# First-line treatment patterns and outcomes among patients with newly diagnosed myelodysplastic syndromes: a global, retrospective observational cohort study

MDS-067

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## Introduction

- Patients with myelodysplastic syndromes (MDS) often require ongoing red blood cell transfusions (RBCTs) to relieve anemia related to ineffective erythropoiesis[1]
- For patients with lower-risk (LR)-MDS, treatment goals focus on the treatment of anemia and reduction in transfusion burden[2,3]
- Understanding existing treatment patterns and their associated outcomes can help tailor clinical management to patients' needs as new treatments are introduced[1,4]
- Real-world first-line (1L) treatment patterns for LR-MDS are not well understood in the context of patient characteristics, treatment duration, and subsequent clinical outcomes

## Objective

- To describe the characteristics, 1L treatment patterns, and clinical outcomes of patients with LR-MDS in United States (US) and European Union (EU) cohorts

## Methods

### Study design

- This was a retrospective study of adults (≥ 18 years of age) receiving 1L systemic treatment for LR-MDS after 2014
  - Patient data came from COTA Vantage data (US) and BC Platforms (EU; Estonia, Poland, and Greece)
- The index date (baseline) was the date of the first systemic therapy for MDS after diagnosis
- Eligible patients had Revised International Prognostic Scoring System classification of Very low-, Low-, or Intermediate-risk MDS and < 5% blasts in bone marrow, serum erythropoietin (EPO) level < 500 U/L (or had a missing value), and Eastern Cooperative Oncology Group performance status (ECOG PS) 0–2 on or before the index date
  - Subgroups of interest included patients who received erythropoiesis-stimulating agents (ESAs) in 1L (single or combination therapy) or other 1L treatments (any non-ESA systemic therapy)
- Patient characteristics, treatment patterns, time to and duration of first hemoglobin (Hb) increase ≥ 1.5 g/dL, rates of secondary hematologic malignancies (hematologic malignancy developed after MDS diagnosis excluding acute myeloid leukemia [AML] eg, non-follicular lymphoma, Hodgkin lymphoma, and follicular lymphoma), and progression to higher-risk (HR) MDS or AML were assessed using descriptive statistics

## Results

### Patient demographics and characteristics

- A total of 421 patients were included (US cohort, n = 351; EU cohort, n = 70) (**Table 1**)
- Overall, median age was 75 years, 43% were female, and 85% were White; characteristics were generally similar for US and EU patients
  - Nearly all patients had an ECOG PS ≤ 1 (81%)
  - Prevalence of overweight and obese patients were higher in the US than the EU cohort

### Clinical characteristics by 1L treatment patterns

- In the overall population, 77% (324/421) of patients received an ESA in 1L and 23% (97/421) received other 1L treatment
- Mean (standard deviation; SD) pre-index Hb levels were low in both the ESA in 1L group 9.0 (1.1) g/dL and the other 1L treatment group 9.9 (2.0) g/dL (**Table 2**)
- The median time from MDS diagnosis to 1L treatment was similar for both groups (**Table 2**)

**Table 1. Baseline patient demographics and characteristics**

| Characteristic | All patients (N = 421) | US patients (n = 351) | EU patients (n = 70) |
|---|---|---|---|
| **Age, median (range), years** | 75.0 (37.0-93.0) | 75.0 (37.0-93.0) | 74.0 (40.0-92.0) |
| **Sex** | | | |
| Female, n (%) | 181 (43) | 146 (42) | 35 (50) |
| **Race, n (%)** | | | |
| White | 359 (85) | 289 (82) | 70 (100) |
| Black or African American | 17 (4) | 17 (5) | 0 |
| Asian | 6 (1) | 6 (2) | 0 |
| Other race | 18 (4) | 18 (5) | 0 |
| Missing/not reported | 21 (5) | 21 (6) | 0 |
| **Duration of follow-up, median (range), months** | 32.4 (0.3-138.8) | 35.8 (0.8-138.8) | 16.7 (0.3-86.9) |
| **BMI, n (%)** | | | |
| Underweight (BMI < 18.5 kg/m$^2$) | 8 (2) | 7 (2) | 1 (1) |
| Normal weight (BMI ≥ 18.5 kg/m$^2$ to < 25 kg/m$^2$) | 85 (20) | 74 (21) | 11 (16) |
| Overweight (BMI ≥ 25 kg/m$^2$ to < 30 kg/m$^2$) | 114 (27) | 100 (28) | 14 (20) |
| Obese (BMI ≥ 30 kg/m$^2$) | 66 (16) | 59 (17) | 7 (10) |
| Missing/unknown | 148 (35) | 111 (32) | 37 (53) |
| **ECOG PS prior to index date, n (%)** | | | |
| 0 | 172 (41) | 160 (46) | 12 (17) |
| 1 | 169 (40) | 138 (39) | 31 (44) |
| 2 | 31 (7) | 19 (5) | 12 (17) |
| 3 | 2 (1) | 0 | 2 (3) |
| Missing | 47 (11) | 34 (10) | 13 (19) |

