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Characterization of Treatment Patterns and Outcomes in Patients With Myelodysplastic Syndromes: Analysis of United States Commercial Claims Database

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INTRODUCTION

- Myelodysplastic syndromes (MDS) constitute a heterogeneous form of blood cancer that primarily affects the elderly, and are characterized by anemia and other cytopenias as well as a high risk of transformation to acute myeloid leukemia (AML).[1]
- Minimum criteria for MDS diagnosis include erythroid, granulocyte, or megakaryocyte dysplasia in 10% of informative cells.[1,2]
- MDS may be further classified into subcategories per the World Health Organization (WHO) system, depending on the percentage of blasts in the bone marrow or peripheral blood, presence or absence of bone marrow multilineage dysplasia, or excess ring sideroblasts.[1,2]
- The International Prognostic Scoring System (IPSS) is the standard prognostic tool in MDS.[1]
  - Patients are classified into risk categories based on the presence of bone marrow blasts, karyotype, cytopenia, and of a 5q deletion (del[5q]).[1,3,4]
- Treatment for patients with MDS may include supportive care (eg, whole-blood and/or platelet transfusion or erythropoiesis-stimulating agent [ESA] therapy), hypomethylating agents, chemotherapy, and lenalidomide for del(5q) MDS.[5]

AIM

- To characterize the burden of disease, treatment patterns, and outcomes of patients with MDS using a large United States claims database.

METHODS

- The Optum Integrated Claims and Electronic Medical Record database (Optum, Inc, Eden Prairie, MN, USA) was retrospectively analyzed.
  - The Optum database includes claims and eligibility information from a national health plan with ~14 million commercial and 500,000 Medicare Advantage enrollees per year.
- Adult patients with an index diagnosis of MDS between 2006 and 2014 were identified.
  - Patients aged younger than 18 years were excluded.
  - Patients with baseline AML, or any AML diagnosis 3 years prior to index diagnosis to 30 days after index diagnosis, were excluded.
  - To ensure index diagnosis, only patients with 365 days of retrospective data preceding the index diagnosis were included.
- MDS was categorized using International Classification of Diseases, revision 9 (ICD-9)[6] based on the earliest recorded diagnosis code.
  - Low-grade (ICD-9 code 238.72: refractory anemia [RA], refractory anemia with excess blasts-1 [RAEB-1], refractory anemia with ringed sideroblasts [RARS], refractory cytopenia with multilineage dysplasia [RCMD], refractory cytopenia with multilineage dysplasia and ringed sideroblasts [RCMD-RS]);
  - High-grade (ICD-9 code 238.73, which includes refractory anemia with excess blasts [RAEB] 2);
  - Del(5q) (ICD-9 code: 238.74);
  - Unspecified (ICD-9 code: 238.75).
- Demographics and clinical outcomes were analyzed by descriptive summary.
- Treatment patterns were summarized by grouping disease-modifying treatments as “lenalidomide,” “azacitidine,” “decitabine,” “imatinib,” or “chemotherapy” (including fludarabine, topotecan, cytarabine, and idarubicin), and supportive care as “ESA” (including darbepoietin and epoetin alfa), along with “others” (including filgrastim, sargramostim, atgam, eltrombopag, romiplostim, and thymoglobulin).
- Kaplan-Meier survival analysis was performed to define progression to AML.

RESULTS

- Of 10,465 MDS patients in the Optum Database, 8493 met the inclusion criteria and were evaluated over a median follow-up of 2.3 years.
- MDS was categorized as low-grade in 2136 (25.2%), high-grade in 367 (4.3%), del(5q) in 198 (2.3%), and unspecified in 5792 (68.2%) patients (**Table 1**).
- Across all MDS categories, median age at diagnosis was 76 years (range, 18-85 years), 77% of patients were aged ≥ 65 years, roughly half were male, the majority were white and non-Hispanic, and most were from the South or Midwest regions of the United States.

