Transitions Across Different Lines of Therapy in Medicare-Enrolled Patient Populations With Multiple Myeloma

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INTRODUCTION

- Multiple myeloma (MM) accounts for approximately 1% of all cancers and 13% of all hematologic malignancies.[1]
- In 2016, it is estimated that 30,330 new cases of will be diagnosed and 12,650 people will die from MM in the United States.[1]
- Most patients diagnosed with symptomatic MM initiate treatment with chemotherapeutic agents.
- Because of the availability of many therapy options for MM patients who have relapsed or are refractory to previous treatments, many patients now receive multiple lines of therapy.[2,3]
- Receipt of multiple lines of therapy has implications for cost and outcomes of care.
- However, little is known about transition rates and reasons for not transitioning across lines of therapies.

METHODS

- Data were ascertained from the Centers for Medicare & Medicaid Services (CMS) 100% Hematologic Cancer File.
- Included Medicare beneficiaries had:
  - Diagnosis of MM (using a combination of the International Classification of Diseases, Revision 9 [ICD-9] codes 203.0X and diagnosis tests or treatment) between January 1, 2008 and December 31, 2011. MM case identification was done using a validated algorithm and the diagnosis date was identified as the disease index date.
  - Initiated treatment with a chemotherapeutic agent specific to MM following the disease index date. The date of treatment initiation was identified as the treatment index date.
  - Continuously enrolled in Medicare Part A, Part B, and Part D between treatment index date and 12 months prior to the disease index date.
  - Aged 18 years or older at the disease index date.
- Excluded patients:
  - Received chemotherapy and/or radiotherapy in the 12 months before the disease index date.
  - Had evidence of bone marrow transplant or stem cell transplant in the 12 months prior to the disease index date.
- Patients advanced lines of therapy after a 90-day gap in all treatments (break) or when a drug was added to a regimen after 90 days (direct switch).
  - Treatment regimens within lines were identified using claims for medications within 90 days of the start of the line.
  - We identified medications from Medicare Part D prescription drug event claims (using NDC codes) and Part B line items and Part A outpatient claims (using HCPCS codes).
  - To further identify patients who initiated multiple lines of therapy, we require them to be continuously enrolled in Medicare Parts A, B, and D between the dates of treatment initiation for the current and previous lines.
- Lines of therapy transition rates, reasons for advancing to the next line, and disposition of those who did not advance were determined.
  - Transition rate was defined as the proportion of patients who initiate the subsequent line of therapy (e.g. the proportion of line 1 patients who initiate second-line therapy).
  - Patients advance from one line of therapy to a subsequent one either via a break in therapy (a minimum of 90-day gap in treatment) or a direct switch (addition of another drug to an existing regimen).
  - Reasons for not initiating a subsequent line of therapy include death, cessation of Medicare Part A, B, or D coverage, or censoring at the end of study period (December 31, 2012).

RESULTS

- Of 73,028 patients with MM diagnosis between January 1, 2008 and December 31, 2011, we identified 15,474 MM patients who met the study inclusion and exclusion criteria and initiated a first-line treatment (age 75.1±8.8 years, 45.6% male, 77.5% white; **Table 1 and Figure 1**).
- 15,474, 8,308, 3,878, 1,608, and 604 MM patients initiated first-, second-, third-, fourth-, and fifth-line treatments, respectively; accounting for transition rates of 53.7%, 46.7%, 41.5%, and 37.6% for lines 1 through 4.
- Of those who initiated a first-line treatment and advanced to second-line treatment (n=8,308), 4,293 (51.7%) had a break in current treatment before line advancement while 4,015 (48.3%) switched directly to second-line therapy **(Table 2)**.

Figure 1. Schematic showing transition across line of therapy for multiple myeloma (MM) patients

