Healthcare Resource Utilization and Costs in Patients with Myelodysplastic Syndromes Treated with Hypomethylating Agents: A SEER-Medicare Analysis

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Background and Objectives

- Myelodysplastic syndromes (MDS) are a group of bone marrow disorders affecting hematopoietic stem cells and progenitors, which result in cytopenias and a risk of acute myeloid leukemia (AML) transformation[1]
- Currently, the hypomethylating agents (HMAs) azacitidine and decitabine are the standard of care in patients with MDS based on results from clinical trials which demonstrate improved response rates and overall survival[2,3]
- However, a significant proportion of patients do not respond to HMA treatment,[4,5] and response among those who do is commonly transient, with an average loss of response within 2 years; once response to HMA is lost, the prognosis is very poor[6]
- Furthermore, the clinical and economic burden of patients with MDS treated with HMAs has not been comprehensively evaluated in real-world practice
- This study aimed to assess healthcare resource utilization (HRU) and costs in patients with MDS treated with HMAs, with a focus on HMA-treatment success and failure

Methods

Data Source

- This study used the linked US Surveillance, Epidemiology, and End Results (SEER)-Medicare database, including data on Medicare beneficiaries with cancer:
  - The SEER program of cancer registries includes individuals with cancer from 01/01/2006-12/31/2015
  - The Medicare claims database includes Part A (institutional) and B (non-institutional) coverage from 01/01/2006-12/31/2016; Medicare Part D (drug events) was not used for this study since HMAs are administered in an outpatient (OP) setting
- An exemption from the Institutional Review Board was obtained from the New England Independent Review Board

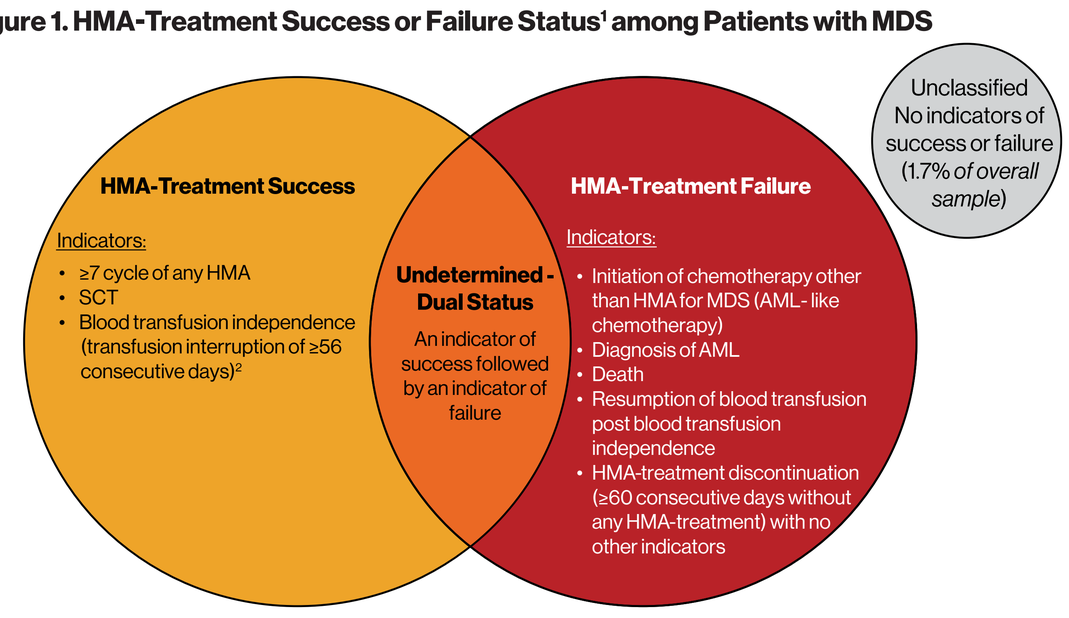
Study Design / Sample Selection

- This study used a retrospective cohort design
- Adult patients with MDS diagnosed on or after 2009 (following the 2008 modification to the World Health Organization MDS classification) who received HMA-treatment with continuous Medicare Part A and B coverage (without Part C) during ≥12 months before and ≥1 month after HMA-treatment initiation were included in the study
- The **index date** was defined as the date of HMA-treatment initiation (azacitidine or decitabine)
- The 12 months preceding the index date constituted the **baseline period**
- The **follow-up period** was defined as the time from the index date to the first event among start of Medicare Part C coverage (i.e., HMO), end of Medicare Parts A and B coverage, end of data availability (i.e., 12/31/2016), or death; the follow-up period varied among patients

