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 years¹
- 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 transplant¹⁻³
- 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 - \geq 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 Score⁵ (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}
- CCI⁸
- 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 \leq 0.50), Intermediate-2 $(> 0.50 \text{ to } \le 0.69)$, High (> 0.69)
- Index medication (among initiators)

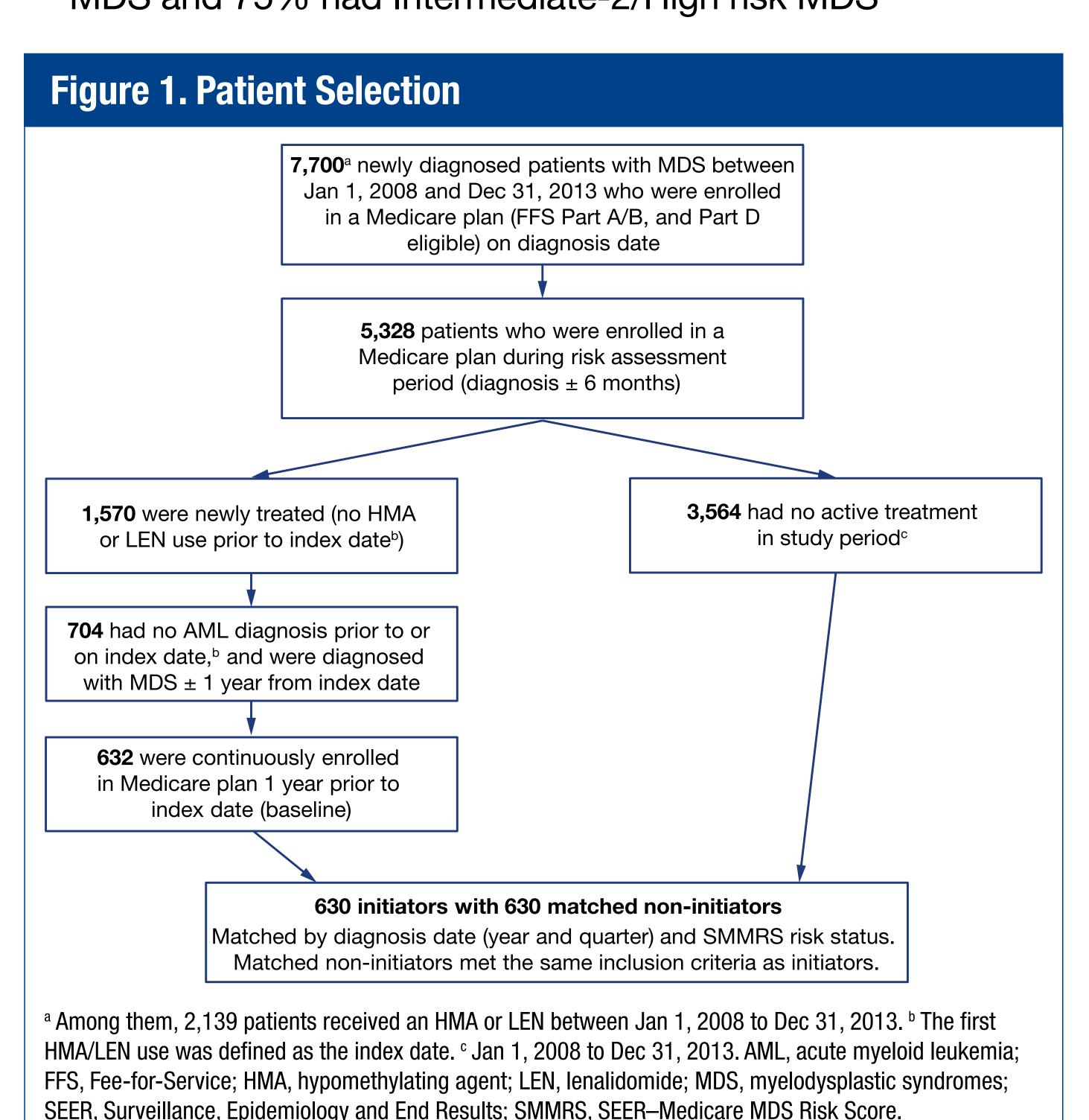
Statistical Analysis

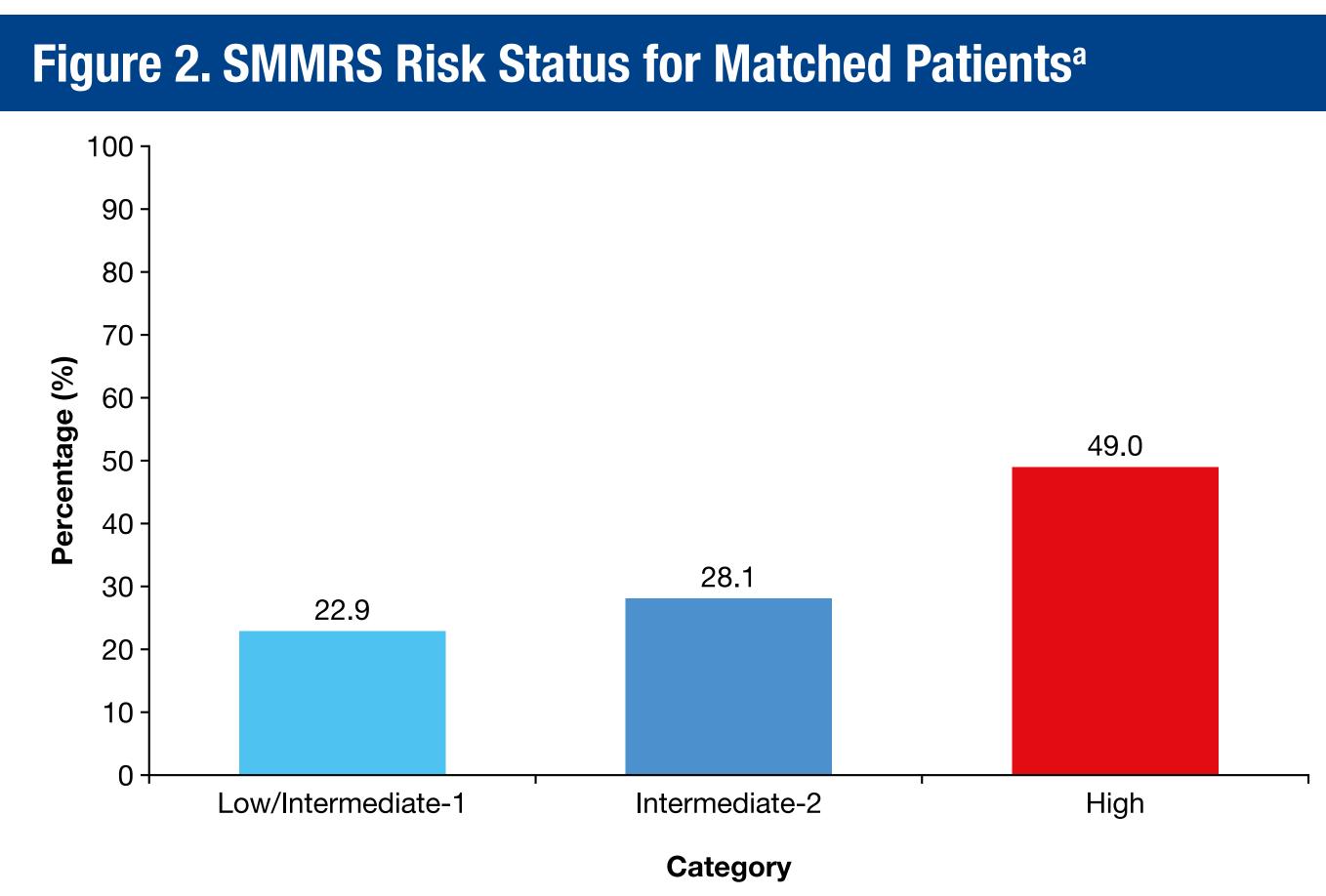
- Descriptive statistics generated for study measures, showing balance post-matching
- Logistic regression conducted to determine key predictors of first-line treatment initiation
- All data transformation and analyses performed using SAS[©] software version 9.4 (SAS Institute, Cary, NC, USA); statistical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





•			Rural location, n (%)	26 (4.1)	15 (2.4)	0.081
704 had no AML diagnosis prior to or on index date, ^b and were diagnosed with MDS ± 1 year from index date			Annual income in residential area, mean (SD), ^a USD	67,213 (31,966)	61,163 (29,919)	0.001
