

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

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INTRODUCTION

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

METHODS

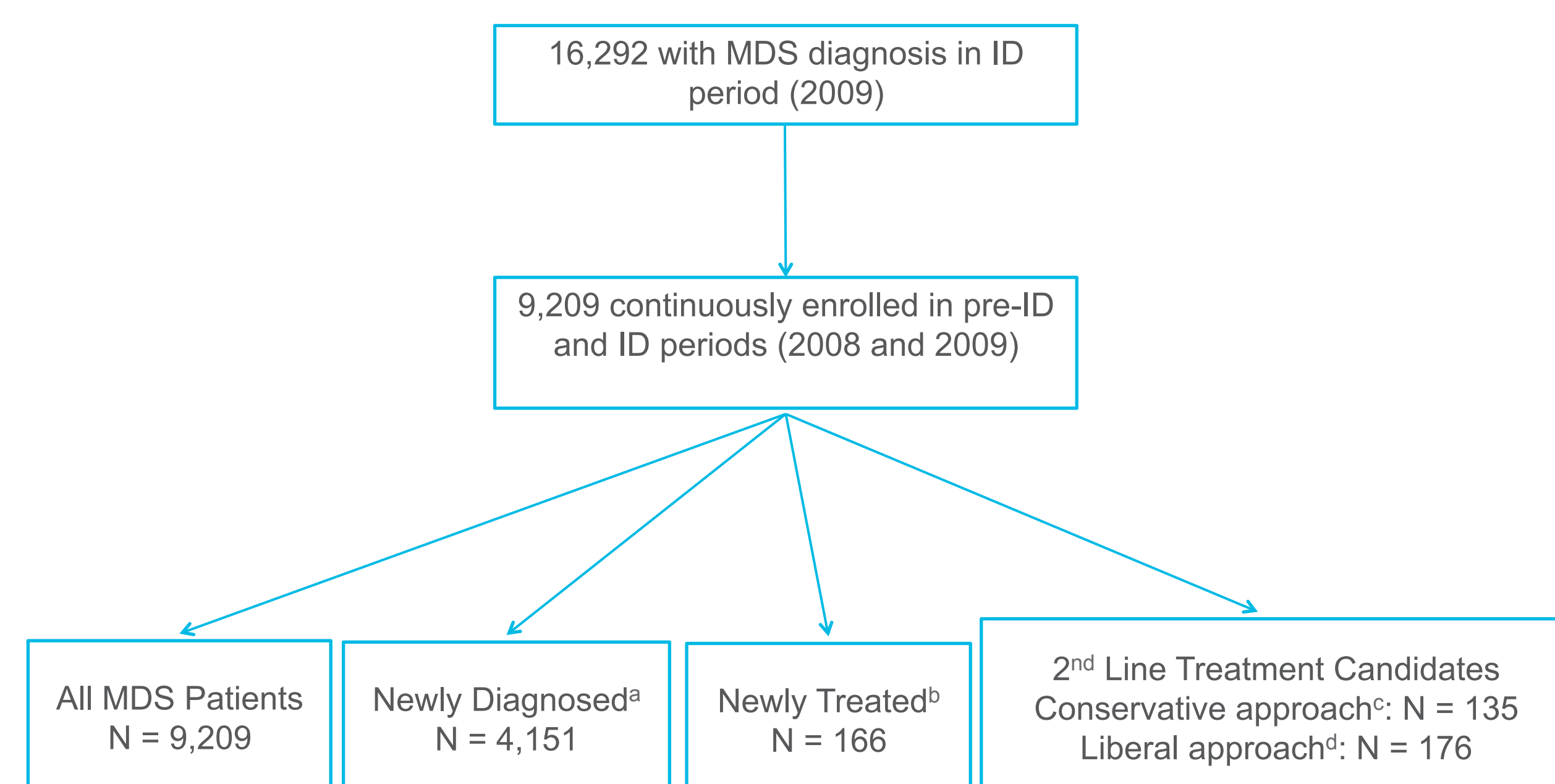
- Study design: Retrospective cohort study using a commercial claims database
- Data source: Optum Clinformatics™ Data Mart
- Patient population:
 - All MDS Patients:** Defined as patients with an MDS-associated medical claim (ICD-9-CM code 238.7x) in the identification (ID) period (1/1/2009-12/31/2009)
 - 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 2nd-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



^a No diagnosis of MDS or unspecified anemia in the pre-ID period.
^b No claim for HMA in the pre-ID period, followed by claim for HMA in the ID period.
^c HMA users who either stopped for at least 2 months or switched to another HMA.
^d 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	All MDS Patients N = 9,209	Newly Diagnosed N = 4,151	Newly Treated N = 166	2 nd Line Treatment Candidates	
					Conservative Approach ^a N = 135	Liberal Approach ^b N = 176
Age, year	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)
Female	no. (%)	5,322 (57.8)	2,422 (58.3)	66 (39.8)	52 (38.5)	64 (36.4)
Region						
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)
Charlson Comorbidity Index	Mean (SD)	3.0 (3.1)	2.8 (3.1)	4.2 (3.2)	4.4 (3.4)	4.0 (3.3)
Number of chronic conditions	Mean (SD)	5.3 (2.6)	5.1 (2.5)	7.0 (2.4)	7.3 (2.6)	6.9 (2.6)

