E1256

Analysis of Overall Survival in Multiple Myeloma Patients With ≥3 Lines of Therapy Including a PI and an IMiD, or Double Refractory to a PI and an IMiD Using Real-world Data

Saad Usmani,[1] Avinash Desai,[2] Tahamtan Ahmadi,[3] Yvette Ng,[2] Gihoon Sung,[2] Maneesha Mehra[2]

[1]Levine Cancer Institute/Carolinas Healthcare System, Charlotte, NC, USA; [2]Janssen Global Services, Raritan, NJ, USA; [3]Janssen Research & Development, LLC, Spring House, PA, USA.

*Presenting author.

INTRODUCTION

- Treatment of multiple myeloma (MM) has improved over the past decade with the introduction of proteasome inhibitors (PIs) and immunomodulatory drugs (IMiDs)[1-3]; however, most patients relapse and long-term outcomes are poor[4-6]
- The natural history of the disease is well chronicled for long-established interventions, but there is limited information on the effects of newer agents in relapsed MM patients outside clinical trials[7]
- In 2012, the International Myeloma Working Group (IMWG) published a study based on medical records, which examined outcomes of patients who were refractory to bortezomib, a PI, and ≥1 IMiD (thalidomide and/or lenalidomide).[7] The study confirmed that outcomes remained poor in patients who were refractory to agents approved at the time of the analysis
- New agents have been approved since the IMWG study was published: pomalidomide (indicated for the treatment of MM patients with ≥2 prior therapies, including lenalidomide and a PI, and progression within 60 days of last therapy) and carfilzomib, (indicated for the treatment of MM patients with ≥2 prior therapies, including bortezomib and an IMiD, and progression within 60 days of last therapy)[8,9]
- Using a United States claims database, this analysis sought to determine treatment patterns and outcomes in patients with relapsed MM, including those exposed to pomalidomide and carfilzomib

AIM

- To define the treatment landscape and natural history of heavily pretreated MM patients who were refractory to both a PI and an IMiD or who had received ≥3 prior lines of therapy (LOTs), including a PI and an IMiD

METHODS

Study Design

- Records of US patients in the IMS LifeLink: IMS Oncology Electronic Medical Records Database from January 2000 to March 2014 were screened
- Patients were eligible for inclusion if they:
  - Had a diagnosis of MM from 2000 to 2011 (ICD-9 codes for MM were 203X, 203.0X, 203.00X, 203.01X, and 203.02X)
  - Did not have another cancer diagnosis prior to their diagnosis of MM
  - Received ≥3 prior LOTs (including a PI and an IMiD) and showed disease progression within 60 days of the completion of most recent treatment regimen, or
  - Were PI and IMiD refractory
- Based on availability of M-protein data, refractory was defined 3 ways (**Table 1**)

Table 1. Definitions of Refractory Status

Definition 1	DOT of current regimen ≤60 days, AND None of current drugs in next regimen, AND No baseline M-protein available
Definition 2	DOT of current regimen ≤60 days, AND None of current drugs in next regimen, AND Baseline M-protein available but no follow-up M-protein showing >25% decline
Definition 3	(DOT of current regimen >60 days, OR One of current drugs in next regimen), AND Both baseline and follow-up M-protein values available, but no >25% decline

DOT, duration of therapy.

- Drugs considered for regimen analysis were PIs (bortezomib, carfilzomib), IMiDs (thalidomide, lenalidomide, pomalidomide), and chemotherapy/steroids (melphalan, cyclophosphamide, dexamethasone)

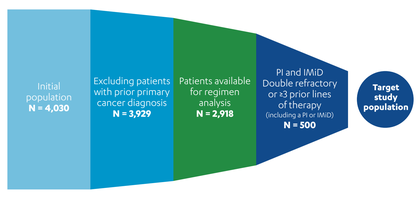
Study Endpoints and Analyses

- Median overall survival (OS) from time of last claim was assessed for the eligible population and in subgroups based on age, gender, Eastern Cooperative Oncology Group (ECOG) performance status at the last LOT, degree of refractoriness, or numbers of prior LOTs

RESULTS

Patients

- Records from 4,030 patients with MM were screened (**Figure 1**)
  - 101 patients were excluded because of a previous cancer diagnosis
  - 2,918 patients were available for regimen analysis
  - 500 patients met the criteria for the target population and were analyzed further



PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Figure 1. Identification of target population.

- Median age at diagnosis was 66 years; median age at eligibility for the study was 70 years (**Table 2**)
- 35% of patients had received ≥3 prior LOTs, including a PI and IMiD, but were not double refractory
- 51%, 12%, and 2% of patients were double, triple, or quadruple refractory, respectively
- Overall, patients received a median of 3 (range, 1-25) prior LOTs at eligibility

Table 2. Patient Demographics

Characteristic	N = 500
Median (range) age, years	
At diagnosis	66 (31-82)
At eligibility	70 (36-85)
Male, n (%)	258 (52)
Median (range) prior LOTs	3 (1-25)
≥3 prior LOTs, including a PI and IMiD, but not double refractory, n (%)	177 (35)
Refractory status, n (%)	
Double refractory	253 (51)
Triple refractory	61 (12)
Quadruple refractory	9 (2)
ECOG score at eligibility, n (%)	N = 208*
0	56 (27)
1	98 (47)
2	41 (20)
3	13 (6)

*ECOG scores at eligibility were missing for 292 patients.
LOT, line of therapy; PI, proteasome inhibitor; IMiD, immunomodulatory drug; ECOG, Eastern Cooperative Oncology Group.