Outcomes and Statistical Analysis

- Indicators of clinical HMA-treatment success or failure observed in claims data are described in **Figure 1**
- HMA-treatment success or failure status was determined based on the sequence of indicators observed up to 12 months post-index or until the first event among a stem cell transplant (SCT), diagnosis of AML, or the end of follow-up period
- The **rate of HMA-treatment success** was defined as the number of patients with HMA-treatment success or Undetermined-dual status divided by the total number of patients with indicators
- The **rate of HMA-treatment failure** was defined as the number of patients with HMA-treatment failure or Undetermined-dual status divided by the total number patients with indicators

Figure 1. HMA-Treatment Success or Failure Status[1] among Patients with MDS



AML = Acute Myeloid Leukemia; HMA = Hypomethylating Agent; MDS = Myelodysplastic Syndrome; SCT = Stem Cell Transplant
Note: 1. AMA-treatment success, HMA-treatment failure, Undetermined-dual, or Unclassified are four mutually exclusive statuses; 2. Silverman LR, et al. J Clin Oncol. 2002;20(10):2429-2440.

- HRU, including inpatient (IP) admissions, emergency department (ED) visits, and days with OP services, were reported using incidence rate (IR) per-100-patients-per-month
- All-cause medical costs from the payers' perspective in 2019 USD were reported per-patient-per-month (PPPM)
- HRU and cost analyses were stratified based on HMA-treatment success or failure status and measured during different periods as described in the scenarios depicted in **Figure 2**; only patients with a study period of ≥1 month were included

Figure 2. Stratification of HRU and Cost Analyses

HMA = Hypomethylating Agent; SCT = Stem Cell Transplant

Results

Patient Characteristics

- A total of 3,046 patients with MDS received HMA treatment (**Table 1**)

Table 1. Description of Patient Characteristics

	Overall N = 3,046
Age (years),[1] Mean ± SD [Median]	77.4 ± 7.6 [78]
Female, N (%)	1,120 (36.8)
US Census region of residence,[1,2] N (%)	
West	1,178 (38.7)
South	761 (25.0)
Northeast	661 (21.7)
Midwest	443 (14.5)
Race/Ethnicity,[3] N (%)	
Non-Hispanic white	2,694 (88.4)
Non-Hispanic black	147 (4.8)
Red Blood Cell Transfusions within 56 days prior to index date,[4] N (%)	3,016 (99.0)
Number of days, Mean ± SD [Median]	14.13 ± 12.62 [11]
MDS with histologic subtypes of RAEB-1/2,[5] N (%)	1,450 (47.6)
Unfit for SCT,[6] N (%)	2,199 (72.2)
Pancytopenia,[5] N (%)	1,796 (59.0)
CCI,[5] Mean ± SD [Median]	2.06 ± 2.01 [2]
Azacitidine,[1] N (%)	2,357 (77.4)
Decitabine,[1] N (%)	689 (22.6)

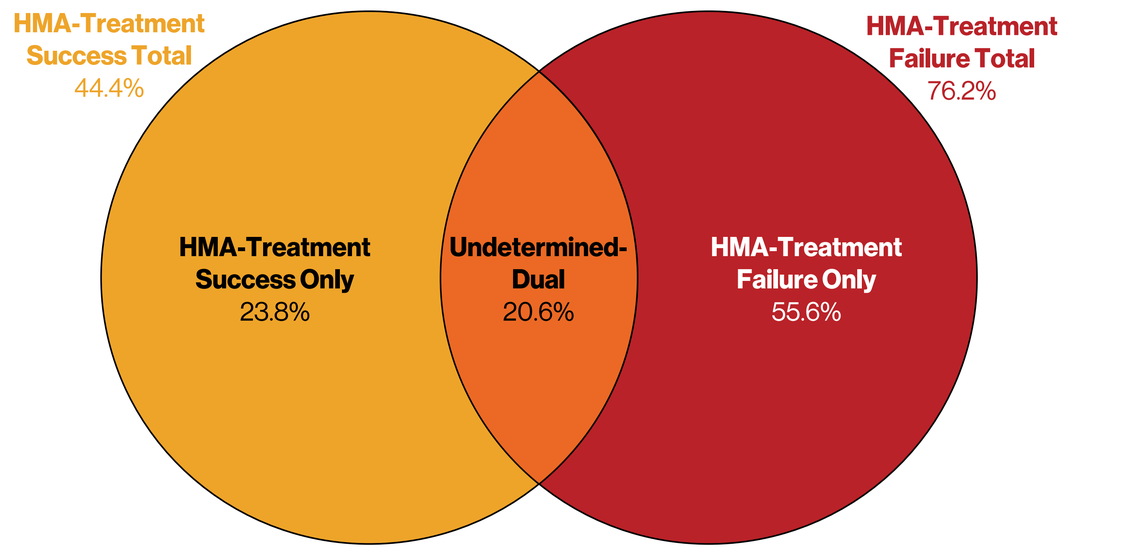
CCI = Charlson Comorbidity Index; HMA = Hypomethylating Agent; MDS = Myelodysplastic Syndrome; RAEB = Refractory Anemia with Excess Blasts; SCT = Stem Cell Transplant; SD = Standard Deviation; US = United States
Notes:
1. As of the index date. 2. Unknown category not reported. 3. Only the most prevalent categories were reported. 4. Silverman LR, et al. *J Clin Oncol*. 2002;20(10):2429-2440. 5. During the 12-month baseline period. 6. Patients with ≥1 of the following indicators: aged +75 years as of the index date, or a diagnosis of congestive heart failure, cirrhosis or end stage renal disease during the 12-month baseline period.