Table 1. Select Characteristics of Included Patients

	Low-grade MDS n = 2136	High-grade MDS n = 367	Del(5q) MDS n = 198	Unspecified MDS n = 5792
Age[a]				
< 65 years, %	25.2	23.7	25.3	22.8
≥ 65 years, %	74.8	76.3	74.7	77.2
Median (range)	75 (18-85)	74 (20-85)	74 (24-85)	76 (18-85)
Sex, %				
Male	51.7	58.0	48.0	53.1
Female	48.0	42.0	52.0	46.8
Race, %				
White	70.8	68.9	69.7	71.8
African American	5.2	2.7	5.6	5.1
Asian	1.6	2.7	2.0	1.3
Other/unknown	22.3	25.6	22.7	21.9
Insurance type, %				
Commercial	66.7	65.3	68.6	66.3
Medicaid	0.3	0.6	1.6	0.4
Medicare	33.1	34.1	29.8	33.3

[a]Proportion of total number of patients within each risk category.

- Platelet counts at diagnosis were available for 33% of patients.
- Most patients had platelet counts > 150,000/μL, regardless of MDS category (**Table 2**).
- In the overall cohort, 500 (5.9%) patients progressed to AML, including patients in each MDS risk category; time from index diagnosis to progression to AML is presented in **Figure 1**.
  - 103 of 2136 patients (4.8%) with low-grade MDS;
  - 78 of 367 patients (21.3%) with high-grade MDS;
  - 12 of 198 patients (6.1%) with del(5q) MDS;
  - 307 of 5792 patients (5.3%) with unspecified MDS.

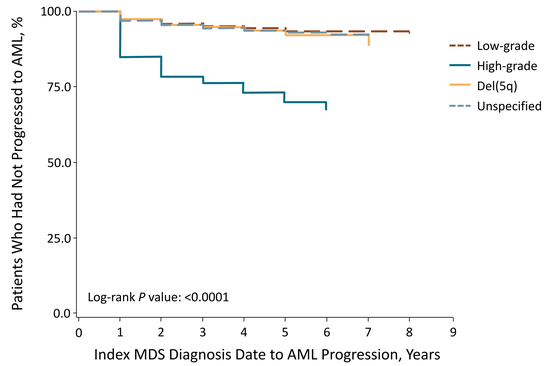
Table 2. Platelet Counts of Included Patients[a]

	Low-grade MDS n = 2136	High-grade MDS n = 367	Del(5q) MDS n = 198	Unspecified MDS n = 5792
Patients with available platelet counts, n	833	15	57	1796
Distribution of platelet count levels, %				
< 50,000/μL	6	2	16	1
50,000-75,000/μL	6	14	4	1
76,000-100,000/μL	8	14	5	9
101,000-150,000/μL	15	14	11	18
> 150,000/μL	66	37	65	53

[a]The closest available result to index MDS diagnosis, within 90 days prior to, and 180 days after, index diagnosis date for each patient, was considered for analysis.

RESULTS

Figure 1. Kaplan-Meier Analysis of Time to Progression to AML



- 54% to 64% of patients in all categories except high-grade MDS did not receive any treatment (**Table 3**).
- In the overall cohort, 40% received ≥ 1 treatment regimen for MDS.
- The most commonly used regimens varied by MDS category (**Table 4**).
  - Epoetin-alfa or darbepoetin in both low-grade and unspecified MDS;
  - Hypomethylating agents (decitabine or azacitidine) in high-grade MDS;
  - Lenalidomide in del(5q) MDS.
- In the overall cohort, 38% of patients who received ≥ 1 regimen and 13% of patients without prescribed treatment went on to have a blood transfusion.
- Among all patients, regardless of treatment, those with high-grade MDS were the most likely to receive transfusions (**Table 3**).

