Disparities in First-Line Treatment Initiation Among US Medicare Beneficiaries With Myelodysplastic Syndromes

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BACKGROUND

- Patients with myelodysplastic syndromes (MDS), characterized by dysplastic blood cell production, have a median survival of ≤ 6 years[1]
- Treatment options include:
  - Off-label use of erythropoiesis-stimulating agents (ESAs)
  - US Food and Drug Administration (FDA)-approved treatment with lenalidomide (LEN) [associated with del(5q) mutation; 2006] or hypomethylating agents (HMAs) (2004 and 2006)
  - Allogeneic hematopoietic cell transplant[1–3]
- Treatment with LEN or HMAs can reduce the need for intensive blood transfusions used in MDS-related anemia
  - Despite benefits of active treatment, prior studies point to relatively low use of LEN and HMAs,[1,3,4] raising concerns about current levels of use and about who is selected or not selected to receive treatment

OBJECTIVES

- To measure current use of first-line treatments for MDS
- To determine patient or disease characteristics associated with first-line treatment initiation

METHODS

Study Design and Data Source

- A retrospective matched cohort study using 2008–2013 data from the linked Surveillance, Epidemiology and End Results (SEER)–Medicare files
- The SEER registry collects clinical, demographic, and cause-of-death information for persons with cancer; cancer diagnoses are confirmed through pathology reports and medical records
- Medicare claims cover health-care services received from the time of Medicare eligibility until death

Patient Identification

- Patients with newly diagnosed MDS between January 1, 2008 and December 31, 2013 who initiated active treatment for MDS
  - MDS diagnosis: International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) codes 9980–9989
  - ≥ 1 claim for an HMA (azacitidine or decitabine) or LEN treatment between January 1, 2009 and December 31, 2013; first claim defined as the index date

METHODS (cont.)

- Initiators of HMAs/LEN were matched 1:1 to non-initiators by diagnosis date (year and quarter) and the SEER–Medicare MDS Risk Score[5] (SMMRS; a validated tool for assigning MDS patients to risk groups based on components including cytopenias, MDS category, age, Charlson Comorbidity Index [CCI], acute hospitalization, transfusion) and assigned the same index date
  - SMMRS risk status was determined using data from 6 months before to 6 months after diagnosis
- All patients resided in SEER regions, had MDS as first cancer diagnosis, and were diagnosed within 12 months of index (baseline)
- This study excluded patients with any of the following characteristics during baseline:
  - Acute myeloid leukemia
  - Not continuously enrolled in Medicare Fee-for-Service Part A/B, or Part D claims for HMA/LEN

Study Measures

- Baseline demographic and clinical characteristics:
  - Age, sex, race/ethnicity, urban/rural location
  - Census tract-level socioeconomic variables[6,7]
  - CCI[8]
  - Presence of del(5q) syndrome (Patient Entitlement and Diagnosis Summary File, ICD-O-3 code 9986/3)
  - Prior blood transfusion
  - Prior use of a hematopoiesis-stimulating agent (HSA; ESA or granulocyte colony-stimulating factor)
  - Year of MDS diagnosis
  - SMMRS score;[5] patients classified into 1 of 4 groups per predicted mortality score: Low (≤ 0.28), Intermediate-1 (> 0.28 to ≤ 0.50), Intermediate-2 (> 0.50 to ≤ 0.69), High (> 0.69)
- Index medication (among initiators)

Statistical Analysis

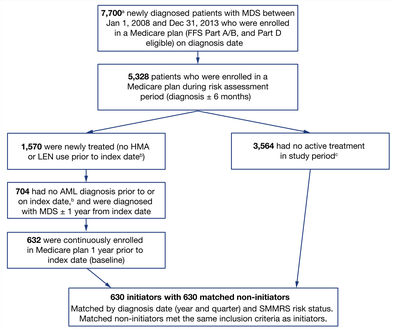
- Descriptive statistics generated for study measures, showing balance post-matching
- Logistic regression conducted to determine key predictors of first-line treatment initiation
- All data transformation and analyses performed using SAS© software version 9.4 (SAS Institute, Cary, NC, USA); statistical significance level 0.05

RESULTS

Baseline and Index Characteristics

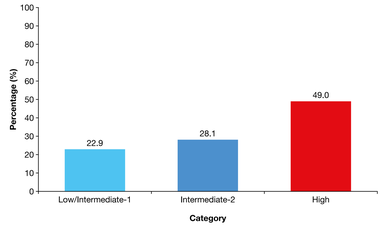
- 2,139 of 7,700 (27.8%) newly diagnosed patients with MDS used an HMA or LEN, of whom 630 met all selection criteria for matched-reference group analysis (Figure 1)
- Approximately 25% of all matched patients had International Prognostic Scoring System (IPSS) Low/Intermediate-1 risk MDS and 75% had Intermediate-2/High risk MDS

Figure 1. Patient Selection



[a] Among them, 2,139 patients received an HMA or LEN between Jan 1, 2008 to Dec 31, 2013. [b] The first HMA/LEN use was defined as the index date. [c] Jan 1, 2008 to Dec 31, 2013. AML, acute myeloid leukemia; FFS, Fee-for-Service; HMA, hypomethylating agent; LEN, lenalidomide; MDS, myelodysplastic syndromes; SEER, Surveillance, Epidemiology and End Results; SMMRS, SEER–Medicare MDS Risk Score.

