

Real-World Treatment Patterns and Outcomes of Triple Exposed Multiple Myeloma (MM) Patients Treated in Community Oncology Practices in the US

Poster No. MM-079

Background

The overall survival of patients with multiple myeloma (MM) has significantly improved in the last two decades with utilization of immunomodulatory drugs, proteasome inhibitors (PIs), and anti-CD38 monoclonal antibodies (mAbs).¹⁻³

Despite these therapeutic advances, MM remains a challenging and incurable disease, with almost all patients experiencing relapse and eventually becoming refractory to the available therapies.⁴⁻⁹

Little is known about the treatment and outcomes of patients with relapsed or refractory MM who have been treated with at least 1 anti-CD38 mAb, 1 proteasome inhibitor, and 1 immunomodulatory agent (triple exposed) in community practices in the US.

The MAMMOTH study by Ghandi et al. showed that 275 patients treated at 14 academic institutions from January 2017 to June 2018 with prior exposure to these 3 agent classes (that is, triple exposed) had median overall survival (OS) of 9.2 months⁷; however, real-world data in the community-based setting are still scarce.

Objective

The aim of this study was to evaluate the real-world treatment patterns and outcomes of patients previously treated with a PI, immunomodulatory drug, and anti-CD38 in US community practices.

Methods

This retrospective observational study used the Integra Connect database, which includes electronic health data from structured and unstructured fields from 12 large community networks, representing over 1000 physicians, combined with administrative claims data from payors.

Patient-level data were completely anonymized and were reported in aggregate. All data collected for this analysis were stored and evaluated in accordance with regulatory requirements and applicable guidance for electronic records.

Patient Population

Adult patients with MM who had received any treatment during the study period from January 1, 2016 to December 31, 2019, with subsequent follow-up through March 31, 2020, for all patients identified in the Integra Connect database by International Classification of Diseases (ICD)-10 codes* and included in the study.[†]

Key inclusion/exclusion criteria

- Patients ≥18 years of age at start of first line of therapy (LOT)
- Patients who met the MM identification criteria with at least 1 treatment[‡]
- Patients who had evidence of starting triple therapy exposure with PI, immunomodulatory agent, and anti-CD-38 mAb (triple exposed)
- The primary study population was defined as patients who completed triple-exposure LOT and received subsequent LOTs during the study period.

Assessments

Assessments included therapies received before, during, and after the triple-exposure LOT; duration of LOTs; response rates; and apparent survival.

Apparent survival, calculated as the number of days between the start date of subsequent line of therapy (sub-LOT) and either the end of the study period or the last office visit date, was measured for all patients who completed their subsequent line of therapy after triple-exposure LOT within the study period. Kaplan-Meier analysis was performed to estimate apparent survival after triple therapy exposure.

Any patient with an office visit in 2020 is considered to have survived.

*ICD-10 codes included C000-C439, C450-C499, C50011-C768, C770-C799, C7B00-C7B09, C800-C802, C8100-C9592, C960-C96Z, C49A0-C4A9, C7A00-C7A09, D0000-D099, D460-D46Z; †Owing to the coronavirus disease 2019 pandemic, patient data in 2020 were censored; and all patients with data in 2020 were considered to have survived. Some patients may not have data in 2020 owing to changes in medical care resulting from the pandemic, which could have a possible impact on this study. ‡Patients were required to have 2 or more evaluation and management claims coded with an MM ICD-9/ICD-10 diagnosis code in any position of the claim on at least 2 separate dates of service during the study period

Disclosures

RS has nothing to disclose. **MX, ND, and PV** are paid employees of IntegraConnect LLC and have received research funding from GSK paid to IntegraConnect LLC. **CH, TB, LS, SF, and EMM** are paid employees of GlaxoSmithKline and hold stocks/shares in GlaxoSmithKline.

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Results

A total of 1399 patients were identified as having MM and having started triple therapy exposure with PI, immunomodulatory agent, and anti-CD-38 mAb.[‡] Among these, 501 patients completed their triple therapy LOT and received subsequent treatment (primary study population).

Of the 501 patients in the primary population the median age (range) was 66 years (35-90), 50% of the population was male, with 42% White, 15% Black, and 43% of unknown race.