Table 3. Patients Receiving Treatment and/or Transfusions Following Index Diagnosis

	Low-grade MDS n = 2136	High-grade MDS n = 367	Del(5q) MDS n = 198	Unspecified MDS n = 5792
Patients who did not receive any treatment regimen, n (%)	1159 (54)	143 (39)	115 (58)	3721 (64)
Patients who received at least 1 treatment regimen, n (%)	977 (46)	224 (61)	83 (42)	2071 (36)
Patients with RBC transfusion, among all patients, n (%)	482 (23)	142 (39)	54 (27)	1265 (22)
Patients with RBC transfusion, among those without any treatment regimen, n (%)	137 (12)	25 (17)	14 (12)	482 (13)
Patients with RBC transfusion, among those with at least 1 treatment regimen, n (%)	345 (35)	117 (52)	40 (48)	783 (38)

Table 4. Distribution of Treatments by MDS Category

Patients receiving treatment, n (%)	Low-grade MDS			High-grade MDS			Del(5q) MDS			Unspecified MDS		
	Treatment line											
	Any n = 2130	1st n = 977	2nd n = 488	Any n = 386	1st n = 224	2nd n = 91	Any n = 177	1st n = 83	2nd n = 47	Any n = 4353	1st n = 2071	2nd n = 992
Lenalidomide[a]	102 (4.8)	32 (3.3)	26 (5.3)	36 (9.3)	18 (8.0)	9 (9.9)	67 (37.9)	37 (44.6)	14 (29.8)	374 (8.6)	157 (7.6)	78 (7.9)
Azacitidine[a]	230 (10.8)	106 (10.8)	57 (11.7)	136 (35.2)	92 (41.1)	27 (29.7)	18 (10.2)	7 (8.4)	6 (12.8)	557 (12.8)	251 (12.1)	151 (15.2)
Decitabine[a]	81 (3.8)	23 (2.4)	22 (4.5)	58 (15.0)	38 (17.0)	15 (16.5)	4 (2.3)	1 (1.2)	1 (2.1)	196 (4.5)	89 (4.3)	44 (4.4)
Imatinib[a]	17 (0.8)	9 (0.9)	1 (0.2)	3 (0.8)	1 (0.4)	2 (2.2)	3 (1.7)	1 (1.2)	2 (4.3)	26 (0.6)	12 (0.6)	8 (0.8)
Chemotherapy[a,b]	19 (0.9)	7 (0.7)	9 (1.8)	17 (4.4)	9 (4.0)	3 (3.3)	1 (0.6)	0	1 (2.1)	57 (1.3)	27 (1.3)	16 (1.6)
ESA[a,c]	1563 (73.4)	732 (74.9)	345 (70.7)	96 (24.9)	48 (21.4)	21 (23.1)	73 (41.2)	30 (36.1)	21 (44.7)	2686 (61.7)	1284 (62.0)	594 (59.9)
Others[d]	119 (5.6)	68 (7.0)	28 (5.7)	40 (10.4)	18 (8.0)	14 (15.4)	11 (6.2)	7 (8.4)	2 (4.3)	461 (10.6)	249 (12.0)	101 (10.2)

[a]Regimens containing listed agent (may reflect use as monotherapy or in combination regimens); [b]Chemotherapy included fludarabine, topotecan, cytarabine, and idarubicin; [c]ESA included darbepoietin and epoetin alfa; [d]Others included filgrastim, sargramostim, atgam, eltrombopag, romiplostim, and thymoglobulin. Note: Above percentages are based on the number of regimens containing the respective drugs as a share of total number of regimens in each MDS disease category. If a regimen consists of a combination of treatments, an order of hierarchy (in decreasing order as presented in the table) was followed and such regimens were counted once in highest available rank based on the treatments in the regimen, and not counted for any other treatment (ie, a regimen including lenalidomide+azacitidine+decitabine would have been counted once as lenalidomide).

CONCLUSIONS

- **Despite the variety of agents available, a significant proportion of MDS patients across all categories did not receive any disease modifying treatment, and many received only supportive care such as ESA or a granulocyte colony-stimulating factor (eg, “Others” category in Table 4).**
- **Limitations of the study:**
  - **It was not possible to determine risk category in a majority of patients.**
  - **Because of the extended timelines involved, duration of transfusion independence and overall survival were not reported in this study.**
- **Rates of transformation to AML and transfusion dependence were consistent with published estimates.**

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