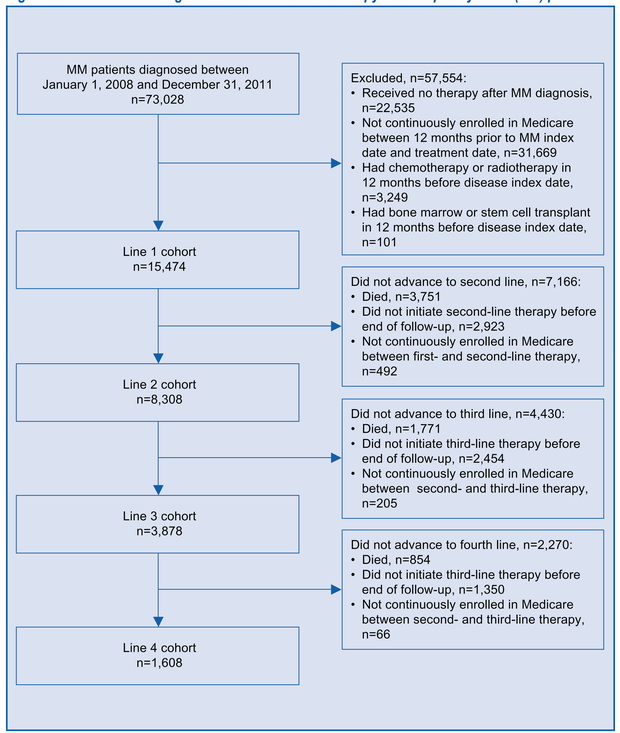

Table 1. Demographic characteristics of study population

	Line 1 cohort	Line 2 cohort	Line 3 cohort	Line 4 cohort
N	15,474	8,308	3,878	1,608
Age mean (SD), years*	75.1 (8.8)	74.2 (8.5)	73.3 (8.2)	72.6 (8.3)
Age, %*				
18–64	8.6	9.2	9.52	10.3
65–74	40.0	44.4	49.2	50.9
75+	51.4	46.4	41.3	38.7
Sex, %				
Male	45.6	46.6	47.1	46.1
Female	54.4	53.4	52.9	53.9
Race, %				
White	77.5	78.5	80.2	80.0
Black	16.3	15.4	14.1	14.2
Other	6.1	6.2	5.8	5.8
Index year				
2008	21.0	6.5	0.9	*
2009	24.0	19.0	11.1	4.0
2010	24.3	24.6	23.8	19.0
2011	25.6	26.9	30.3	35.3
2012	5.1	23.0	33.9	41.7
Charlson comorbidty index				
0	18.2	2.1	2.1	2.1
1–3	56.3	62.1	64.6	62.9
4+	25.5	35.7	33.3	35.0
Selected comorbid conditions				
Congestive heart failure	17.4	21.2	22.7	24.6
Diabetes	27.6	29.9	31.1	31.2
COPD	18.9	23.5	26.9	30.5
Chronic kidney disease	35.9	41.8	45.4	48.2
Anemia	58.8	72.9	79.4	82.8
Osteoporosis	12.1	15.0	17.0	19.0
Neutropenia	1.6	7.3	13.7	17.4
Thrombocytopenia	6.8	13.5	19.2	22.6
Peripheral neuropathy	5.1	14.7	22.2	26.5

*Age as at MM disease index date.
COPD, Chronic obstructive pulmonary disease; MM, multiple myeloma; SD, standard deviation.

- Similar patterns of advancement were observed for the other treatment lines.
- The most common reason for not advancing to the next treatment across all lines of therapy was censoring due to study end, while the least common reason was cessation of Medicare coverage **(Table 3)**.
  - Patients who were censored at end of study may have initiated subsequent lines of therapy. However, we are unable to identify such occurrences due to lack of data.
  - Thus, it is possible that true transition rates across lines of therapy are higher than the observed rates in this study.

Table 2. Pathways for advancing through lines of therapy among Medicare-enrolled multiple myeloma patients

Therapy	Advanced to next line n (%)	Pathway for advancing to next line n (%)
First line	15,474 (100.0)	
Advanced	8,308 (53.7)	8,308 (100.0)
Break in therapy		4,293 (51.7)
Direct switch		4,015 (48.3)
Second line	8,308 (100)	
Advanced	3,878 (46.7)	3,878 (100.0)
Break in therapy		1,871 (48.3)
Direct switch		2,007 (51.8)
Third line	3,878 (100.0)	
Advanced	1,608 (41.7)	1,608 (100.0)
Break in therapy		827 (51.3)
Direct switch		781 (48.6)
Fourth line	1,608 (100.0)	
Advanced	604 (37.6)	604 (100.0)
Break in therapy		305 (50.5)
Direct switch		299 (49.5)

Table 3. Reasons for not advancing to a next line of therapy among Medicare-enrolled multiple myeloma patients

Therapy	Did not advance to next line n (%)	Reason for not advancing to next line n (%)
First line	15,474 (100.0)	
Did not advance	7,166 (46.3)	7,166 (100.0)
Died		3,751 (52.3)
Lost coverage		492 (6.9)
Censored		2,923 (40.8)
Second line	8,308 (100)	
Did not advance	4,430 (53.3)	4,430 (100.0)
Died		1,771 (40.0)
Lost coverage		205 (4.6)
Censored		2,454 (55.4)
Third line	3,878 (100.0)	
Did not advance	2,270 (58.5)	2,270 (100.0)
Died		854 (37.6)
Lost coverage		66 (2.9)
Censored		1,350 (59.5)
Fourth line	1,608 (100.0)	
Did not advance	1,004 (62.4)	1,004 (100.0)
Died		354 (35.3)
Lost coverage		20 (2.0)
Censored		630 (62.8)

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CONFLICT OF INTEREST DISCLOSURES

Dr. Yusuf and Ms. Natwick report no conflicts of interest. Ms. Felici was an employee of Onyx Pharmaceuticals, Inc., an Amgen subsidiary, South San Francisco, CA. Dr. Werther is an employee of Amgen, Inc.

CONCLUSIONS

- Population sizes transitioning through lines of therapy were derived from Medicare population of MM patients.
- These estimates of patient numbers and their distribution across lines of therapy can provide an insight into understanding treatment patterns.

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