30, 2019
  - LR defined according to IPSS (Low, Intermediate-1) or IPSS-R (Very low, Low, or Intermediate [prognostic score ≤ 3.5]), or as documented by a physician in the patient's EMR, or computed through evaluation of curated individual prognostic factors
- Patients had ≥ 2 distinct clinical encounters (defined as any evidence of interaction with the health system), with ≥ 1 encounter subsequent to the initiation of ESA therapy

Exclusion criteria

- Treatment with: an ESA prior to MDS diagnosis; luspatercept or lenalidomide at any time during follow-up; any of the following prior to initiating ESA therapy: granulocyte colony-stimulating factors (G-CSF), hypomethylating agents (HMAs), thrombopoietin receptor agonists, immunosuppressive therapies, androgens
- Hematopoietic stem cell/bone marrow transplantation (HSCT/BMT) after LR-MDS diagnosis and prior to initiating ESA therapy

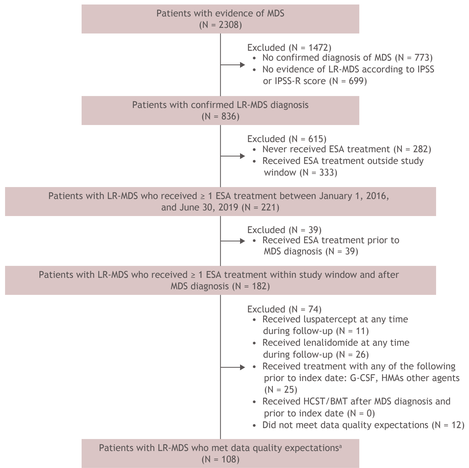
Statistical analysis

- Patients were followed from the time of ESA initiation (index date) until the corresponding outcome/event of interest, progression to higher-risk MDS or AML, death, date of last contact (defined as a health system interaction that provides evidence of vital status), or end of study period (June 30, 2021), whichever occurred first
- Descriptive statistics were used in the analysis: frequencies and proportions are reported for categorical variables, and median and interquartile range (IQR) are reported for continuous variables
- Categories for missing values were created and included in the analysis
- Kaplan-Meier product-limit estimator was used to evaluate OS
- Analyses were conducted in all patients and for the subgroup of patients who discontinued and reinitiated ESA therapy

Results

- Of the 2308 patients with evidence of MDS, 108 had LR-MDS and initiated ESA therapy within the study window (**Figure 1**)

Figure 1. CONSORT flow diagram



[a]Patients who meet data quality expectations are those who have all data elements required for inclusion in the analysis.

Patient characteristics

- Patients had a median age of 79 years at diagnosis (IQR 73-85), were predominantly male (58%), White (97%), and overweight or obese (52%) (**Table 1**)
- The median follow-up period was 17.0 months (IQR 7.2-34.7)

Distribution of ESA therapy

- The most commonly used ESA was darbepoetin alfa (60% of patients), followed by epoetin alfa (38%) and epoetin alfa-epbx (2%) (**Table 2**)
- 56% of patients discontinued and reinitiated ESA therapy
- Examples of patient treatment journeys for those who discontinued and reinitiated ESA therapy are shown in **Figure 2**

Patient outcomes by end of follow-up

- Of the 33 patients with ≥ 1 baseline transfusion, 52% did not achieve transfusion independence (TI; **Table 3**); 53% and 43% did not achieve TI at 6 and 12 months, respectively
- Among the 61 patients who discontinued and reinitiated ESA therapy, 2% progressed to AML
- Median OS for patients who discontinued and reinitiated ESA therapy was 45 months (**Figure 3**)

Table 1. Demographic and clinical characteristics

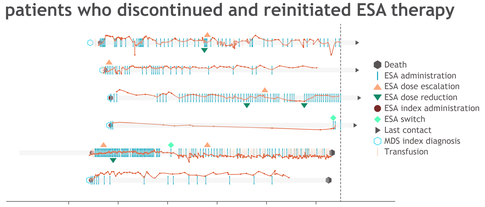
	All patients (N = 108)	Patients who discontinued and reinitiated ESA therapy (N = 61)
Follow-up time, median (IQR), months	17.0 (7.2-34.7)	27.2 (13.8-44.6)
Age at LR-MDS diagnosis, median (IQR), years	79 (73-85)	79 (72-84)
Male, n (%)	63 (58)	37 (61)
BMI categories, n (%)		
Underweight/normal (< 25.0 kg/m^2)	34 (31)	19 (31)
Overweight (25.0 to < 30.0 kg/m^2)	32 (30)	16 (26)
Obese - Class 1 (30.0 to < 35.0 kg/m^2)	15 (14)	11 (18)
Obese - Class 2 (35.0 to < 40.0 kg/m^2)	8 (7)	4 (7)
Obese - Class 3 (≥ 40.0 kg/m^2)	1 (1)	1 (2)
Unknown	18 (17)	10 (16)
Primary race, n (%)		
White	105 (97)	60 (98)
Black/African American	2 (2)	1 (2)
Asian	1 (1)	0

BMI, body mass index.

