PSY30

Evaluation of Survival Outcomes of Post-Frontline Anti-Myeloma Treatments in Multiple Myeloma Patients Based on Data From SEER-Medicare Database

Ajay Nooka,[1,*] Peter Voorhees,[2] Shaji Kumar,[3] Maneesha Mehra,[4] Annette Lam,[4] Mary Slavcev,[4] Jon Ukropec,[5] Anandaroop Dasgupta[6]

[1]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [2]Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC, USA; [3]Mayo Clinic, Rochester, MN, USA; [4]Janssen Global Services, LLC, Raritan, NJ, USA; [5]Janssen Global Services, LLC, Spring House, PA, USA; [6]SmartAnalyst Inc., New York, NY, USA.

*Presenting author.

BACKGROUND

- Lenalidomide+dexamethasone (Rd) and bortezomib+dexamethasone (Vd) are standard-of-care regimens for multiple myeloma (MM) and are used both in frontline treatment and in subsequent lines of therapy[1]
- Recently, several phase 3 studies have reported the progression-free survival (PFS) and overall survival (OS) of relapsed or refractory MM (RRMM) patients treated with Rd or Vd as the control regimen[2-7]
  - A significant PFS benefit of adding a novel drug to Rd or Vd was observed across many of these studies
- However, a study of RRMM patients revealed that the real-world PFS associated with proteasome inhibitors (PIs) and immunomodulatory drugs (IMiDs) was shorter than that observed in clinical trials[8]
  - Additionally, real-world data reporting on outcomes of MM patients treated with Rd or Vd post-frontline are limited
- The SEER (Surveillance, Epidemiology, and End Results)-Medicare database contains linked population-based data derived from 2 large databases: the SEER registry and the Medicare database
  - SEER registry: contains demographic, clinical, and mortality information on cancer patients within geographically designated areas
  - Medicare database: contains information regarding inpatient and outpatient visits and services, prescription drug claims, and home health services claims for Medicare beneficiaries

OBJECTIVES

- To characterize patients treated with Rd or Vd for RRMM in a real-world setting
- To evaluate survival outcomes of treatment with Rd or Vd in patients who have received at least 1 prior line of therapy

METHODS

Patients

Inclusion Criteria

- An index MM diagnosis in the SEER-Medicare database on or after January 1, 2007
- Enrollment in Medicare Part A (inpatient services coverage), Part B (outpatient services coverage), and Part D (prescription drug coverage) at the time of the index MM diagnosis
  - This allowed us to track all inpatient, outpatient, and drug claims after MM diagnosis
  - The Medicare Part D dataset contains prescription drug claims from on or after January 1, 2007
- ≥1 anti-MM treatment documented
- No enrollment in Medicare Advantage at the time of the index MM diagnosis
  - The Centers for Medicare & Medicaid Services do not receive all inpatient and outpatient claims for patients enrolled in Medicare Advantage
- No prior primary cancers

Study Design and Data Analysis

- Business rules were used to identify each patient's lines of therapy
  - Data from patients treated post-frontline with Rd and Vd were analyzed separately
- Patients in each line of therapy cohort were characterized
- A survival analysis was conducted using the following business rules:
  - Occurrence of death was treated as an event
  - Patients who did not die were censored on the study end date of December 31, 2013
  - Calculation of time to event:
    - If a patient had an event, then: Duration = Event date – Index MM date + 1
    - If a patient was censored, then: Duration = Censor date – Index MM date + 1
- Rate models were used to estimate the incidences of death during the preprogression phase in the Rd and Vd cohorts

RESULTS

Patient Selection

- The SEER-Medicare database included 22,773 patients diagnosed with MM (**Table 1**)
  - 4,632 of these patients were eligible for analysis
    - 2,725 of these patients had ≥1 line of therapy and were included in the analysis

Table 1. Attrition Table for Inclusion/Exclusion Criteria for the Study

Criteria	N
Number of patients diagnosed with MM in the SEER-Medicare database	22,773
Number of patients with an MM diagnosis on or after January 1, 2007	18,778
Number of patients with Medicare Part A, Part B, and Part D coverage who were not enrolled in Medicare Advantage at the time of index MM diagnostics	5,675
Number of patients without a prior primary cancer	4,632
Number of patients with at least 1 prior line of therapy	2,725

MM, multiple myeloma; SEER, Surveillance, Epidemiology, and End Results.