632 were continuously enrolled in Medicare plan 1 year prior to index date (baseline) 630 initiators with 630 matched non-initiators Matched by diagnosis date (year and quarter) and SMMRS risk status. Matched non-initiators met the same inclusion criteria as initiators. a Among them, 2,139 patients received an HMA or LEN between Jan 1, 2008 to Dec 31, 2013. The first HMA/LEN use was defined as the index date. 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.		Percentage of residents with \geq 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)		
Figure 2. SMMRS Risk Status for Matched Patients ^a			CCI, mean (SD)	4.0 (3.2)	4.2 (3.1)	0.254
100 7	tatus ivi matchicu ra		Any blood transfusion at baseline, n (%)	429 (68.1)	309 (49.0)	< 0.00
90 - 80 -			HSA use at baseline, n (%)			< 0.001
70 - % 60 -			No use	366 (58.1)	428 (67.9)	
60 - 50 -	49.0		< 12 weeks	199 (31.6)	162 (25.7)	
ercen 40 -			≥ 12 weeks	65 (10.3)	40 (6.3)	
28.1			Index medication, n (%)			NA
20 - 10 -			Azacitidine	368 (58.4)	NA	
0 Low/Intermediate-1	Intermediate-2	High	Decitabine	132 (21.0)	NA	
	Category		LEN	132 (21.0)	NA	
^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.			^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.			