Figure 2. SMMRS Risk Status for Matched Patients[a]



[a] SMMRS risk status and MDS diagnosis date (year and quarter) were identical for initiators and non-initiators after matching. Low and Intermediate-1 categories combined due to small cell counts to comply with SEER–Medicare cell size suppression policy. MDS, myelodysplastic syndromes; SEER, Surveillance, Epidemiology and End Results; SMMRS, SEER–Medicare MDS Risk Score.

Table. Matched Cohort – Baseline and Index Characteristics

	HMA/LEN Initiators n = 630	Non-Initiators n = 630	*P* Value
Age at MDS diagnosis, mean (SD) [median], years	76.2 (8.6) [77]	82.0 (8.8) [83]	< 0.001
Age at index, mean (SD) [median], years	77.0 (8.6) [78]	82.8 (8.8) [84]	< 0.001
Female, n (%)	325 (51.6)	343 (54.4)	0.615
del(5q) syndrome, n (%)	46 (7.3)	17 (2.7)	< 0.001
Race/ethnicity, n (%)			0.034
White	543 (86.2)	523 (83.0)	
Black	23 (3.7)	41 (6.5)	
Hispanic	23 (3.7)	34 (5.4)	
Other	41 (6.5)	32 (5.1)	
Rural location, n (%)	26 (4.1)	15 (2.4)	0.081
Annual income in residential area, mean (SD),[a] USD	67,213 (31,966)	61,163 (29,919)	0.001
Percentage of residents with ≥ 4 years of college education, mean (SD)[a]	31.9 (19.3)	28.8 (18.3)	0.005
Percentage of residents living below poverty, mean (SD)[a]	11.7 (8.8)	14.3 (10.9)	< 0.001
< 20%, n (%)	477 (82.7)	416 (74.8)	
20–40%, n (%)	96 (16.6)	116 (20.9)	
> 40%, n (%)	NA	24 (4.3)	
CCI, mean (SD)	4.0 (3.2)	4.2 (3.1)	0.254
Any blood transfusion at baseline, n (%)	429 (68.1)	309 (49.0)	< 0.001
HSA use at baseline, n (%)			< 0.001
No use	366 (58.1)	428 (67.9)	
< 12 weeks	199 (31.6)	162 (25.7)	
≥ 12 weeks	65 (10.3)	40 (6.3)	
Index medication, n (%)			NA
Azacitidine	368 (58.4)	NA	
Decitabine	132 (21.0)	NA	
LEN	132 (21.0)	NA	

[a] Census-tract level variable.
CCI, Charlson Comorbidity Index; HMA, hypomethylating agent; HSA, hematopoiesis-stimulating agent; LEN, lenalidomide; NA, not applicable; MDS, myelodysplastic syndromes; SD, standard deviation.

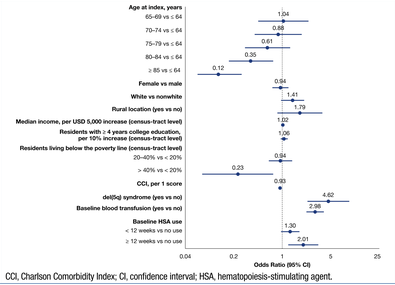
RESULTS (cont.)

- HMA (n = 498) and LEN (n = 132) initiators (vs matched non-initiators) were (Table):
  - Younger at diagnosis (76.2 vs 82.0 years; *P* < 0.001)
  - Predominantly white (86.2% vs 83.0%; *P* = 0.034)
  - More often diagnosed with del(5q) syndrome (7.3% vs 2.7%; *P* < 0.001)
- The majority (58.4%) of HMA/LEN initiators had azacitidine as their index medication (Table)

Predictors of First-Line Treatment Initiation With HMA or LEN

- Predictors of treatment initiation with HMA or LEN were presence of del(5q) syndrome, prior blood transfusion, and prior HSA use (< 12 weeks vs no use; ≥ 12 weeks vs no use) (Figure 3)
- Advanced age (80–84 vs ≤ 64 years; ≥ 85 vs ≤ 64 years), census-tract residents below the poverty line (> 40% vs < 20%), and increasing CCI decreased the likelihood of treatment initiation (Figure 3)

Figure 3. Logistic Regression Model Results: Likelihood of Receiving Active Treatment



CCI, Charlson Comorbidity Index; CI, confidence interval; HSA, hematopoiesis-stimulating agent.

DISCUSSION

- Treatments are determined predominantly by clinical factors, such as blood transfusion requirement, prior HSA use, and the presence of del(5q) syndrome, yet we found evidence of disparities in first-line treatment initiation among MDS patients based on age and income
  - Patients with advanced age (≥ 80 years) and residing in areas with greater poverty were less likely to receive first-line treatment

DISCUSSION (cont.)

- Data in this study are limited because they are based on registry and claims information; however, our findings are consistent with studies that show age and income disparities in the treatment of other conditions, such as depression[9,10]
- Our observation that nonclinical factors may affect clinician decision-making about treatments deserves additional study
- Treatment decisions may also be based on patient preferences, and patient-centered outcomes research into this topic would be useful

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DISCLOSURES

C.R.C.: Celgene Corporation – steering committee member for the Celgene Connect MDS/AML Registry. S.R.R., E.C., S.G., M.S.B.: Partnership for Health Analytic Research (PHAR), LLC, a health services research company hired by Celgene Corporation to conduct this study – employment. M.McG.: Celgene Corporation – employment.

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