Current Real-World Treatment Patterns and Outcomes in Patients With Relapsed/Refractory Multiple Myeloma

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Introduction

- Since 2013, several new agents with novel mechanisms of action have been approved for relapsed/refractory multiple myeloma (RRMM), including new-generation immunomodulatory drugs.[1-6]
- Current treatment options include combinations of newer agents with existing standard of care regimens, as well as triplet and quadruplet regimens.[7]
- National Comprehensive Cancer Network treatment guidelines recommend bortezomib (BTZ), lenalidomide (LEN), and dexamethasone for first-line therapy (1LT) of both transplant and non-transplant candidates; guideline recommendations following 1LT are relatively inclusive of therapies with market approval,[7] allowing physicians to select the regimen deemed most appropriate for a given patient.
- Limited real-world data exist to describe current utilization, treatment patterns, and clinical outcomes of the different treatments for RRMM.

Objective

- To assess treatment patterns and outcomes of patients with RRMM who received ≥2 lines of therapy from 2011–2017 using electronic medical records (EMRs) and charts from US community oncology practices.

Methods

Study design

- A comprehensive electronic chart review using data from the International Oncology Network (ION) practices and the ION EMR data warehouse.
- Patients (N=1601) were identified through programmatic queries of standardized elements within structured fields available through the ION EMR management software.
  - Inclusion criteria included:
    - Diagnosis of multiple myeloma (MM) based on International Classification of Diseases, 9th and 10th Revision, Clinical Modification codes
    - Initiation of chemotherapy 1LT between January 1, 2011, and May 31, 2017
    - Receipt of ≥2 treatment regimens
    - ≥18 years of age at initiation of 1LT
    - No evidence of other primary malignant cancer during the study period
    - ≥90 days of follow-up after initiation of 1LT treatment.
- Of the 1601 patient charts identified, a sample of 1005 charts that were readily available were reviewed alongside the database analysis to maximize the completeness and robustness of study results.
  - Patients were excluded if they had:
    - MM that was not being actively treated/managed (confirmed within physician notes)
    - Diagnosis or treatment for MM outside the ION network
    - Diagnosis of any other malignancy
    - Missing/incomplete physician notes.
- Patients were stratified into "older" versus "newer" treatment cohorts based on whether the therapies used in each treatment line were approved before/during 2012 versus 2013 or later.

Outcome measures

- Outcome measures assessed included:
  - Baseline demographics and clinical characteristics
  - Treatment patterns (including time on treatment, length of treatment-free intervals, and retreatment with a particular therapy)
  - Adverse events (AEs)
  - Median real-world progression-free survival (PFS)
  - Median real-world overall survival (OS).
- A change in treatment line was defined as a change in regimen due to progression and not due to toxicity or other reasons.

Data analysis

- Patient data were examined from the date of initiation of 1LT for MM until death, loss to follow-up, or study end date, whichever was earliest.
- This study was hypothesis generating, thus no statistical tests were performed; descriptive statistics are used throughout.

Results

Patients

- Of the 1005 charts reviewed, 456 patients met study criteria and were included in the analysis.
  - The most common reasons for exclusion were diagnosis/treatment outside of the ION network (n=113) and not initiating 2LT during the study period (n=390).
- The median age at diagnosis was 70.4 years, 39.5% of patients were female, and 66.0% had bone involvement at diagnosis (**Table 1**).
- International Staging System stage within 1 month of diagnosis was I in 28.7%, II in 27.9%, and III in 43.4% of patients with a known stage (**Table 1**).

Table 1. Demographic and clinical characteristics

Demographic characteristics	N	%
Total population	456	
Age at MM onset date, Median (range), years	70.4	(38.9–95.1)
Gender		
Female	180	39.5
Race/ethnicity		
White	173	37.9
African American	39	8.6
Hispanic	1	0.2
Asian	5	1.1
Other	1	0.2
Missing	237	52.0
Patient insurance		
Commercial	9	2.0
Medicaid	11	2.4
Medicare	338	74.1
Other	0	0.0
Missing	98	21.5
Geographic region of practice		
Midwest	60	13.2
Northeast	0	0.0
South	313	68.6
West	83	18.2
Year of MM onset		
2011	131	28.7
2012	111	24.3
2013	88	19.3
2014	75	16.4
2015	39	8.6
2016	10	2.2
2017	2	0.4

