Real-world impact of luspatercept versus erythropoiesis-stimulating agents on the healthcare resource utilization of patients with myelodysplastic syndromes in the United States

MDS-059

Brian J. Ball,[1] Rui Song,[2] Enrico Zanardo,[3] Lynn Huynh,[2] Manasi Mohan,[2] Megan Pinaire,[2] Derek Tang,[4] Mihran Yenikomshian,[2] Ashley Swanson,[4] Svetlana Gavrilov,[4] Samantha Slaff[4]

[1]Department of Hematology & Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, CA; [2]Analysis Group, Inc., Boston, MA; [3]Analysis Group, Inc., Denver, CO; [4]Bristol Myers Squibb, Princeton, NJ; USA

Introduction

- Myelodysplastic syndromes (MDS) are a group of hematologic malignancies characterized by ineffective hematopoiesis, persistent cytopenias, and risk of progression to acute myeloid leukemia (AML)[1,2]
- Patients with MDS often require frequent red blood cell (RBC) transfusions for the treatment of anemia[1]
  - Erythropoiesis-stimulating agents (ESAs) are an established treatment for lower-risk (LR)-MDS associated anemia; however, some patients do not respond, or stop responding to ESAs, and become transfusion dependent (TD), which is associated with increased healthcare resource utilization (HRU)[3,4]
- Luspatercept can effectively reduce transfusion burden (TB) in patients with LR-MDS who are ESA-naive or after failing an ESA[5,6]
  - Luspatercept was approved in the United States (US) in August 2023 for the treatment of anemia in ESA-naive patients, and in April 2020 for patients who have failed an ESA[7,8]
- Real-world evidence regarding the effectiveness of luspatercept versus ESAs on HRU among patients with MDS is limited

Objective

- To compare HRU among patients with MDS treated with luspatercept or ESAs in US clinical practice

Methods

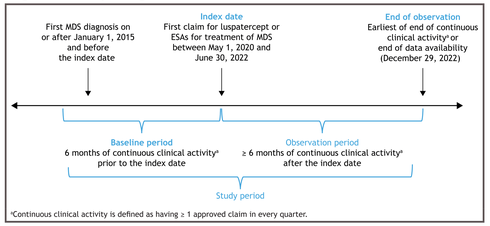
Data source

- This retrospective claims-based cohort study used data from the Symphony Health database[9,10]
- Symphony Health is a de-identified, provider-sourced, open-claims database representing US patients across a range of payers (eg, Medicare, Medicaid, commercial, and cash), providing information on demographic and clinical characteristics, as well as prescription and medical claims

Study design (Figure 1)

- Patient identification window for initiating luspatercept or ESAs was May 1, 2020 to June 30, 2022
- The index date was the date of first claim for luspatercept or ESAs
- The baseline period was defined as the 6 months before the index date
- The follow-up period ranged from the index date to the end of clinical activity or data availability (December 29, 2022) and was ≥ 6 months

Figure 1. Study design



[a]Continuous clinical activity is defined as having ≥ 1 approved claim in every quarter.

Study population

- Inclusion criteria
  - Both cohorts: ≥ 1 inpatient (IP) claim or ≥ 2 outpatient (OP) claims with a diagnosis of MDS (initial diagnosis on or after January 1, 2015) before the first claim for luspatercept treatment for the luspatercept cohort or ESA treatment for the ESA cohort, which defines the index date; ≥ 18 years of age on the index date; ≥ 6 months of clinical activity prior to and after the index date
  - Luspatercept cohort: no claim for ESAs in the 6 months before or on the index date
  - ESA cohort: no claim for luspatercept at any time
- Exclusion criteria for both cohorts
  - Any claims with other MDS treatments (hypomethylating agents [HMAs], granulocyte colony-stimulating factor [G-CSF], or immunomodulatory drug [IMiD] agents) in the 6 months prior to or on the index date
  - Diagnosis for AML or use of chemotherapy at any time during the study period, or diagnosis for refractory anemia with excess blasts (RAEB) before or on the index date (presumed to have high-risk MDS)
  - Diagnosis for β-thalassemia, myelofibrosis, aplastic anemia, or breast cancer during the baseline period

Study measures and outcomes

- Patient demographics and clinical characteristics were assessed during the baseline period and on the index date
  - A patient was non-TD (NTD) if they had 0 unique dates with transfusions in the 8-week period on/before the index date; a patient was TD if they had ≥ 1 unique date with transfusions in the 8-week period on/before index date
  - Charlson Comorbidity Index (CCI) comorbidities and MDS-related conditions were assessed using the total data availability on or prior to the index date
  - HRU was assessed during the 6-month baseline period and annualized to per-patient-per-year (PPPY)
- All-cause HRU included IP admissions, OP visits, and other/unknown visits
- MDS-related HRU was identified as HRU encounters with a diagnosis code in any position for MDS, anemia, neutropenia, or thrombocytopenia