Rates of HMA-Treatment Success and Failure

- Sequences of indicators of clinical success or failure with a prevalence ≥1% are described in **Figure 3**
- The estimated rate of HMA-treatment success was 44.4% (this rate was 23.8% when excluding those with an Undetermined-dual status) and the estimated rate of HMA-treatment failure was 76.2%; 20.6% of patients were included in both rates

Figure 3. Rates of HMA-Treatment Success and Failure among Patients with MDS

Sequences of Indicators with a Prevalence ≥1% (N = 3,046)	N (%)
≥7 cycles of any HMA	Success (17.5%)
Diagnosis of AML	Failure (16.6%)
Death	Failure (14.1%)
HMA-treatment discontinuation	Failure (10.1%)
HMA-treatment discontinuation → Death	Failure (8.8%)
≥7 cycles of any HMA → HMA-treatment discontinuation	Undetermined-dual (5.9%)
HMA-treatment discontinuation → Diagnosis of AML	Failure (4.8%)
HMA-treatment discontinuation → ≥7 cycles of any HMA	Success (3.6%)
≥7 cycles of any HMA → Diagnosis of AML	Undetermined-dual (3.2%)
HMA-treatment discontinuation → Blood transfusion independence → Resumption of blood transfusion	Undetermined-dual (2.4%)
≥7 cycles of any HMA → Death	Undetermined-dual (2.1%)
Stem Cell Transplant	Success (1.2%)
≥7 cycles of any HMA → HMA-treatment discontinuation → Death	Undetermined-dual (1.0%)

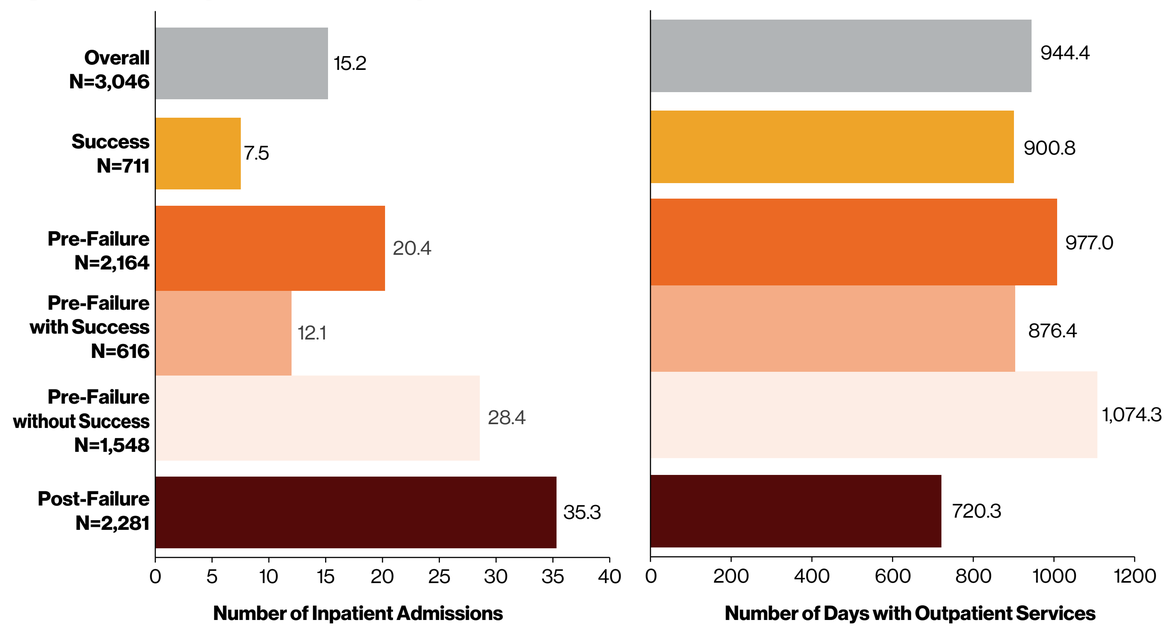


AML = Acute Myeloid Leukemia; SCT = Stem Cell Transplant; HMA = Hypomethylating Agent; MDS = Myelodysplastic Syndrome
Notes: Sequence of indicators observed up to 12 months post-index or until the first event among SCT, diagnosis of AML, or the end of follow-up period; an indicator of SCT was observed in 3.5% of patients overall at any time.