Patient Characteristics

- **Table 2** shows the demographic and clinical characteristics of the 4,632 patients that were eligible for analysis

Table 2. Patient Demographic and Clinical Characteristics

Characteristic	N = 4,632
Race, n (%)	
Caucasian	3,248 (70.1)
African American	840 (18.1)
Asian	247 (5.3)
Hispanic	189 (4.1)
Native North American	21 (0.5)
Other	87 (1.9)
Gender, n (%)	
Female	2,351 (50.8)
Male	2,281 (49.2)
Age, y	
Mean (SD)	75.1 (9.3)
Median	75
Range	33-99
Patients aged <45 y, %	7.9
Patients aged 45-64 y, %	0.5
Patients aged ≥65 y, %	91.6
Follow-up period, mo	
Mean (SD)	24.9 (22.4)
Median	19
Range	1-85
Patients with <1 y of follow-up, %	41.2
Patients with 1-2 y of follow-up, %	13.9
Patients with ≥2 y of follow-up, %	44.9

SD, standard deviation; MM, multiple myeloma.
The follow-up period was derived by calculating the number of days between the index MM diagnosis date and the date when the patient's coverage ended or when the patient died, whichever was earlier.

- The overall frequency distribution of treatment regimens by year of index MM diagnosis is listed in **Table 3**

Table 3. Overall Frequency Distribution of Treatment Regimens by Year of Index MM Diagnosis

	Year of index MM diagnosis		
Regimen, %	2007-2009 (N = 6,122)	≥2010 (N = 3,588)	2007-2013 (N = 9,710)
Bortezomib+dexamethasone	22.7	26.5	24.0
Lenalidomide+dexamethasone	22.8	26.1	24.0
Dexamethasone	17.5	15.4	16.7
Other steroids	12.8	9.3	11.4
Thalidomide+dexamethasone	11.2	4.0	8.5
Bortezomib+lenalidomide+dexamethasone	3.8	8.8	5.7
Bortezomib+cyclophosphamide+dexamethasone	1.5	3.0	1.9
Bortezomib+thalidomide+dexamethasone	1.6	1.9	1.2
Pomalidomide+dexamethasone	0.9	0.9	1.0
Carfilzomib	0.5	0.4	0.6
Other chemotherapy regimens	4.5	4.7	4.2

MM, multiple myeloma.
Percentages are based on the total number of regimens (N) available within the associated interval displayed in the column header.

- The frequency distribution of treatment regimens by number of prior lines of therapy is listed in **Table 4**
  - Among patients who received ≥2 lines of therapy (LOT2+ patients), 579 instances were with Rd and 447 instances were with Vd

Table 4. Frequency Distribution of Treatment Regimens by LOT

Regimen, n (%)	LOT1 (N = 2,725)	LOT2 (N = 1,476)	LOT3+ (N = 1,640)
Bortezomib containing	**1,405**	**728**	**793**
Bortezomib only	602 (43)	271 (37)	250 (32)
Bortezomib+dexamethasone	470 (33)	227 (31)	220 (28)
Bortezomib+lenalidomide+dexamethasone	210 (15)	127 (17)	151 (19)
Bortezomib+thalidomide+dexamethasone	56 (4)	46 (6)	43 (5)
Other	67 (5)	57 (8)	129 (16)
Lenalidomide containing[a]	**736**	**548**	**479**
Lenalidomide only	153 (21)	204 (37)	215 (45)
Lenalidomide+dexamethasone	579 (79)	339 (62)	240 (50)
Other	4 (1)	5 (1)	24 (5)
Thalidomide containing[b]	**519**	**115**	**101**
Thalidomide+dexamethasone	296 (57)	46 (40)	42 (42)
Thalidomide only	212 (41)	64 (56)	54 (53)
Other	11 (2)	5 (4)	5 (5)
Other[c]	**65**	**85**	**267**
Pomalidomide or carfilzomib containing	0 (0)	8 (9)	145 (54)
Chemotherapy	65 (100)	77 (91)	122 (46)