Statistical analysis

- The rate of all-cause and MDS-related HRU was analyzed using descriptive statistics and reported on a PPPY basis by dividing the number of visits during the observation period by the observation period length (in years) per patient
- The rate of all-cause and MDS-related HRU was compared between cohorts using incidence rate ratios (IRRs), with 95% confidence intervals (CIs), and *P* value estimates from generalized estimating equations models with Poisson distribution and robust variance estimator
  - Comparative models were adjusted for age at index, sex, region, baseline CCI score, baseline, and baseline HRU to account for confounders

Results

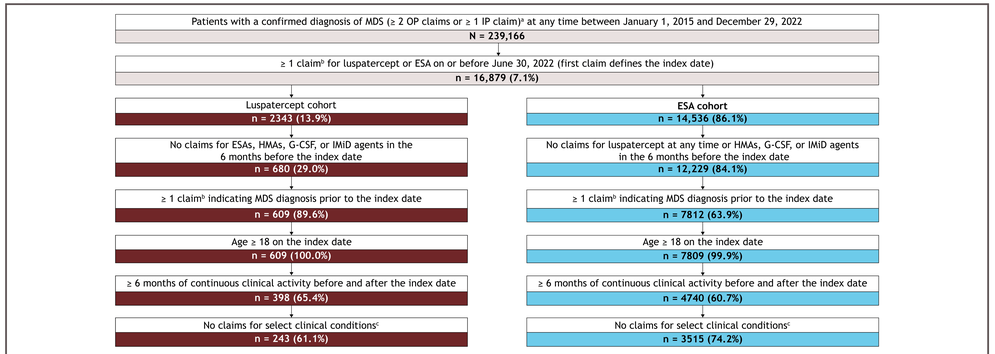
Sample selection

- Overall, 3758 patients were included in the study (n = 243 in the luspatercept cohort; n = 3515 in the ESA cohort) (**Figure 2**)

Patient baseline characteristics

- The median (interquartile range [IQR]) follow-up time was 14.6 (10.4-22.6) months in the luspatercept cohort and 14.4 (9.5-20.9) months in the ESA cohort (**Table 1**)

Figure 2. Sample selection



[a]Patients with ≥ 2 diagnosis claims for MDS during the study period were included, even if place of service was designated as other, unknown, or missing; [b]For prescription claims, only approved claims were used; [c]The following clinical conditions were excluded: a) Diagnosis of β-thalassemia, myelofibrosis, aplastic anemia, or breast cancer during the baseline period; b) Diagnosis of AML or treatment with chemotherapy during the full data availability; c) Diagnosis of RAEB on or before the index date.

Table 1. Patient baseline characteristics

	Luspatercept cohort (n = 243)	ESA cohort (n = 3515)
Age at index date, years		
Mean (SD)	73.6 (7.3)	74.4 (7.7)
Median (IQR)	77.0 (70.0-79.0)	78.0 (72.0-79.0)
Male sex, n (%)	147 (60.5)	1916 (54.5)
Follow-up time, months		
Mean (SD)	16.4 (7.2)	15.6 (7.1)
Median (IQR)	14.6 (10.4-22.6)	14.4 (9.5-20.9)
Time from first MDS diagnosis to index date, months		
Mean (SD)	25.0 (19.9)	13.9 (18.9)
Median (IQR)	22.3 (7.5-39.1)	4.4 (0.8-20.7)
Index treatment, n (%)[a]		
Luspatercept	243 (100)	0
Darbepoetin alfa	0	1092 (31.1)
Epoetin alfa	0	690 (19.6)
Epoetin alfa-epbx	0	1594 (45.3)
Epoetin beta	0	141 (4.0)
CCI score		
Mean (SD)	3.3 (2.9)	4.2 (2.9)
Median (IQR)	3.0 (1.0-5.0)	4.0 (2.0-6.0)
MDS-related conditions, n (%)		
Anemia	235 (96.7)	3456 (98.3)
Hypertension	171 (70.4)	2980 (84.8)
Dyspnea	126 (51.9)	1869 (53.2)
Fatigue	114 (46.9)	1538 (43.8)
Chest pain	91 (37.4)	1467 (41.7)
Weakness	74 (30.5)	1286 (36.6)
All-cause HRU, mean (SD), PPPY		
IP admissions	1.0 (2.6)	1.6 (3.2)
OP visits	23.5 (24.2)	21.8 (25.5)
Other visits	3.8 (13.3)	6.6 (24.3)
Unknown visits	6.8 (12.9)	4.6 (8.8)
RBC transfusion status, n (%)		
NTD	167 (68.7)	3005 (85.5)
TD	76 (31.3)	510 (14.5)
1 transfusion	22 (28.9)	297 (58.2)
2 or 3 transfusions	38 (50.0)	171 (33.5)
≥ 4 transfusions	16 (21.1)	42 (8.2)

[a]Patients in the ESA cohort could have received ≥ 1 type of ESA at the index date.
SD, standard deviation.