HRU

- The median study period duration was 5.9 months for the overall sample, 12 months for patients with HMA-treatment success, 4.3 months during the pre-HMA-treatment failure period, and 1.8 months post-HMA-treatment failure
- Overall, patients had an IR of 15.2 IP admissions, 7.9 ED visits, and 944.4 days with OP services per-100-patients-per-month (**Figure 4**)
- Post-HMA-treatment failure, patients had 35.3 IP admissions per-100-patients-per-month

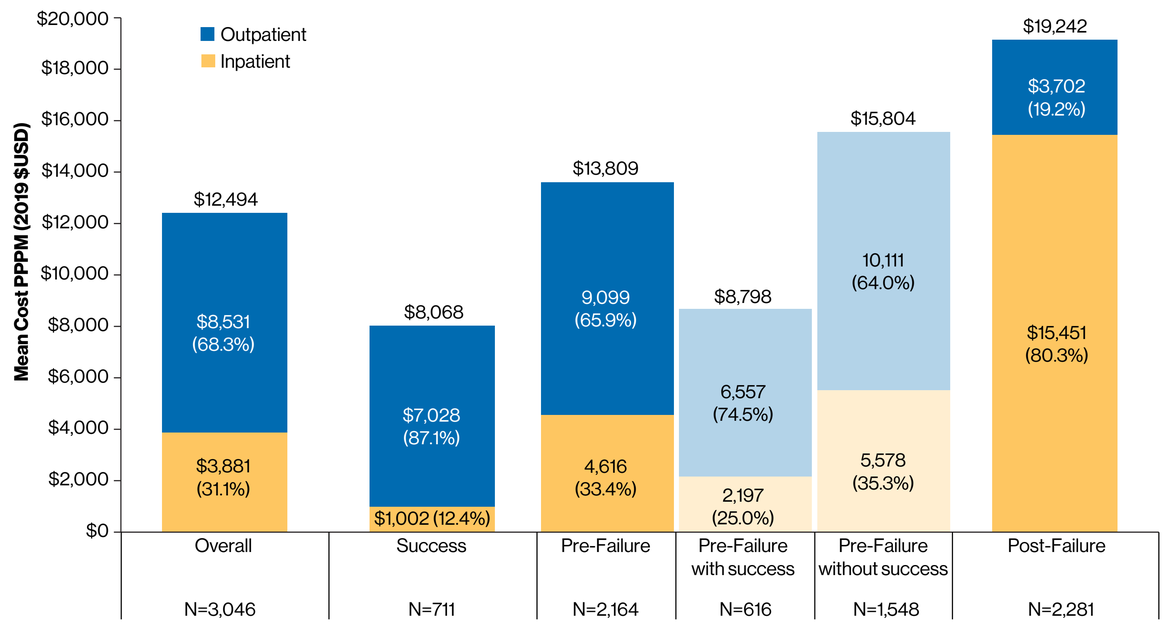
Figure 4. Monthly Incidence Rate per 100 Patients



Medical Costs

- Overall, mean total all-cause medical costs were $12,494 PPPM (Medicare perspective; **Figure 5**); in addition, the mean patient out-of-pocket cost was $2,521 PPPM
- OP costs were the main contributor of total all-cause medical costs for the overall sample (68.3%), while IP costs were the main driver post-HMA-treatment failure (80.3%)

Figure 5. Monthly All-cause Medical Costs



PPPM = Per-Patient-Per-Month; USD = United States Dollars
Note: Emergency department costs were <1% of the total.

Limitations

- Since laboratory test results were not available, clinical indicators were used to assess response to HMA-treatments to estimate the rate of HMA-treatment success and failure via a claim-based algorithm developed in collaboration with a clinical expert
- The study sample was limited to Medicare-insured individuals; thus, generalizability to the overall US population may be limited
- Administrative claims data include diagnosis and procedure codes that are recorded for reimbursement purposes, which may be subject to coding errors or data omissions

Conclusions

- This US real-world observational study using administrative claims and cancer-linked data shows that despite the availability of HMA therapies, more than three quarters of patients failed HMA treatment within 6 months of initiation
- The incidence rate of inpatient admissions was the highest post-HMA-treatment failure, which translated into medical costs that were ~4x higher compared to the costs for those with HMA-treatment success
- These data highlight the unmet clinical needs of HMA-treated patients with MDS and demonstrate the substantial economic burden associated with those who do not achieve treatment success

References

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