Clinical characteristics	N	%[a]
Total population	456	
ISS stage (provider reported)[b]	251	55.0
I	*72*	*28.7*[c]
II	*70*	*27.9*[c]
III	*109*	*43.4*[c]
ECOG PS at diagnosis	143	31.4
0	*32*	*22.4*[c]
1	*76*	*53.1*[c]
2	*29*	*20.3*[c]
≥3	*6*	*4.2*[c]
Immunoglobulin class	429	94.1
IgA	*43*	*10.0*[c]
IgG	*147*	*34.3*[c]
light-chain only kappa	*44*	*10.3*[c]
light-chain only lambda	*46*	*10.7*[c]
LDH at MM onset	121	26.5
Normal	*64*	*52.9*[c]
Low (<140 IU/L)	*28*	*23.1*[c]
High (>280 IU/L)	*29*	*24.0*[c]
Bone involvement at baseline	301	66.0
Baseline smoking status	390	85.5
Current smoker	*50*	*12.8*[c]
Past smoker	*139*	*35.6*[c]
Never smoked	*201*	*51.5*[c]

[a]Patients with unknown data excluded by variable. [b]ISS stage either by physician report or first reported laboratory values for serum beta-2-microglobulin and serum albumin within 1 month of diagnosis. [c]Expressed as percentages of the total number of patients with data available in that category.

ECOG PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma.

Treatment patterns

- In total, 183 (40.1%) patients received 3LT, 75 (16.4%) received 4LT, and 29 (6.4%) received 5LT.
- 1LT and 2LT were dominated by BTZ, LEN, and the combination of the two, with 93.3% of patients using these agents as 1LT and 69.8% as 2LT.
- These patients often received the agent(s) as retreatment in 2LT and beyond (for patients who received BTZ or LEN alone, 55.6% were retreated with BTZ, and 47.0% retreated with LEN, respectively; for patients who received BTZ/LEN combination, 51.3% were retreated with BTZ and 46.2% retreated with LEN).
- In 3LT and beyond, there was greater use of newer drugs compared with 1LT and 2LT, including pomalidomide, carfilzomib, elotuzumab, panobinostat, daratumumab, and ixazomib (**Table 2A**). The use of these newer drugs also increased over time (**Table 2B**).

Table 2A. Percentage of patients using newer treatments[a], by LT

Treatment, %	1LT	2LT	3LT	4LT	5LT
Carfilzomib	2.2	17.8	31.7	28.0	31.0
Pomalidomide	0.9	12.1	26.2	33.3	37.9
Daratumumab	0	1.8	6.6	13.3	17.2
Elotuzumab	0	1.5	2.7	4.0	3.4
Ixazomib	0	1.5	3.8	8.0	6.9
Panobinostat	0	0.4	0	4.0	3.4

Table 2B. Percentage of patients using newer treatments[a] in any LT, by year

Treatment, %	Index year						
	2011 (n=131)	2012 (n=111)	2013 (n=88)	2014 (n=75)	2015 (n=39)	2016 (n=10)	2017 (n=2)
Carfilzomib	35.1	36.0	35.2	38.7	48.7	20.0	50.0
Pomalidomide	22.9	27.9	27.3	33.3	38.5	30.0	50.0
Daratumumab	2.3	3.6	5.7	14.7	25.6	20.0	0
Elotuzumab	1.5	2.7	1.1	5.3	12.8	0	0
Ixazomib	2.3	1.8	4.5	9.3	7.7	20.0	0
Panobinostat	2.3	0.9	1.1	1.3	2.6	0	0

[a]With or without other agents. LT, line of therapy.

- Median (mean) time on treatment decreased from 7.5 (10.7) months in 1LT to ≤2.3 (≤3.7) months in 4LT and 5LT (**Figure 1**).
- Median (mean) time to next treatment decreased from 1.6 (5.7) months between 1LT and 2LT to 0.5 (1.1) months between 4LT and 5LT (**Figure 2**).
- The most common reasons for discontinuation were disease progression and drug toxicity/intolerability. Other reasons included death and active surveillance.

Adverse events

- The most commonly reported AEs for all lines of therapy were fatigue (71.6%–78.3%), bone pain (45.3%–69.1%), and anemia (54.8%–69.3%; **Table 3**).
- The incidence of edema decreased from 1LT to 5LT; other AEs were variable across treatment lines (**Table 3**).