Table 2. Distribution of initial ESA therapy

Initial ESA received, n (%)	All patients (N = 108)	Patients who discontinued and reinitiated ESA therapy (N = 61)
Darbepoetin alfa	65 (60)	32 (52)
Epoetin alfa	41 (38)	28 (46)
Epoetin alfa-epbx	2 (2)	1 (2)

Figure 2. Patient journey examples for subgroup of patients who discontinued and reinitiated ESA therapy



Each row corresponds to a different patient treatment journey.
Each red dot corresponds to a hemoglobin measure; the red line connecting the dots depict the pattern of hemoglobin levels for a given patient over time.

Table 3. Patient outcomes by end of follow-up

	All patients (N = 108)	Patients who discontinued and reinitiated ESA therapy (N = 61)
Transfusion dependent at ESA initiation, n (%)		
No	75 (69)	44 (72)
Yes	33 (31)	17 (28)
Failure to achieve TI (among transfusion-dependent patients), n (%)	n = 33	n = 17
No	16 (48)	12 (71)
Yes	17 (52)	5 (29)
Progression to AML, n (%)		
No	103 (95)	60 (98)
Yes	5 (5)	1 (2)
Vital status during follow-up, n (%)		
Alive	55 (51)	32 (52)
Deceased	53 (49)	29 (48)

Figure 3. OS among patients who discontinued and reinitiated ESA therapy

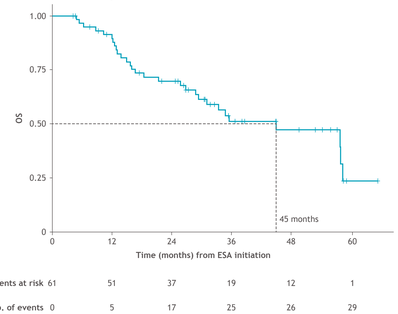


Table 4. HCRU during follow-up

	All patients (N = 108)	Patients who discontinued and reinitiated ESA therapy (N = 61)
Number of health system visits per patient-month of follow-up, median (IQR)	3.7 (0.71-7.5)	3.2 (0.6-4.9)
Patients with ≥ 1 outpatient visit, n (%)	90 (83)	54 (89)
Patients with ≥ 1 emergency department visit, n (%)	52 (48)	38 (62)
Patients with ≥ 1 inpatient visit, n (%)	75 (69)	44 (72)
Total length of hospitalization(s), median (IQR), days	10.0 (4.0-20.5)	12.0 (4.8-27.8)
Immunosuppressive therapy, n (%)	1 (1)	1 (2)
Treatment with antibiotics, n (%)	59 (55)	33 (54)
Iron chelation therapy, n (%)	3 (3)	2 (3)

HCRU during follow-up among patients who discontinued and reinitiated ESA therapy

- The median number of health system visits per patient-month was 3.2 (IQR 0.6-4.9) (**Table 4**)
- 89%, 62%, and 72% of patients had ≥ 1 outpatient, emergency department, or inpatient visit, respectively, with median length of hospitalization 12 days (IQR 4.8-27.8)
- Most patients (54%) received an antibiotic at least once during follow-up; use of immunosuppressive therapy (2%) or iron chelation (3%) was rare (**Table 4**)

Limitations

- This study is limited by the utilization of secondary data derived from EMRs; reliance upon accurate and complete records
- As the prevalence of LR-MDS is low in the general population, the study size is small
- This study was conducted in patients receiving care within a community health setting in the USA; therefore, results may not be generalizable to other healthcare settings or countries

Conclusions

- In this real-world study of community practice in the USA, reinitiation of ESA treatment after prior discontinuation in LR-MDS was prevalent
- The frequency of ESA-treated patients with LR-MDS who did not achieve TI and the demonstrated burden on health systems suggest the need to consider alternative treatment and management options for patients with LR-MDS

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Disclosures

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