

# Treatment Patterns Among Patients with Myelodysplastic Syndromes: Observations of 1st-Line Therapy, Discontinuation and the Need of Additional Therapies

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## BACKGROUND

- The myelodysplastic syndromes (MDS) typically affect older individuals.
- High-risk MDS patients are usually treated first with hypomethylating agents (HMAs; azacitidine [AZA] or decitabine [DEC]).<sup>1</sup>
- Presently, there are no approved therapeutic treatment options for those who have failed initial treatment with an HMA; 2<sup>nd</sup>-line therapeutic approaches are unproven and may include lenalidomide (LEN), switching to a different HMA, or supportive care.
- There is little published information on the treatment patterns of MDS patients after failed HMA therapy who become eligible for 2<sup>nd</sup>-line therapy.

## OBJECTIVE

- To describe treatment patterns of MDS patients who have failed or become intolerant to HMA therapy.

## METHODS

### Study Design and Data Source

- Retrospective cohort study of a large US, HIPAA-compliant, commercial health insurance claims database.
- Timeframe: 1/1/2008 to  $\geq 6$  months after patients became candidates for 2<sup>nd</sup>-line MDS treatment, until the end of enrollment, or study end (12/31/2012).

### Study Population

- We identified patients with an MDS-associated medical claim (ICD-9-CM diagnosis codes 238.7x) being treated with an HMA in the identification (ID) period (1/1/2009–12/31/2011) who were considered to have failed initial HMA treatment (AZA or DEC).
- The index date was the date on which patients were defined as eligible for 2<sup>nd</sup>-line therapy (i.e., initiated HMA treatment but then stopped for  $\geq 2$  months, switched to another HMA, or have been on the same HMA for  $> 7$  months).

## Outcomes

- 1<sup>st</sup>- and 2<sup>nd</sup>-line treatment patterns:
  - MDS-specific therapy: AZA, DEC, or LEN.
  - Utilization of hematologic supportive care agents, including erythropoiesis-stimulating agents (ESA), growth factors (i.e., granulocyte and granulocyte-macrophage colony-stimulating factors), and blood transfusions.
- 1<sup>st</sup>-line treatment only: Number of AZA or DEC cycles, defined as continuous treatment periods without a gap of  $>7$  days, and the gap between observed cycles could not be  $\geq 60$  days.

## RESULTS

### Baseline Patient and Disease Characteristics

- Of 38,702 patients diagnosed with MDS in the ID period, 1,366 used an HMA (Figure 1).
- Among 402 patients eligible for 2<sup>nd</sup>-line MDS therapy (Figure 1), mean age was 72.9 years and 40% were female (Table 1).
- 386 (96.0%) patients had a cytopenia, including anemia (92.8%), neutropenia (53.0%), or thrombocytopenia (52.7%; Table 1).
- The mean Charlson comorbidity score was 3.6 (Table 1).
- AML/MDS dual diagnosis was present in 24.1% of patients at baseline (Table 1).

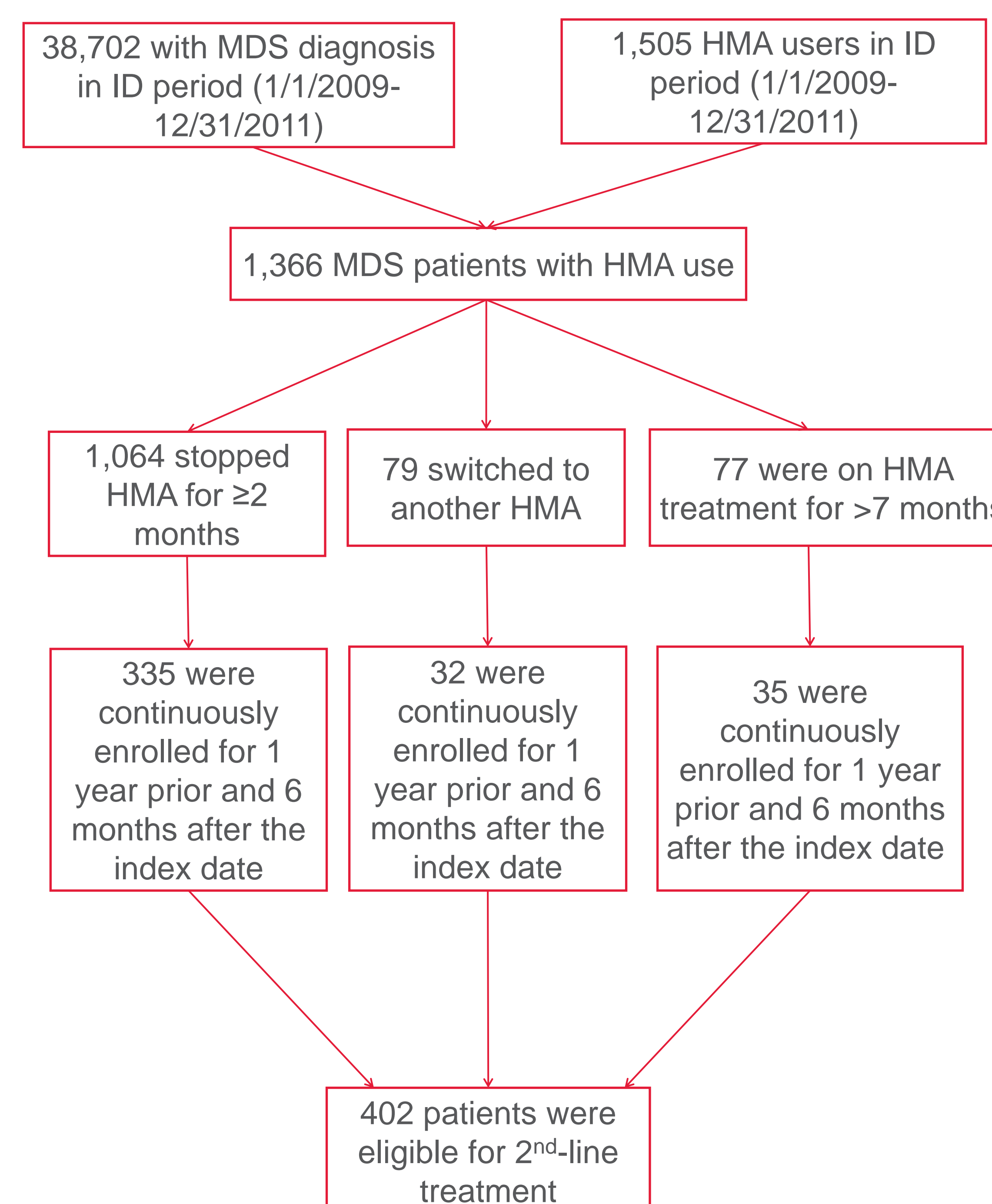
### 1<sup>st</sup> Line Treatment Patterns