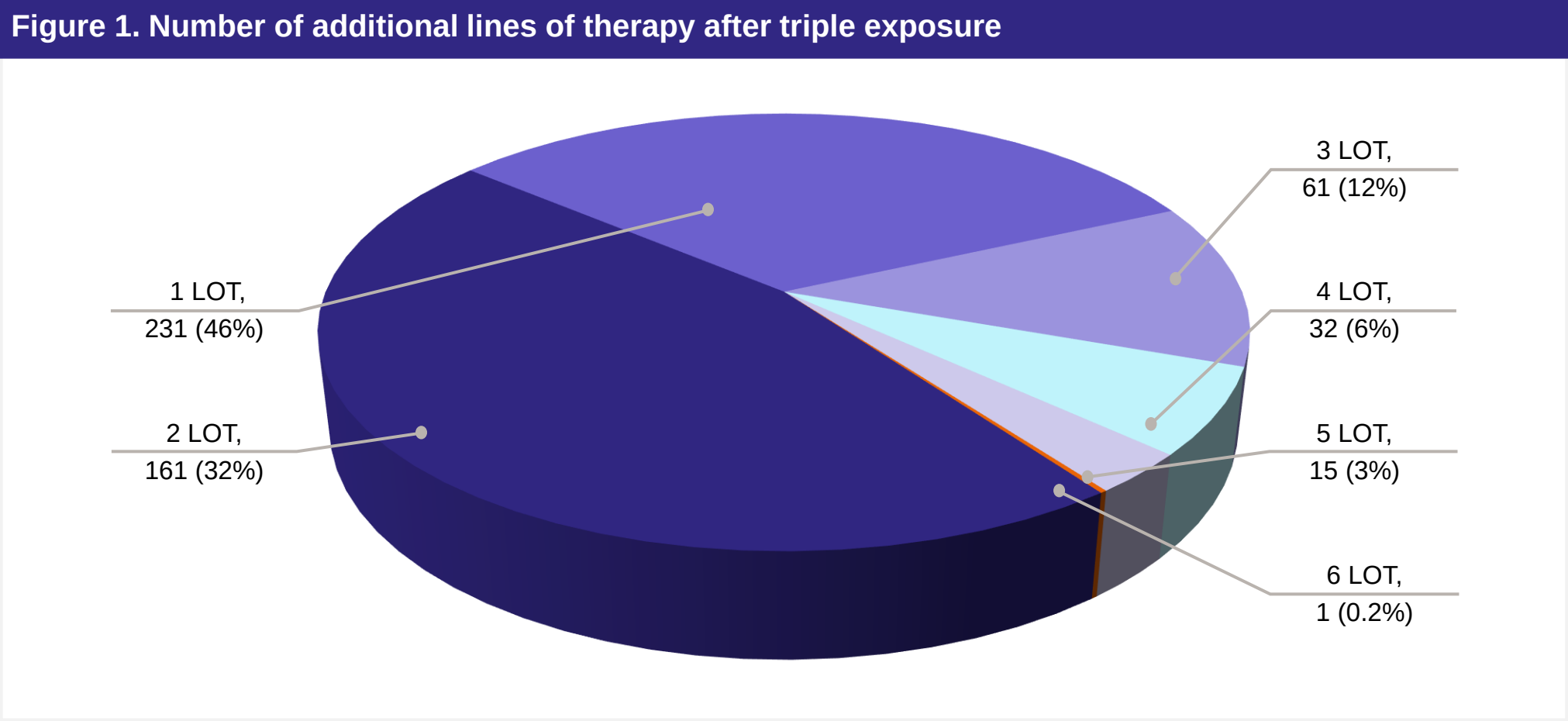
Triple exposure was achieved with a median of 3 LOTs, and the median number of days from the start of LOT1 to completion of triple-exposure LOT was 995 (**Table 1**).

[‡]Patients who completed their triple therapy and did not start a subsequent LOT (n=411). A total of 487 patients were excluded as they did not complete their triple therapy during the study period

Table 1. Number of lines of therapy and duration (days)				
Exposure variables				
	Mean	SD	Median	
Number of LOTs from LOT1 through final triple exposure agent	3.5	1.4	3	
Number of days from start of LOT1 to start of final triple exposure agent	956.2	728.5	785	
Number of days from start of LOT1 to end of triple exposure	1158.2	775	995	

Figure 1 shows how many additional lines of therapy patients received at time of data cutoff post triple exposure.

At time of data cutoff, almost half had received 1 additional LOT, approximately one-third had received 2 additional LOTs, and 22% received 3 or more additional LOTs after triple exposure (**Figure 1**).