Percentages may not sum to 100% due to rounding. BMI, body mass index.

**Table 2. Clinical characteristics by 1L treatment patterns**

| Characteristic | ESA in 1L (n = 324) | Other 1L treatment ( n = 97) |
|---|---|---|
| **Hb level (baseline)** | | |
| Patients with Hb level available, n (%) | 285 (88) | 82 (85) |
| Mean (SD), g/dL | 9.0 (1.1) | 9.9 (2.0) |
| Median (range), g/dL | 9.1 (4.9-12.6) | 9.9 (6-16.2) |
| **Hb level (baseline), n (%)** | | |
| < 8 g/dL | 40 (14) | 14 (17) |
| ≥ 8 g/dL to < 10 g/dL | 193 (67) | 27 (33) |
| ≥ 10 g/dL | 52 (18) | 41 (50) |
| **EPO level (baseline), n (%)** | | |
| Patients with a test | 68 (21) | 8 (8) |
| ≤ 200 U/L | 55 (81) | 7 (88) |
| > 200 U/L | 13 (19) | 1 (13) |
| **MDS diagnosis to 1L treatment, months** | | |
| Mean (SD) | 11.8 (25.0) | 5.7 (11.7) |
| Median (range) | 1.8 (0.03-193) | 1.6 (0.03-71) |

Percentages may not sum to 100% due to rounding.

### 1L treatment patterns

- In the US and EU cohorts, 81% and 57% of patients received an ESA in 1L, respectively
- Overall, 86% of patients receiving an ESA in 1L did so as a monotherapy (US cohort, 87%; EU cohort, 76%) (**Table 3**)
  - Darbepoetin alfa monotherapy was the most commonly used 1L therapy in the ESA in 1L group overall (44%) and in both geographical cohorts (US cohort, 43%; EU cohort, 48%)
  - AZA monotherapy was the most common 1L therapy in the other 1L treatment group overall (60%) and in both geographical cohorts (US cohort, 71%; EU cohort, 37%)
- Median duration of 1L treatment was longer for patients who received an ESA in 1L than those who did not in the overall cohort (12.4 vs 6.4 months, respectively), the US cohort (12.2 vs 8.7 months, respectively) and the EU cohort (13.8 vs 4.7 months, respectively) (**Table 3**)

