

# Population Incidence of MDS Following Hypomethylating Agent (HMA) Treatment Failure: Analysis of US Commercial Claims Data

Sudipto Mukherjee, MD, MPH<sup>1</sup>; Christopher R Cogle, MD<sup>2</sup>; Sandra E Kurtin, RN, MS, AOCN, ANP-C<sup>3</sup>; Tanya GK Bentley, PhD<sup>4</sup>; Michael S Broder, MD, MSHS<sup>4</sup>; Eunice Chang, PhD<sup>4</sup>; Moira E Lawrence, PhD<sup>5</sup>; Thomas J McKearn, MD, PhD<sup>5</sup>; Scott Megaffin<sup>5</sup>; Michael E Petrone, MD, MPH<sup>5</sup>

<sup>1</sup>Cleveland Clinic Foundation, Cleveland, OH; <sup>2</sup>University of Florida, Gainesville, FL; <sup>3</sup>University of Arizona, Tucson, AZ; <sup>4</sup>Partnership for Health Analytic Research, LLC, Beverly Hills, CA; <sup>5</sup>Onconova Therapeutics, Inc., Newtown, PA

## INTRODUCTION

- Treatments for high-risk MDS patients are limited mainly to hypomethylating agents (HMAs) and clinical trials.<sup>1</sup>
- However, 80% of MDS patients receiving HMAs fail to achieve remission, with nearly all patients eventually developing chemoresistant disease.<sup>2</sup>
- For patients who have failed initial treatment with HMAs, a variety of 2<sup>nd</sup>-line therapies are available. However, these interventions have been only modestly effective to date.<sup>3,4</sup>
- In this analysis, we documented the incidence of MDS following HMA treatment failure and characterized patient populations with MDS receiving 1<sup>st</sup>-line and 2<sup>nd</sup>-line therapy.

## METHODS

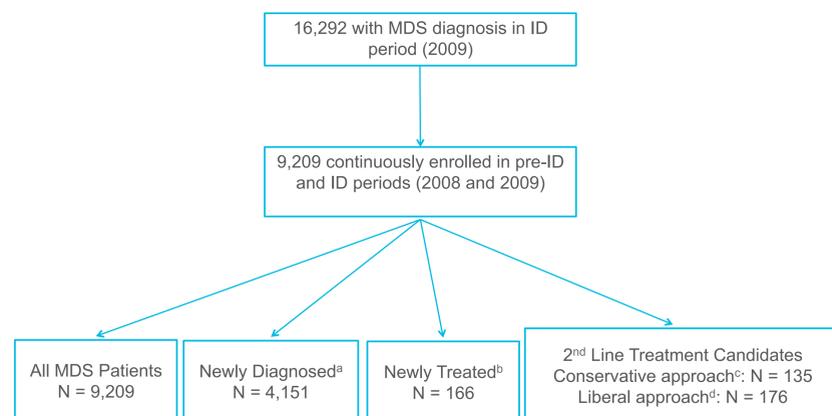
- Study design: Retrospective cohort study using a commercial claims database
- Data source: Optum Clinformatic™ Data Mart
- Patient population:
  - All MDS Patients:** Defined as patients with an MDS-associated medical claim (ICD-9-CM code 238.7x) in the identification (ID) period (1/1/2009-12/31/2009)
  - Newly diagnosed:** Among All MDS Patients, persons with no MDS diagnosis in the pre-ID period (1/1/2008-12/31/2008)
  - Newly treated with HMAs:** Defined as Newly Diagnosed patients with a claim for HMA treatment in the ID period, but not in the pre-ID period
  - Candidates for 2<sup>nd</sup>-line treatment:** MDS patients who used an HMA in the ID period and:
    - Stopped for ≥2 months,
    - Switched to another HMA,
    - OR remained on the first HMA for >7 months.
- Key outcomes:
  - MDS incidence
  - Treatment patterns in newly diagnosed MDS patients
  - MDS incidence in patients treated with HMAs
- Software used for analyses: SAS® version 9.4 (SAS Institute, Cary, NC)

## RESULTS

### General Characteristics and Trends

- During 2009, in a cohort of 5,942,153 enrollees, there were 9,209 prevalent cases of MDS
- Consistent with current understanding of MDS, the majority of the 9,209 MDS patients identified in our study were at least 65 years of age or older
- Over 80% of all MDS patients underwent a “watch and wait” strategy, receiving no chemotherapy and no supportive care
- A modest proportion of patients received supportive care (18.6%), defined as receipt of erythropoiesis-stimulating agents (ESAs) or growth factors
- A smaller proportion of patients received chemotherapy (3.9%), most commonly azacitidine (197/359, 54.9%)

Figure 1. Selection of Study Cohort



<sup>a</sup> No diagnosis of MDS or unspecified anemia in the pre-ID period.  
<sup>b</sup> No claim for HMA in the pre-ID period, followed by claim for HMA in the ID period.  
<sup>c</sup> HMA users who either stopped for at least 2 months or switched to another HMA.  
<sup>d</sup> HMA users who either stopped for at least 2 months, switched to another HMA, or remained on the same HMA for more than 7 months.