LOT, line of therapy.
Percentages may not total 100% due to rounding.
[a]Includes all lenalidomide-containing regimens that do not contain bortezomib.
[b]Includes all thalidomide-containing regimens that do not contain bortezomib and lenalidomide.
[c]Includes all regimens that do not contain bortezomib, lenalidomide, and thalidomide.

Characterization of SEER-Medicare LOT2+ Patients Who Received Rd or Vd

- The baseline characteristics of SEER-Medicare LOT2+ patients who received Rd (LOT2+ Rd cohort) or Vd (LOT2+ Vd cohort) are shown in **Table 5**
  - Transfusions were received by 34% of Rd and 37% of Vd patients

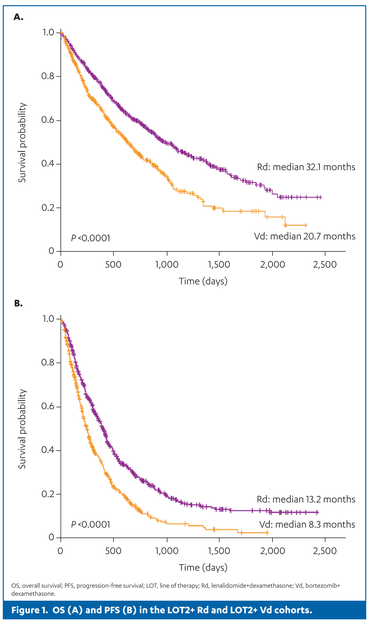
Table 5. Baseline Characteristics of SEER-Medicare LOT2+ Rd and LOT2+ Vd Patients

Characteristic	Rd	Vd
Number of LOT2+ instances	579	447
Number of distinct patients	507	394
% male	50	48
Age at start of line of therapy, y		
Mean	73.5	73.3
Median	74	74
Number of prior lines of treatment		
Mean	1.7	1.9
Median	1	1
% received transfusions	34	37
Prior exposure to		
PI only, n (%)	202 (34.9)	72 (16.1)
IMiD only, n (%)	178 (30.7)	162 (36.2)
PI and IMiD, n (%)	189 (32.6)	209 (46.8)
Refractory to		
PI only, n (%)	176 (30.4)	9 (2.0)
IMiD only, n (%)	29 (5.0)	257 (57.5)
Both PI and IMiD, n (%)	62 (10.7)	34 (7.6)

SEER, Surveillance, Epidemiology, and End Results; LOT, line of therapy; Rd, lenalidomide+dexamethasone; Vd, bortezomib+dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Survival Outcomes in the LOT2+ Rd and LOT2+ Vd Cohorts

- The median OS was 32.1 months in the LOT2+ Rd cohort and 20.7 months in the LOT2+ Vd cohort (**Figure 1A**)
- The median PFS was 13.2 months in the LOT2+ Rd cohort and 8.3 months in the LOT2+ Vd cohort (**Figure 1B**)
- In the preprogression phase, the mortality rate was 0.0144 per patient-month of follow-up in the LOT2+ Rd cohort and 0.0286 per patient-month of follow-up in the LOT2+ Vd cohort

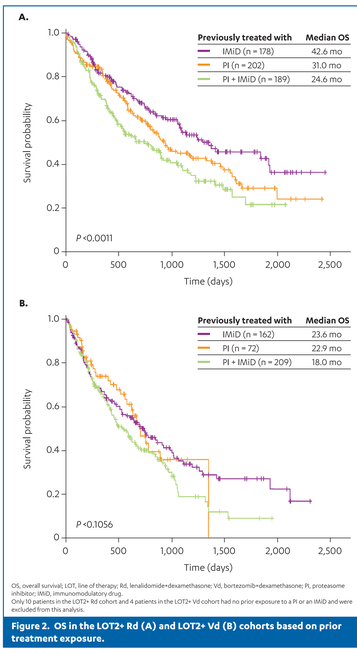


OS, overall survival; PFS, progression-free survival; LOT, line of therapy; Rd, lenalidomide+dexamethasone; Vd, bortezomib+dexamethasone.