^a HMA users who either stopped for at least 2 months or switched to another HMA.
^b 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 1st-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
Watch and wait (no chemotherapy and no supportive care)	no. (%)	7,373 (80.1)	3,691 (88.9)	-
Chemotherapy (with or without supportive care)	no. (%)	359 (3.9)	107 (2.6)	166 (100.0)
HMA	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)
Immunomodulatory				
Lenalidomide	no. (%)	120 (1.3)	35 (0.8)	11 (6.6)
Supportive care (with or without chemotherapy)	no. (%)	1,716 (18.6)	414 (10.0)	123 (74.1)
Erythropoiesis-stimulating agents	no. (%)	1,454 (15.8)	270 (6.5)	95 (57.2)
Growth factors	no. (%)	471 (5.1)	213 (5.1)	76 (45.8)

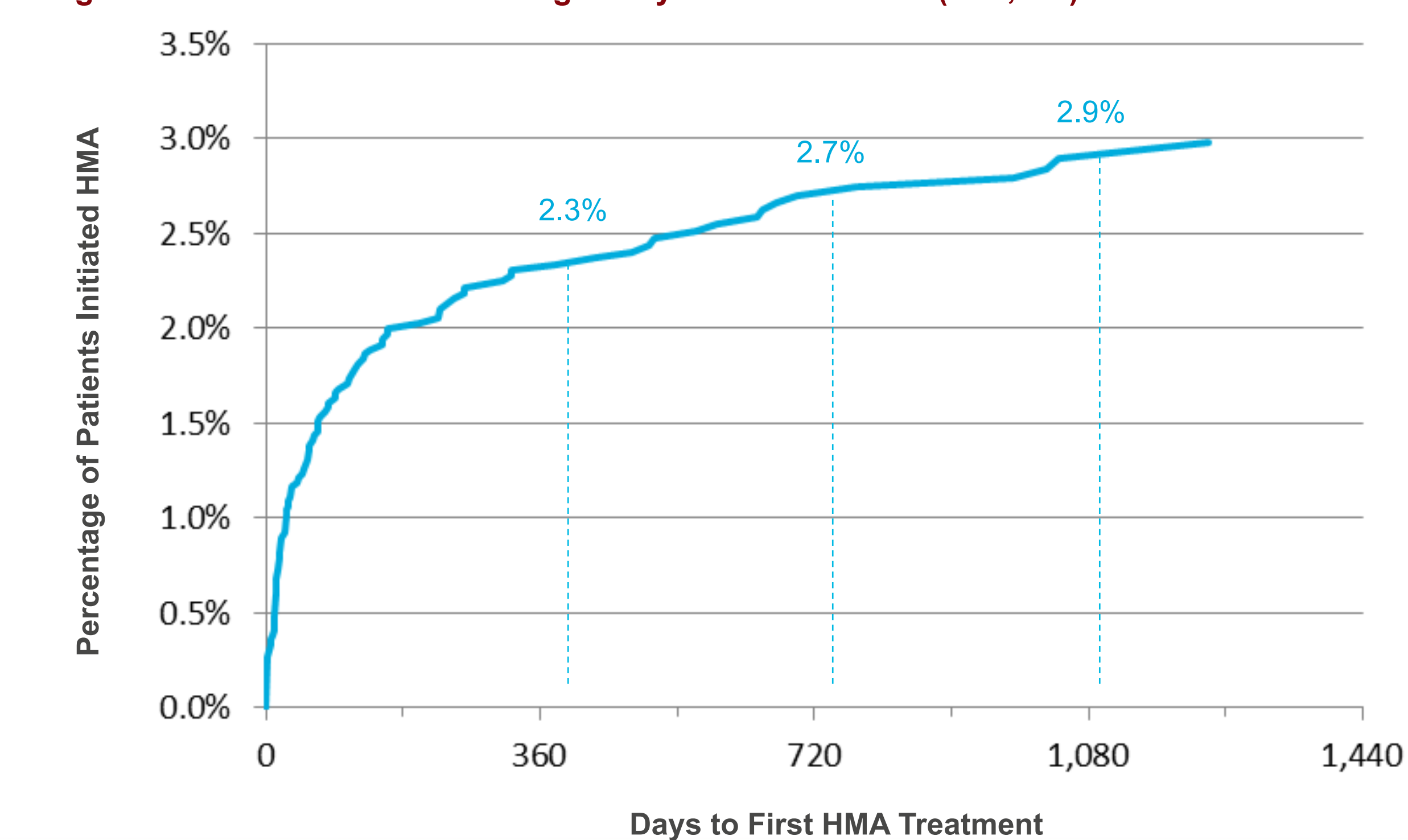
^a Patients might receive more than one type of treatment in 2009.