**Table 3. 1L treatment patterns by ESA treatment**

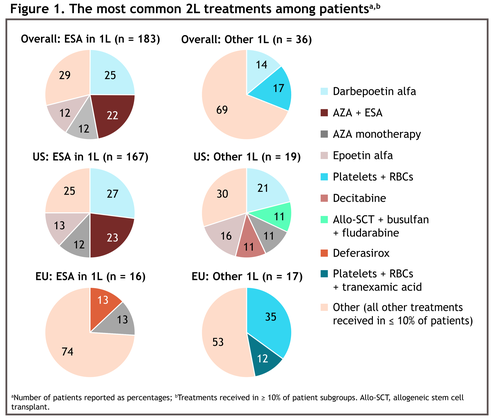
| Treatment | All patients | | US | | EU | |
|---|---|---|---|---|---|---|
| | ESA in 1L (n = 324) | Other 1L treatment (n = 97) | ESA in 1L (n = 284) | Other 1L treatment (n = 67) | ESA in 1L (n = 40) | Other 1L treatment (n = 30) |
| **1L regimen/agents,[a] n (%)** | | | | | | |
| Darbepoetin alfa | 142 (44) | 0 | 123 (43) | 0 | 19 (48) | 0 |
| Epoetin alfa | 124 (38) | 0 | 117 (41) | 0 | 7 (18) | 0 |
| Epoetin zeta | 4 (1) | 0 | 0 | 0 | 4 (10) | 0 |
| Epoetin alfa epbx | 9 (3) | 0 | 9 (3) | 0 | 0 | 0 |
| Deferasirox + epoetin alfa | 4 (1) | 0 | 0 | 0 | 4 (10) | 0 |
| AZA | 0 | 58 (60) | 0 | 47 (71) | 0 | 11 (37) |
| AZA + darbepoetin alfa | 14 (4) | 0 | 14 (5) | 0 | 0 | 0 |
| AZA + epoetin alfa | 4 (1) | 0 | 4 (1) | 0 | 0 | 0 |
| AZA + decitabine | 0 | 6 (6) | 0 | 6 (9) | 0 | 0 |
| AZA + platelets + RBCs | 0 | 6 (6) | 0 | 0 | 0 | 6 (20) |
| Decitabine | 0 | 6 (6) | 0 | 6 (9) | 0 | 0 |
| **Duration of 1L treatment, months** | | | | | | |
| Mean (SD) | 20.7 (22.5) | 15.9 (23.0) | 20.8 (22.9) | 19.4 (25.4) | 19.9 (20.0) | 8.6 (14.6) |
| Median (range) | 12.4 (0-116.4) | 6.4 (0-135.6) | 12.2 (0-116.4) | 8.7 (0-135.6) | 13.8 (0-78.1) | 4.7 (0.1-65.0) |

[a]Treatment received in > 1% of full patient population. AZA, azacitidine; RBC, red blood cell.

### Second-line (2L) treatment patterns

- Overall, more than half (57%, 183/324) of the ESA in 1L group and 38% (36/97) of the other 1L treatment group received a 2L therapy
- In the US cohort, more than half (59%, 167/284) of the ESA in 1L group and 29% (19/67) of the other 1L treatment group received a 2L therapy
- In the EU cohort, 40% (16/40) of the ESA in 1L group and more than half (57%, 17/30) of the other 1L treatment group received a 2L therapy
- The most common 2L therapies among patients are reported in **Figure 1**

**Figure 1. The most common 2L treatments among patients[a,b]**




[a]Number of patients reported as percentages; [b]Treatments received in ≥ 10% of patient subgroups. Allo-SCT, allogeneic stem cell transplant.

### 2L treatment patterns

- In the overall cohort, median duration of 2L treatment was 7.1 months for patients who received an ESA in 1L and 3.7 months for patients who did not

### 2L treatment modification after 1L ESAs

- Of the 183 patients who received a 2L therapy (**Table 4**)
  - 30% added another therapy to their existing ESA regimen
  - 23% switched to a different ESA from their existing ESA regimen
  - 26% changed to another regimen that did not include an ESA
  - 10% removed a non-ESA therapy from their regimen
  - 10% made no change to their treatment regimen

**Table 4. 2L treatment modification after 1L ESAs**

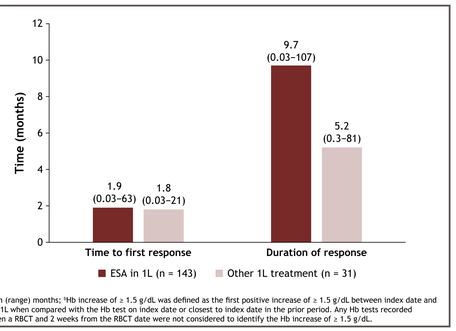
| | Overall | US | EU |
|---|---|---|---|
| | ESA in 1L (n = 183) | ESA in 1L (n = 167) | ESA in 1L (n = 16) |
| **2L treatment modification, n (%)[a,b]** | | | |
| Added therapy to existing ESA[c] | 55 (30) | 52 (31) | 3 (19) |
| Switched to different ESA | 42 (23) | 41 (25) | 1 (6) |
| Changed to non-ESA regimen | 47 (26) | 35 (21) | 12 (75) |
| Removed a non-ESA therapy | 19 (10) | 19 (11) | 0 |
| No change | 19 (10) | 19 (11) | 0 |