Table. Matched Cohort – Baseline and Index Characteristics

76.2 (8.6) [77]

77.0 (8.6) [78]

325 (51.6)

46 (7.3)

543 (86.2)

41 (6.5)

Age at MDS diagnosis, mean

Age at index, mean (SD)

del(5q) syndrome, n (%)

Race/ethnicity, n (%)

(SD) [median], years

[median], years

Female, n (%)

Black

Hispanic

HMA/LEN Initiators Non-Initiators P Value

n = 630

343 (54.4)

523 (83.0)

34 (5.4)

32 (5.1)

82.0 (8.8) [83] < 0.001

82.8 (8.8) [84] < 0.001

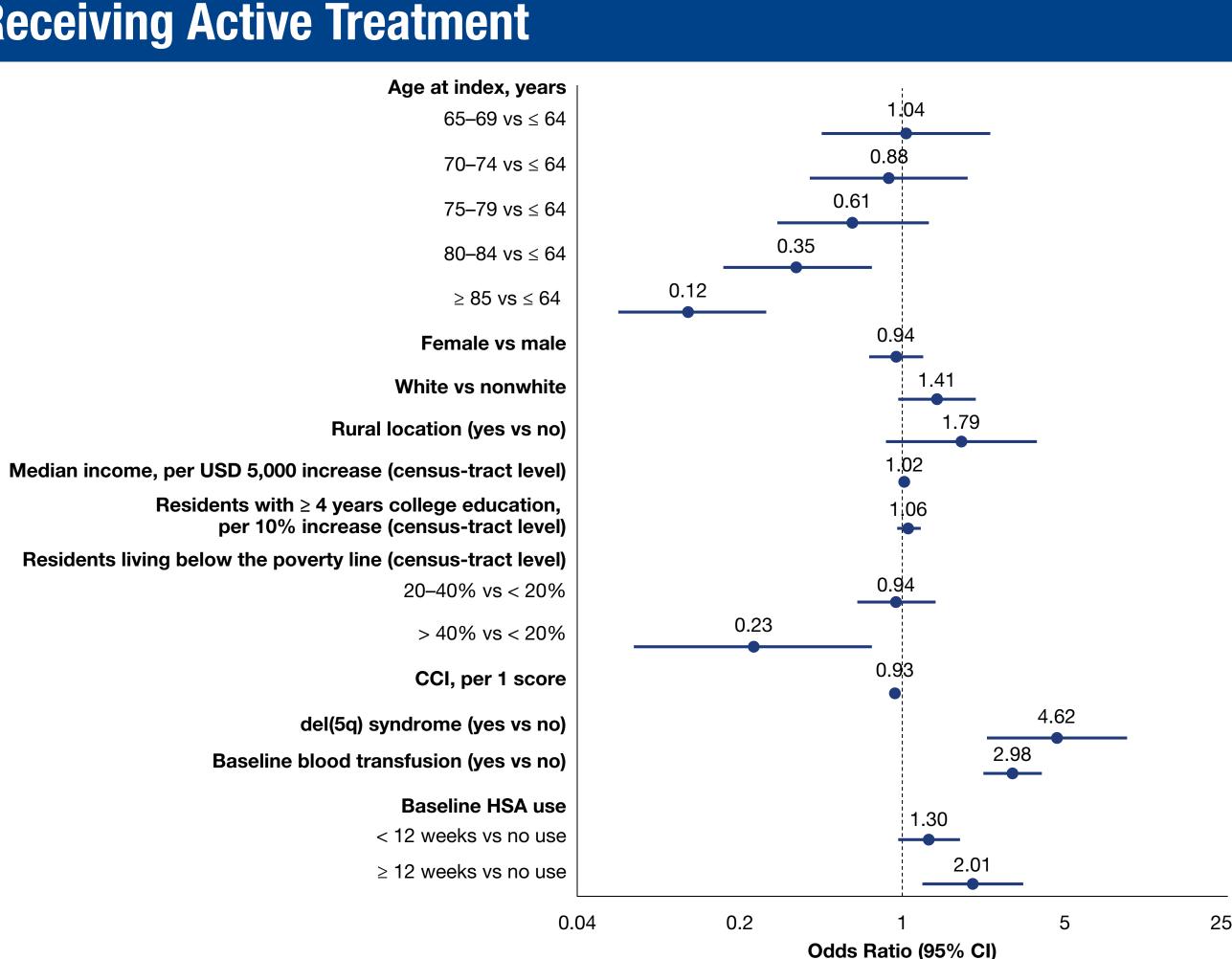
RESULTS (cont.)

- 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.