Figure 1. Length of treatment by LT

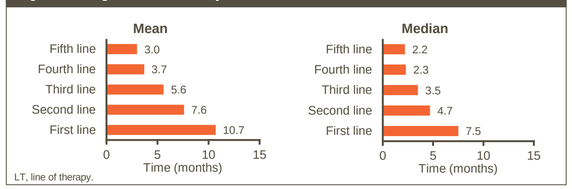


Figure 2. Time to next therapy, reported among patients receiving the next LT

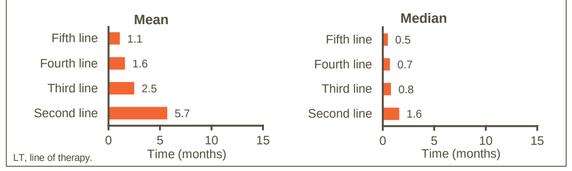


Table 3. Adverse events occurring in ≥5% of patients by LT

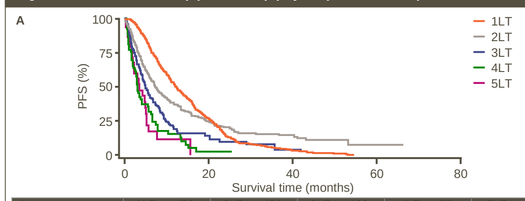
Adverse event, %	LT				
	1	2	3	4	5
Fatigue	78.3	74.3	71.6	77.3	75.9
Anemia	69.3	54.8	59.6	62.7	62.1
Bone pain	69.1	62.5	57.4	45.3	55.2
Neuropathy	48.5	39.3	32.8	28.0	37.9
Thrombocytopenia	31.8	30.3	29.5	33.3	34.5
Edema	30.3	23.0	21.3	18.7	6.9
Neutropenia	19.5	18.2	13.7	20.0	27.6
Leukopenia	15.4	12.9	8.7	10.7	17.2
Pneumonia	12.5	8.3	6.6	8.0	6.9
Blurred vision	7.0	3.5	4.9	4.0	6.9

LT, line of therapy.

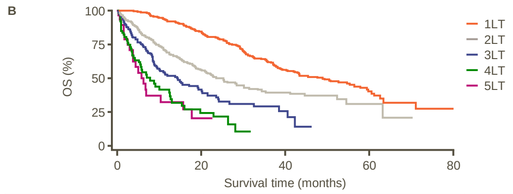
Treatment outcomes

- Overall, median (mean) PFS ranged from 12.0 (14.5) months in 1LT to 3.5 (4.6) months in 5LT, and median (mean) OS ranged from 48.8 (45.8) months in 1LT to 5.8 (8.3) months in 5LT (**Figure 3**).
- A trend for increased median PFS and median OS with newer versus older drugs was observed across most treatment lines; the magnitude of the "new" treatment benefit was pronounced in 1LT (**Figure 4**).

Figure 3. Real-world PFS[a] (A) and OS[b] (B) by LT (all treatments)



All treatments	1LT (n=456)	2LT (n=456)	3LT (n=183)	4LT (n=75)	5LT (n=29)
Progressed, n (%)	465 (100)	308 (67.5)	133 (72.7)	59 (78.7)	23 (79.3)
Median PFS (95% CI), months	12.0 (11.0, 13.5)	7.2 (6.3, 8.6)	4.9 (4.2, 6.0)	3.0 (2.4, 4.1)	3.5 (1.9, 5.0)



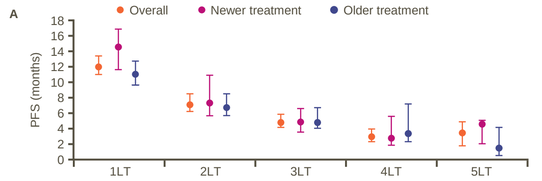
All treatments	1LT (n=456)	2LT (n=456)	3LT (n=183)	4LT (n=75)	5LT (n=29)
Died, n (%)	183 (40.1)	183 (40.1)	91 (49.7)	46 (61.3)	19 (65.5)
Median OS (95% CI), months	48.8 (40.3, 57.9)	23.6 (20.2, 30.2)	14.3 (9.5, 20.1)	7.9 (5.2, 12.5)	5.8 (2.9, 15.8)

[a]Disease progression was defined by either: documentation of disease progression, increasing disease severity or new disease site; documentation of initiation of hospice care; or death. If progression was not indicated in the EMR, then PFS was censored at either the date of last administration of the current treatment regimen or last visit prior to next line of therapy, whichever occurred latest.