Daratumumab was used in 100% of patients, and was reused in subsequent LOTs in 31% (**Table 2**). Note: daratumumab was the only anti-CD38 mAb approved during the study timeframe.

Among PIs, bortezomib was predominantly used with 91% utilization, followed by carfilzomib with 81%, and then ixazomib with 32%; the reuse of these agents ranged from 20% to 48% (**Table 2**).

Among the immunomodulatory agents, lenalidomide was utilized in 93% of patients, pomalidomide in 82%, and thalidomide in 9%, with high rates of reuse among treatments in this class as well (**Table 2**).

Overall, classes with most treatment recycling were among PIs and immunomodulatory agents, with carfilzomib (48%) and pomalidomide (47%), respectively. Nearly one-third (31%) of patients were re-treated with daratumumab (**Table 2**).

Table 2. Therapies received to reach triple exposure and treatments received subsequent to triple exposure		
	Percent of patients receiving specific agents leading to triple exposure	Percent of patients receiving specific agents in LOTs subsequent to triple exposure
	n (%)	
Anti-CD38: Daratumumab	501 (100)	157 (31.3)
PI: Bortezomib Carfilzomib Ixazomib	456 (91.0) 404 (80.6) 161 (32.1)	148 (29.5) 241 (48.1) 98 (19.6)
Immunomodulatory agents: Lenalidomide Pomalidomide Thalidomide	466 (93.0) 412 (82.2) 45 (9.0)	155 (30.9) 234 (46.7) 30 (6.0)
Cytotoxic chemotherapy* Cytotoxic chemotherapy*	253 (50.5)	151 (30.1)
Others Selinexor Panobinostat Elotuzumab	33 (6.6) 51 (10.2) 180 (35.9)	34 (6.8) 39 (7.8) 138 (27.5)

*Cytotoxic agents included bendamustine, 34 (6.8); doxorubicin, 46 (9.2); melphalan, 50 (10.0); cisplatin, 20 (4.0); doxorubicin liposomal, 27 (5.4); carmustine, 2 (0.4); etoposide, 24 (4.8). Agents subsequent to triple exposure included bendamustine, 30 (6.0); doxorubicin, 36 (7.2); melphalan, 29 (5.8); cisplatin, 17 (3.4); doxorubicin liposomal, 20 (4.0); carmustine, 3 (0.6); etoposide, 18 (3.6)

Twenty-one percent of patients received repeat treatment with triple-class agents exclusively (**Table 3**).

Subsequent treatments for nearly 80% of patients included a combination of triple-class agents and other agents such as elotuzumab, panobinostat or selinexor, while <5% received exclusively agents outside of PIs, immunomodulatory agents, and daratumumab (**Table 3**).

The rates of reuse indicate a high proportion of quad- and penta-refractory patients.

Table 3. Classes of treatments used after triple-exposure therapy (sub-LOT)		
Percent of patients exclusively receiving triple-exposure (PI, immunomodulatory agent, anti-CD38) agents as a sub-LOT	N	%
Total	103	20.6
Receiving exclusively previously administered triple-exposure agents as sub-LOT	25	5.0
Receiving only new triple-exposure agents as sub-LOT	35	7.0
Receiving both previously administered and new triple-exposure agents as sub-LOT	43	8.6
Percent of patients receiving triple-exposure (PI, immunomodulatory agent, anti-CD38) agents and combination of other agents as a sub-LOT	N	%
Total	398	79.4
Receiving exclusively non–triple-exposure agents in sub-LOT	24	4.8
Receiving non–triple-exposure agents and previously administered triple-exposure agents in sub-LOT	111	22.2
Receiving non–triple-exposure agents and new triple-exposure agents in sub-LOT	79	15.8
Receiving non–triple-exposure agents, new triple-exposure agents, and previously administered triple-exposure agents in sub-LOT	184	36.7