Table 1. Patient Demographics and Baseline Comorbidities

	All MDS Patients N = 9,209	2 <sup>nd</sup> Line Treatment Candidates				
		All MDS Patients N = 9,209	Newly Diagnosed N = 4,151	Newly Treated N = 166	Conservative Approach <sup>a</sup> N = 135	Liberal Approach <sup>b</sup> N = 176
<b>Age, year</b>	Mean (SD)	63.9 (17.1)	59.0 (18.6)	72.8 (9.1)	72.9 (8.4)	73.1 (8.2)
≤49	no. (%)	1,771 (19.2)	1,173 (28.3)	4 (2.4)	2 (1.5)	2 (1.1)
50-64	no. (%)	2,312 (25.1)	1,169 (28.2)	27 (16.3)	22 (16.3)	28 (15.9)
65-74	no. (%)	1,772 (19.2)	735 (17.7)	43 (25.9)	37 (27.4)	48 (27.3)
≥75	no. (%)	3,354 (36.4)	1,074 (25.9)	92 (55.4)	74 (54.8)	98 (55.7)
<b>Female</b>	no. (%)	5,322 (57.8)	2,422 (58.3)	66 (39.8)	52 (38.5)	64 (36.4)
<b>Region</b>						
Midwest	no. (%)	2,167 (23.5)	987 (23.8)	33 (19.9)	31 (23.0)	41 (23.3)
Northeast	no. (%)	1,060 (11.5)	449 (10.8)	16 (9.6)	10 (7.4)	12 (6.8)
South	no. (%)	3,955 (42.9)	1,767 (42.6)	74 (44.6)	57 (42.2)	77 (43.8)
West	no. (%)	2,027 (22.0)	948 (22.8)	43 (25.9)	37 (27.4)	46 (26.1)
<b>Charlson Comorbidity Index</b>	Mean (SD)	3.0 (3.1)	2.8 (3.1)	4.2 (3.2)	4.4 (3.4)	4.0 (3.3)
<b>Number of chronic conditions</b>	Mean (SD)	5.3 (2.6)	5.1 (2.5)	7.0 (2.4)	7.3 (2.6)	6.9 (2.6)

<sup>a</sup> HMA users who either stopped for at least 2 months or switched to another HMA.  
<sup>b</sup> HMA users who either stopped for at least 2 months, switched to another HMA, or remained on the same HMA for more than 7 months.

### Newly-Diagnosed MDS Patients

- There were 4,151 patients newly diagnosed with MDS (incidence 69.9/100,000); among these patients, 2.3% had initiated HMA by 1 year of diagnosis
- Incidence peaked among men in the 65- to 74-year-old age group; among women, the incidence peaked in the 50- to 64-year-old age group
- The proportion undergoing “watch and wait” management in newly-diagnosed patients approached 89%
- Chemotherapy (2.6%) was used infrequently in newly diagnosed MDS patients
- Azacitidine was used more than twice as often as decitabine

### Newly-Treated MDS Patients

- The incidence of newly-treated MDS was 2.8 per 100,000 enrollees
- All 166 newly-treated patients received chemotherapy; the most common agent was azacitidine (127/166, 76.5%)
- Newly-treated patients remained on 1<sup>st</sup>-line HMA therapy for a median 117 (decitabine) or 154 (azacitidine) days prior to discontinuation, or about 4-5 months.

Table 2. Treatment Patterns among MDS Patients, Newly Diagnosed Patients, and Newly Treated Patients in 2009

		All MDS Patients N = 9,209	Newly Diagnosed N = 4,151	Newly Treated N = 166
<b>Watch and wait</b> (no chemotherapy and no supportive care)	no. (%)	7,373 (80.1)	3,691 (88.9)	-
<b>Chemotherapy</b> (with or without supportive care)	no. (%)	359 (3.9)	107 (2.6)	166 (100.0)
<b>HMA</b>	no. (%)	257 (2.8)	77 (1.9)	166 (100.0)
Azacitidine	no. (%)	197 (2.1)	59 (1.4)	127 (76.5)
Decitabine	no. (%)	83 (0.9)	22 (0.5)	50 (30.1)
<b>Immunomodulatory</b>				
Lenalidomide	no. (%)	120 (1.3)	35 (0.8)	11 (6.6)
<b>Supportive care</b> (with or without chemotherapy)	no. (%)	1,716 (18.6)	414 (10.0)	123 (74.1)
<b>Erythropoiesis-stimulating agents</b>	no. (%)	1,454 (15.8)	270 (6.5)	95 (57.2)
<b>Growth factors</b>	no. (%)	471 (5.1)	213 (5.1)	76 (45.8)