- Patients received a wide range of treatments at eligibility, including carfilzomib and pomalidomide (**Table 3**)
- All patients received 1 LOT after eligibility; 298 received 2 LOTs, and 169 received 3 LOTs
- 22% of patients received carfilzomib or pomalidomide as their first LOT after meeting criteria
  - Carfilzomib and pomalidomide were given as single agents >80% of the time

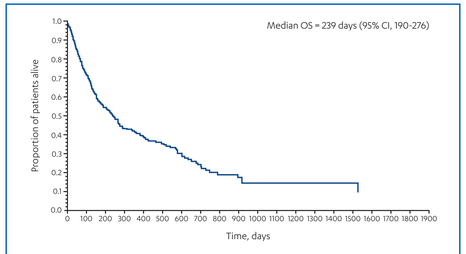
Table 3. Treatment Regimen Received at Eligibility

Regimen	Patients at identification, % (N = 500)
Bortezomib only (no IMiDs/cytotoxic agent)	28.8
Lenalidomide/thalidomide only	24.0
Bortezomib + lenalidomide/thalidomide (±cytotoxic agent)	21.2
Bortezomib + cytotoxic agent	6.8
Any cytotoxic agent	5.2
Any carfilzomib	5.8
Steroid only	4.0
Any pomalidomide	2.8
Lenalidomide/thalidomide + cytotoxic agent	1.0
Bendamustine	0.4

IMiD, immunomodulatory drug.

Overall Survival

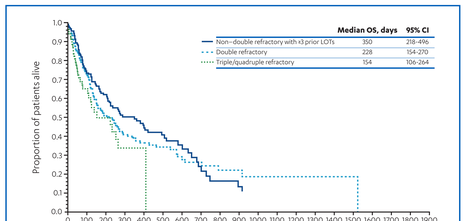
- Median OS from time of last claim for all eligible patients (N = 500) was 239 days (95% confidence interval [CI], 190-276; **Figure 2**)



OS, overall survival; CI, confidence interval; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Figure 2. OS in patients with ≥3 prior LOTs (including a PI and an IMiD) or double refractory to a PI and an IMiD.

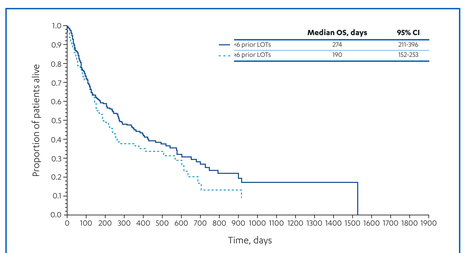
- Median OS for triple/quadruple refractory patients was shorter (154 days; 95% CI, 106-264) than double refractory only (228 days; 95% CI, 154-270) and non–double refractory patients with ≥3 prior LOTs (350 days; 95% CI, 218-496; *P* = 0.0695; **Figure 3**)
  - The median OS of double refractory patients was not significantly shorter than median OS among patients with ≥3 prior LOTs (including a PI and an IMiD) that were not double refractory (*P* <0.28)



OS, overall survival; LOT, line of therapy; PI, proteasome inhibitor; IMiD, immunomodulatory drug; CI, confidence interval.

Figure 3. OS in double and triple/quadruple refractory patients and patients with ≥3 prior LOTs (including a PI and an IMiD).

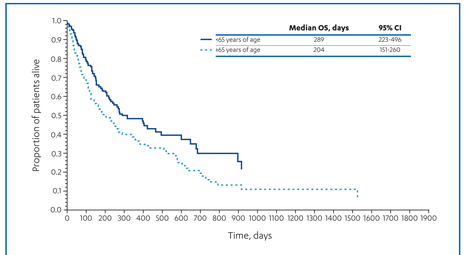
- Median OS was 274 days (95% CI, 211-396) in patients with <6 prior LOTs versus 190 days (95% CI, 152-253) in those with ≥6 prior LOTs (*P* = 0.09; **Figure 4**)



OS, overall survival; LOT, line of therapy; CI, confidence interval.

Figure 4. OS in patients with <6 or ≥6 prior LOTs.

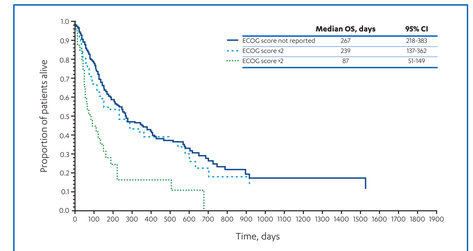
- Median OS was longer in patients <65 years (289 days; 95% CI, 223-496) compared with patients ≥65 years (204 days; 95% CI, 151-260; *P* <0.01; **Figure 5**)



OS, overall survival; CI, confidence interval.

Figure 5. OS in patients ≥65 or <65 years of age.

- Patients with an ECOG score ≤2 had a longer median OS (239 days; 95% CI, 137-362) versus patients with ECOG scores >2 (87 days; 95% CI, 51-149; *P* <0.0001; **Figure 6**)



OS, overall survival; ECOG, Eastern Cooperative Oncology Group; CI, confidence interval.

Figure 6. OS in patients based on ECOG score.

- There were no significant differences in median OS between females (260 days; 95% CI, 176-396) and males (228 days; 95% CI, 165-274; *P* = 0.73)

CONCLUSIONS

- **Median OS among patients who were double refractory to PIs and IMiDs, including pomalidomide and carfilzomib, or who had received ≥3 prior therapies (including a PI and an IMiD) was 239 days (approximately 8 months)**
  - **This result is similar to that reported by the 2012 IMWG study where a median OS of 9 months was observed[7]**
- **Patient characteristics that were associated with shorter median OS included age ≥65 years, ECOG score >2, ≥6 prior LOTs, and triple/quadruple refractory disease**
- **In spite of the approval of pomalidomide and carfilzomib, outcomes remain poor in patients with relapsed MM**
- **Novel agents are urgently needed for patients with heavily pretreated, refractory MM**

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