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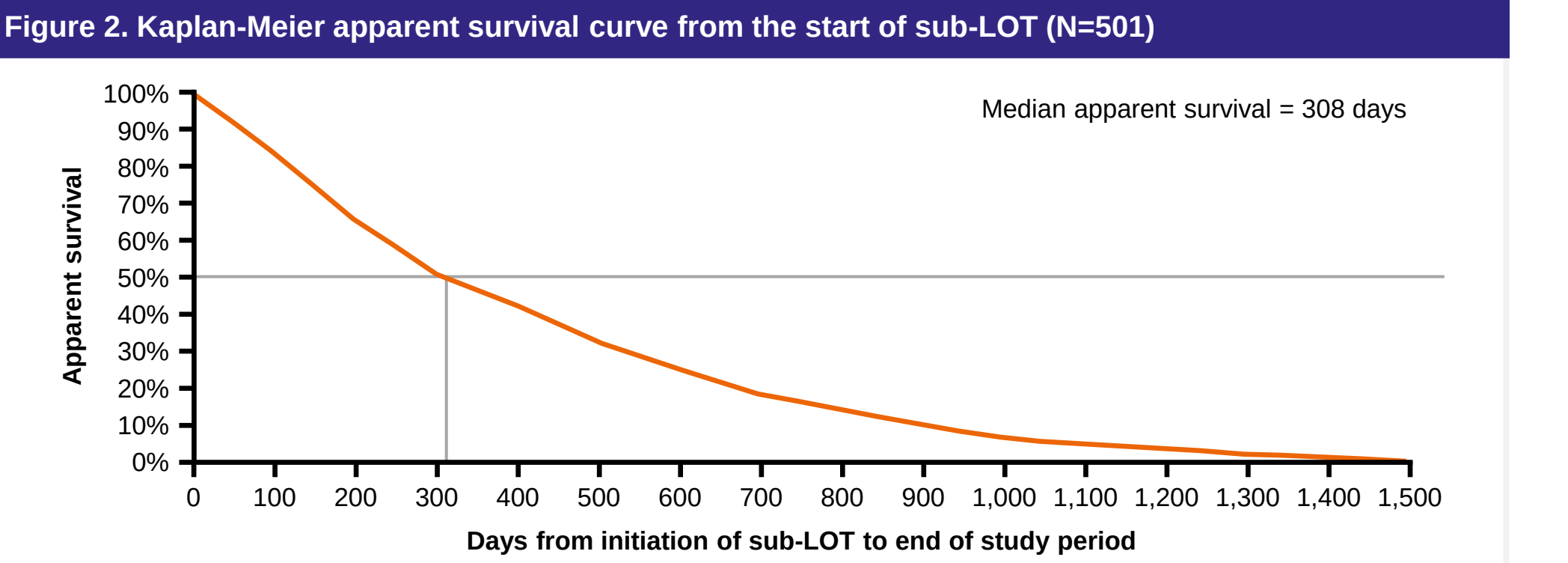
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The median duration of sub-LOT immediately after triple exposure was 78 days, and median apparent survival from time of initiation of subsequent lines of therapy was less than a year (308 days) (**Table 4**, **Figure 2**).

Table 4. Time to subsequent treatment post triple-exposure and duration of treatment					
Summary Level Outcome Variables					
	Mean	SD	Median	Range	N
Number of days between end of triple exposure and start of sub-LOT	36.04	64.06	18.00	(1, 691)	501
Duration of sub-LOT (days)	124.99	151.34	78.00	(0, 1125)	429
Number of LOTs subsequent to triple exposure	1.89	1.06	2.00	(1, 6)	501

Figure 2 depicts apparent survival from initiation of treatment after triple exposure.



Apparent survival was defined as the length of time from the start of sub-LOT through the date of the last office visit, is a real-surrogate for measuring overall survival. The Kaplan-Meier analysis was not adjusted for any covariates.

Conclusions

In this retrospective observational study, we observed high degree of reuse of PIs, immunomodulatory agents, and anti-CD38 classes in lines of therapy subsequent to triple exposure.

Consistent with findings in the academic-based MAMMOTH study,⁷ we observed poor outcomes with short duration in subsequent lines of therapy and short overall survival.

Contrary to the above MAMMOTH study, our analysis found that patients reached triple exposure with a lower median number of LOTs and months.

This difference in median LOTs to triple exposure may be due to the approval of daratumumab for earlier lines of therapy during the defined study period, in which we observed patients receiving triple therapy sooner, without any observed impact on survival.

Although the clinical data used in this study are robust, there are some limitations to be considered:

- Medical records and claims data analysis rely on complete and accurate documentation and coding, which were not fully auditable.
- Patient experience is truncated based on data availability.
- Results from this analysis may not be representative for different populations or different time periods.

The high proportion of triple-class agent reuse, short durations of additional treatments post triple-class exposure, and poor survival in this setting all highlight the previously noted need for new agents with novel mechanisms to improve survival and quality of life in these triple-refractory patients.

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