- 283 (70.4%) and 123 (30.6%) of patients had used AZA and DEC, respectively.
- Patients averaged 6.1 (SD=5.1) HMA treatment cycles (6.4 (5.4) for AZA or 5.4 (4.0) for DEC) prior to being considered potential candidates for 2<sup>nd</sup>-line therapy.
- 193 (48.0%) patients had “early” discontinuation (47.1% for AZA, 50.0% for DEC), defined as less than ( $<$ ) 5 treatment cycles before stopping or switching among HMAs.
- Among all 402 patients eligible for 2<sup>nd</sup>-line therapy, 320 (79.6%) received hematologic supportive care interventions: 208 (51.7%) received transfusions, 206 (51.2%) ESA, and 170 (42.3%) growth factors, at least one or more times.

Table 1. Patient and Disease Characteristics

Characteristic	Value
Age, year, mean (SD)	72.9 (9.1)
Female, no. (%)	160 (39.8)
Charlson comorbidity index, mean (SD)	3.6 (2.9)
Number of chronic conditions, mean (SD)	6.8 (2.3)
AML/MDS dual diagnosis, no. (%)	97 (24.1)
Cytopenias potentially associated with HMA use, no. (%)	386 (96.0)
Pancytopenia	202 (50.2)
Anemia	373 (92.8)
Thrombocytopenia	212 (52.7)
Leukopenia	93 (23.1)
Neutropenia	213 (53.0)

Figure 1. Patient Selection Flowchart



## 2<sup>nd</sup> Line Treatment Interventions

- Among 402 patients eligible for 2<sup>nd</sup>-line therapy, 32 (8.0%) switched to another HMA.
- The following treatments were received during 6 months' followup among these 402 patients:
  - AZA: 121 (30.1%)
  - DEC: 74 (18.4%)
  - Lenalidomide: 18 (4.5%)
  - Supportive care: 247 (61.4%; Table 2)

Table 2. Supportive Care Interventions

Characteristic	Value
Supportive Care, no. (%)	247 (61.4)
Blood Transfusions, no (%)	161 (40.0)
ESAs, no. (%)	122 (30.3)
Growth Factors, no. (%)	116 (28.9)

## CONCLUSION

- These data suggest that a significant proportion of MDS patients are candidates for 2<sup>nd</sup>-line treatment after AZA and DEC.
- Discontinuation of 1<sup>st</sup>-line MDS treatment with less than ( $<$ ) 5 HMA treatment cycles is frequent in higher-risk patients.
- AZA was used more often than DEC or LEN as 1<sup>st</sup>-line MDS therapy.
- The clinical reasons for early HMA discontinuation warrant further investigation, as does the frequency of need for co-administered hematologic supportive care interventions.
- Switching HMA occurs in a minority of patients after failing 1<sup>st</sup> line HMA therapy
- Safe and effective 2<sup>nd</sup>-line therapies that reduce cytopenias are needed for these patients.

## REFERENCES

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- Bordononi RE, et al. Hematologic outcomes of myelodysplastic syndromes treatment with hypomethylating agents in community practice. *Clin Lymphoma Myeloma Leuk.* 2011 Aug;11(4):350-4.