Figure 1. OS (A) and PFS (B) in the LOT2+ Rd and LOT2+ Vd cohorts.

OS in the LOT2+ Rd and LOT2+ Vd Cohorts Based on Prior Treatment Exposure

- **Figure 2** shows OS in the LOT2+ Rd (**Figure 2A**) and LOT2+ Vd (**Figure 2B**) cohorts based on prior exposure to a PI, an IMiD, or a PI and an IMiD
  - In the LOT2+ Rd cohort, the median OS was:
    - 42.6 months among those with prior IMiD exposure
    - 31.0 months among those with prior PI exposure
    - 24.6 months among those with prior PI and IMiD exposure
  - In the LOT2+ Vd cohort, the median OS was:
    - 23.6 months among those with prior IMiD exposure
    - 22.9 months among those with prior PI exposure
    - 18.0 months among those with prior PI and IMiD exposure

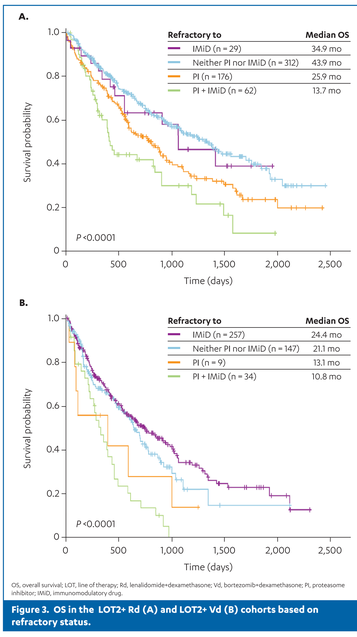


OS, overall survival; LOT, line of therapy; Rd, lenalidomide+dexamethasone; Vd, bortezomib+dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug.
Only 10 patients in the LOT2+ Rd cohort and 4 patients in the LOT2+ Vd cohort had no prior exposure to a PI or an IMiD and were excluded from this analysis.

Figure 2. OS in the LOT2+ Rd (A) and LOT2+ Vd (B) cohorts based on prior treatment exposure.

OS in the LOT2+ Rd and LOT2+ Vd Cohorts Based on Refractory Status

- **Figure 3** shows OS in the LOT2+ Rd (**Figure 3A**) and LOT2+ Vd (**Figure 3B**) cohorts based on refractory status
  - In the LOT2+ Rd cohort, the median OS was:
    - 43.9 months among those not refractory to either a PI or an IMiD
    - 34.9 months among those refractory to an IMiD
    - 25.9 months among those refractory to a PI
    - 13.7 months among those refractory to both a PI and an IMiD
  - In the LOT2+ Vd cohort, the median OS was:
    - 21.1 months among those not refractory to either a PI or an IMiD
    - 24.4 months among those refractory to an IMiD
    - 13.1 months among those refractory to a PI
    - 10.8 months among those refractory to both a PI and an IMiD



OS, overall survival; LOT, line of therapy; Rd, lenalidomide+dexamethasone; Vd, bortezomib+dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Figure 3. OS in the LOT2+ Rd (A) and LOT2+ Vd (B) cohorts based on refractory status.

CONCLUSIONS

- **Patients treated with Rd or Vd have poorer outcomes than those in recent clinical trials[2-6]**
  - **More elderly patients were included in our real-world analysis compared with recent clinical trials**
  - **These findings are consistent with those obtained from another real-world study[8]**
- **Our results highlight the need for effective treatments that improve outcomes for patients with RRMM**

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DISCLOSURES

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