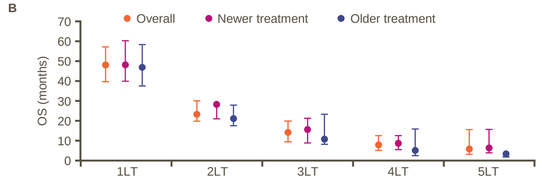
[b]OS was defined as time from the date of treatment initiation to the date of death. Patients without a recorded death date were censored for OS at their last visit date or the end of the study period, whichever came first.

CI, confidence interval; EMR, electronic medical record; LT, line of therapy; OS, overall survival; PFS, progression-free survival.

Figure 4. Median real-world PFS[a] (A) and OS[b] (B) by LT overall and by newer and older treatments



Median PFS (95% CI), months	1LT	2LT	3LT	4LT	5LT
Newer treatment	14.5 (11.6, 16.8)	7.5 (5.9, 11.1)	4.9 (3.6, 6.7)	2.9 (1.9, 5.6)	4.6 (2.1, 5.1)
Older treatment	11.4 (9.6, 12.4)	6.8 (5.7, 8.5)	4.8 (4.1, 6.7)	3.4 (2.3, 7.2)	1.5 (0.6, 4.2)



Median OS (95% CI), months	1LT	2LT	3LT	4LT	5LT
Newer treatment	48.2 (40.0, 60.3)	28.1 (20.7, NA)	15.4 (8.7, 21.3)	8.7 (5.5, 12.4)	6.3 (3.7, 15.6)
Older treatment	47.0 (37.6, 58.6)	21.3 (17.7, 28.0)	10.9 (8.2, 23.2)	5.1 (2.2, 15.9)	3.4 (1.6, NA)

[a]Disease progression was defined by either: documentation of disease progression; increasing disease severity; new disease site; documentation of initiation of hospice care; or death. If progression was not indicated in the EMR, then PFS was censored at either the date of last administration of the current treatment regimen or last visit prior to next line of therapy, whichever occurred latest.

[b]OS was defined as time from the date of treatment initiation to the date of death. Patients without a recorded death date were censored for OS at their last visit date or the end of the study period, whichever came first.

CI, confidence interval; EMR, electronic medical record; LT, line of therapy; NA, not available; OS, overall survival; PFS, progression-free survival.

Conclusions

- Forty percent of patients received therapy beyond 2LT, demonstrating a great unmet need in the treatment of RRMM.
- While BTZ and LEN were predominant in 1LT and 2LT, substantial fragmentation was seen ≥3LT, highlighting the lack of defined treatment pathways for these patients.
- BTZ and LEN were often used as retreatment after 1LT, with around half of previously-treated patients receiving these in combination or as a single agent again in later lines.
- As expected, treatments in 3LT and beyond offered shorter benefits as the disease progressed; median time on treatment and PFS decreased with increasing treatment line.
- Fatigue, anemia, and bone pain were the three most frequent AEs across all lines of treatment.
- Median PFS and OS with newer agents in ≥3LT ranged from 2.9 months to 4.9 months and 6.3 months to 15.4 months, respectively; this is slightly lower than that observed in recent clinical trials of novel agents such as pomalidomide and daratumumab (median PFS: 3.7–8.8 months[8,9] and median OS: 12.7–17.5 months[8-10]).
- While there remains a need to replicate these results within a larger dataset where statistical comparisons can be made and confounding factors controlled for, a trend for improved PFS and OS outcomes with more-recently approved treatments was suggested, particularly when used in earlier lines of treatment.

References

1. FDA. Pomalidamide (POMALYST©) Prescribing Information. 2013.
2. FDA. Elotuzumab (EMPLICITI®) Prescribing Information. 2015.
3. FDA. Panobinostat (FARYDAK©) Prescribing Information. 2016.
4. FDA. Daratumumab (DARZALEX®) Prescribing Information. 2018.
5. FDA. Ixazomib (NINLARO©) Prescribing Information. 2015.
6. FDA. Carfilzomib (KYPROLIS©). Prescribing Information. 2012.
7. NCCN. *Clinical Practice Guidelines in Oncology. Multiple Myeloma. v1.2019.* 2018.
8. Chari A, et al. *Blood* 2017;130:974–81.
9. Lonial S, et al. *Lancet* 2016;387:1551–60.
10. San Miguel J, et al. *Lancet Oncol* 2013;14:1055–66.

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Disclosures

- J Willson, AB, JO, and JN are employees of, and own stocks/shares in, GSK. OL, DS-M, and J Willey are employees of Xcenda, which was contracted by GSK to conduct this study.

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