[a]One patient had unknown 2L treatment in the US cohort; [b]Added therapy to existing ESA = No ESA change, added other drugs; Switched to different ESA = Changed ESA + other therapy(s); Changed to non-ESA regimen = Changed to a new regimen that did not include ESA; Removed a non-ESA therapy = No ESA change, removed other drugs; No change = Retreated with same ESA monotherapy agent; [c]No granulocyte colony-stimulating factor was used in added therapy; added therapies included AZA, lenalidomide, decitabine and luspatercept.

### Hb increase ≥ 1.5 g/dL during 1L treatment

- Overall 41% of patients achieved a Hb increase ≥ 1.5 g/dL
  - More ESA in 1L patients (44%) than other 1L treatment patients (32%) had an increase in Hb ≥ 1.5 g/dL
- The median time from baseline to an increase in Hb ≥ 1.5 g/dL was similar in both groups (**Figure 2**)
- The median duration of response for Hb ≥ 1.5 g/dL was greater in patients who received an ESA in 1L (**Figure 2**)
- In the ESA in 1L group, a similar proportion of patients in baseline EPO categories ≤ 200 U/L and > 200 U/L achieved an increase in Hb ≥ 1.5 g/dL (49% vs 46%, respectively)

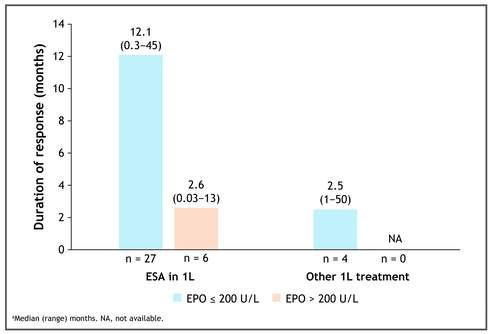
**Figure 2. Time to first response and duration of response of Hb increase ≥ 1.5 g/dL[a,b]**




[a]Median (range) months; [b]Hb increase of ≥ 1.5 g/dL was defined as the first positive increase of ≥ 1.5 g/dL between index date and end of 1L when compared with the Hb test on index date or closest to index date in the prior period. Any Hb tests recorded between a RBCT and 2 weeks from the RBCT date were not considered to identify the Hb increase of ≥ 1.5 g/dL.

- The duration of Hb increase ≥ 1.5 g/dL was substantially lower for patients treated with ESA in 1L who had a baseline EPO level > 200 U/L than those with a baseline EPO level ≤ 200 U/L (**Figure 3**)

**Figure 3. Duration of Hb increase ≥ 1.5 g/dL by baseline EPO level[a]**




[a]Median (range) months. NA, not available.

### Disease progression rates and second hematologic malignancies

- Overall, 10% of patients progressed to HR-MDS/AML
  - 9% of those treated with ESA in 1L and 10% who received other 1L treatments progressed to HR-MDS/AML
- Overall, 8% of patients had a second hematologic malignancy (hematologic malignancy developed after MDS diagnosis)
  - 8% of those treated with ESA in 1L and 8% who received other 1L treatments had a second hematologic malignancy

## Conclusions

- Patients with newly diagnosed LR-MDS in the US and EU cohorts had generally similar baseline characteristics
- Patients received either ESAs or other 1L treatments for approximately 1.5 years on average, even though the majority did not achieve clinically meaningful Hb improvement (≥ 1.5 g/dL increase)
  - Patients who discontinued ESAs in 1L were often retreated with ESAs in 2L
- Patients who received an ESA in 1L but had a baseline EPO level > 200 U/L were unlikely to sustain meaningful improvements in Hb levels
- These findings suggest a substantial need for more effective clinical management approaches to improve outcomes in 1L and 2L, and delay disease progression in LR-MDS

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## Acknowledgments

- The authors would like to acknowledge Matthew Wong for his contributions
- The study was supported by Bristol Myers Squibb
- All authors contributed to and approved the presentation; writing and editorial assistance was provided by Niamh Burke, PhD, of Excerpta Medica, funded by Bristol Myers Squibb

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