Table 3. MDS Incidence, Stratified by Age and Sex^a

Sex	Age (years)	Newly Diagnosed Patients (N=4,151)	Newly Treated Patients (N=166)	Potential 2 nd -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

^a Results expressed as number per 100,000 enrollees.

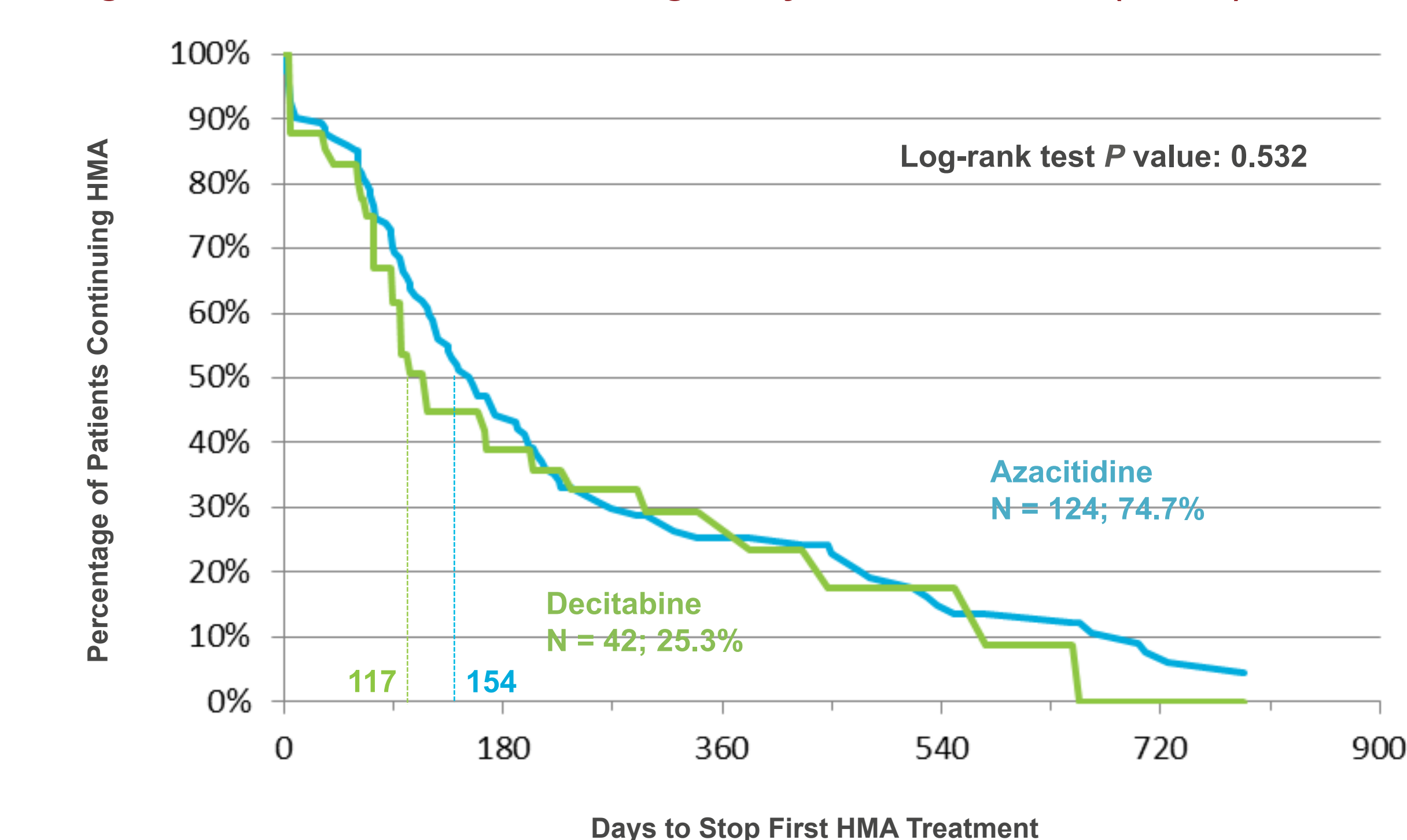
Figure 2. Time to First HMA among Newly Treated Patients (N=4,151)



MDS Patients Eligible for 2nd-line Therapy

- An estimated 135 to 176 MDS patients were potential 2nd-line treatment candidates (incidence 2.3-3.0/100,000):
- For 1st-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.^{5,6}
- Patients receiving first-line HMA therapy used the drug a median of 4-5 months before stopping.
- Patients considered eligible for 2nd-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.³

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