- Median (IQR) age was 77.0 (70.0-79.0) years in the luspatercept cohort and 78.0 (72.0-79.0) years in the ESA cohort
- The mean (SD) time from first MDS diagnosis to index date was 25.0 (19.9) months in the luspatercept cohort and 13.9 (18.9) months in the ESA cohort
- At treatment initiation, 68.7% of patients in the luspatercept cohort and 85.5% in the ESA cohort were NTD
- **Table 2** presents the descriptive rates of all-cause and MDS-related HRU after treatment initiation
  - The mean (SD) for all-cause IP admissions was 1.1 (2.0) PPPY for the luspatercept cohort and 1.4 (2.6) PPYY for the ESA cohort, and for all-cause OP visits was 23.5 (23.1) PPPY for the luspatercept cohort and 33.9 (39.9) PPPY for the ESA cohort
  - The mean (SD) for MDS-related IP admissions was 0.8 (1.9) PPPY for the luspatercept cohort and 0.9 (2.2) PPPY for the ESA cohort, and for MDS-related OP visits was 14.3 (15.8) PPPY for the luspatercept cohort and 14.6 (16.6) PPPY for the ESA cohort

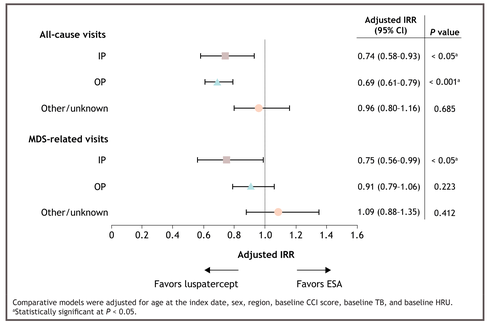
Table 2. Post-index HRU by treatment group

	Luspatercept cohort (n = 243)	ESA cohort (n = 3515)
All-cause HRU, mean (SD), PPPY[a]		
IP admissions	1.1 (2.0)	1.4 (2.6)
OP visits	23.5 (23.1)	33.9 (39.9)
Other/unknown visits	12.9 (19.6)	14.1 (24.9)
Other visits	5.5 (17.1)	7.1 (22.3)
Unknown visits	7.5 (11.8)	7.0 (13.3)
MDS-related[b] HRU, mean (SD), PPPY[b]		
IP admissions	0.8 (1.9)	0.9 (2.2)
OP visits	14.3 (15.8)	14.6 (16.6)
Other/unknown visits	8.2 (11.6)	7.8 (13.2)
Other visits	1.2 (4.3)	1.3 (4.4)
Unknown visits	7.0 (11.2)	6.6 (12.7)

[a]HRU was assessed during the total available follow-up time and annualized to PPPY; [b]Claims with MDS, anemia, neutropenia, or thrombocytopenia diagnosis codes in any position were considered *MDS-related*.

- All-cause IP admission and OP visit rates were significantly lower among patients treated with luspatercept than with ESAs, with a 26% lower rate of IP admissions and a 31% lower rate of OP visits (**Figure 3**)
- MDS-related IP admission rates were also significantly lower in the luspatercept cohort while MDS-related OP visits were numerically lower in the luspatercept cohort with a 25% lower rate of IP admissions and a 9% lower rate of OP visits (**Figure 3**)

Figure 3. Post-index HRU: luspatercept versus ESAs



Comparative models were adjusted for age at the index date, sex, region, baseline CCI score, baseline TB, and baseline HRU.
[a]Statistically significant at $P < 0.05$.

Conclusions

- This study showed a significantly lower rate of all-cause IP admissions and OP visits among patients with MDS receiving luspatercept versus ESAs in US clinical practice
  - Rates of MDS-related IP admissions were also significantly lower with luspatercept, and rates of OP visits were numerically lower with luspatercept versus ESAs
- This study was conducted in an administrative claims database and may not be generalizable to uninsured populations; claims data have the potential for missing or misclassified HRU encounters, although this would likely affect both cohorts similarly
- Future real-world studies with larger sample sizes are needed to further assess the differential effectiveness of luspatercept versus ESAs overall and among clinically relevant subgroups of patients with MDS

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