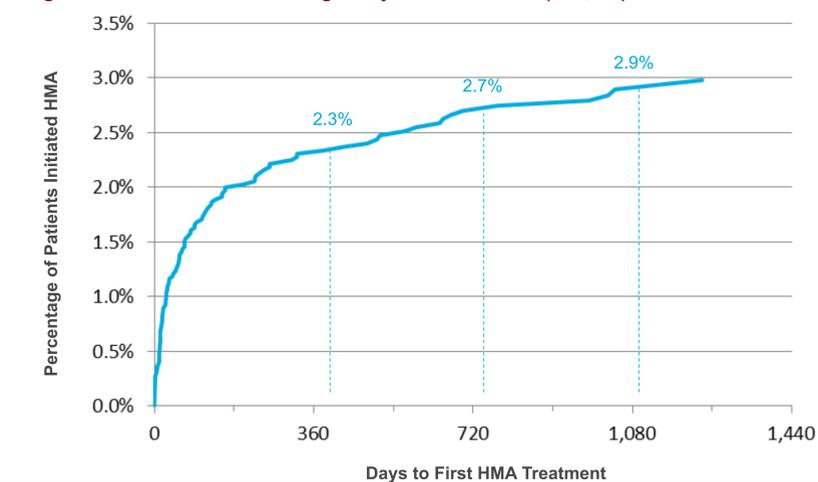
<sup>a</sup> Patients might receive more than one type of treatment in 2009.

Table 3. MDS Incidence, Stratified by Age and Sex<sup>a</sup>

Sex	Age (years)	Newly Diagnosed Patients (N=4,151)	Newly Treated Patients (N=166)	Potential 2 <sup>nd</sup> -line Treatment Candidates (N=176)
Female	All	75.7	2.1	2
	≤49	56.6	0.1	0
	50-64	111.5	2.1	1.1
	65-74	101.2	4	5.3
	≥75	68.5	4.4	4.4
Male	All	63.1	3.6	4.1
	≤49	29.6	0.2	0.1
	50-64	86.5	2.5	3.8
	65-74	106.1	8.5	8.5
	≥75	97.1	10.5	11.7
All	All ages	69.9	2.8	3

<sup>a</sup> Results expressed as number per 100,000 enrollees.

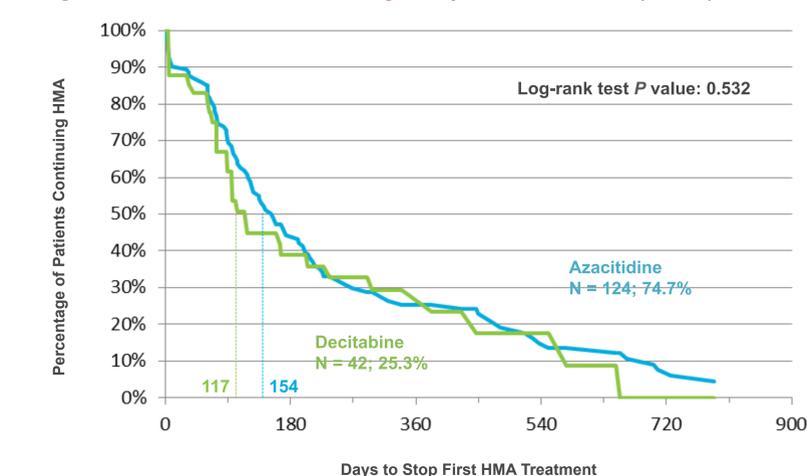
Figure 2. Time to First HMA among Newly Treated Patients (N=4,151)



### MDS Patients Eligible for 2<sup>nd</sup>-line Therapy

- An estimated 135 to 176 MDS patients were potential 2<sup>nd</sup>-line treatment candidates (incidence 2.3-3.0/100,000):
- For 1<sup>st</sup>-line therapy, patients previously used:
  - Azacitidine (66.7%-69.9%)
  - ESAs (52.3%-53.5%)
  - Growth factors (46.0%-48.9%)

Figure 3. Time on First HMA among Newly Treated Patients (N=166)



## CONCLUSION

- The majority (over 80%) of MDS patients, whether newly diagnosed or established, are managed with a “watch and wait” strategy.
- The incidence of newly-diagnosed MDS patients in this study was 69.9/100,000 which is consistent with published literature on US populations.<sup>5,6</sup>
- Patients receiving first-line HMA therapy used the drug a median of 4-5 months before stopping.
- Patients considered eligible for 2<sup>nd</sup>-line therapy (N=135-176) were much more likely to have received supportive care (73.9-76.3%) compared to the overall MDS population (18.6%).
- Results from this analysis can inform population-based estimates of the MDS burden of disease among Medicare and commercially-insured patients, as the prognosis for patients in whom HMA therapy has failed is grim.<sup>3</sup>

## REFERENCES

- Wang, et al. *Leukemia Research* 2011.
- Steensma, et al. *Hematology/Oncology Clinics of North America* 2010.
- Prebet, et al. *Journal of Clinical Oncology* 2011.
- Jabbour, et al. *Cancer* 2010.
- Cogle, et al. *Blood* 2011.
- Goldberg, et al. *Journal of Clinical Oncology* 2010.