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Real-World Disease Burden and Treatment Patterns Among Triple-Class–Exposed Patients With Relapsed/Refractory Multiple Myeloma and Extramedullary Disease in the United States: A Retrospective Analysis Using Flatiron Health Electronic Medical Records

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Key Takeaway

Among patients with TCE RRMM, the median OS in patients with EMD was only one-third that of patients without EMD (12.6 months vs 36.4 months, respectively), highlighting the need for novel, effective treatment options for patients with TCE RRMM and EMD

Conclusions

This real-world analysis demonstrated that patients with TCE RRMM, both with and without EMD, are often retreated in a subsequent LOT with the same drugs or drug classes previously administered, underscoring the limited treatment options in this population

Moreover, patients with TCE RRMM and EMD consistently experienced poorer outcomes, as evidenced by shorter PFS, OS, TTD, and TTNT compared to patients with TCE RRMM without EMD

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Poster

https://www.congresshub.com/ASH2025/Oncology/Talquetamab/Biran

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Introduction

- Patients with triple-class–exposed (TCE) relapsed/refractory multiple myeloma (RRMM) are defined as those who have received ≥1 proteasome inhibitor (PI), ≥1 immunomodulatory drug (IMiD), and ≥1 anti-CD38 monoclonal antibody (mAb)[1]
- These patients typically have limited treatment options and poor prognosis with standard treatments[2-4]
- The presence of extramedullary disease (EMD) is associated with particularly adverse outcomes in clinical trial settings
  - In pivotal trials of patients with heavily pretreated RRMM, EMD has been linked to lower response rates and shorter survival; however, these trial populations may not represent the full spectrum of disease burden observed in routine practice[5-8]
- In real-world investigations of patients with TCE RRMM, EMD data remain scarce, with limitations, such as small sample sizes, that make it difficult to characterize disease burden and survival outcomes in this high-risk population[9]
- Therefore, this retrospective study examined the disease burden of patients with TCE RRMM, with and without EMD, who started a subsequent line of therapy (LOT), with a focus on patient characteristics, treatment patterns, and clinical outcomes

Methods

Study design and patient population

- In this real-world, retrospective, observational, longitudinal study, adult patients ≥18 years of age in the United States with RRMM who started a subsequent (index) LOT after becoming TCE, with an index date between May 3, 2018, and July 31, 2024, were identified from the Flatiron Health Research Database (FHRD)[10]
  - The FHRD provides longitudinal, disease- and treatment-level patient records from over 2.2 million patients with cancer treated by more than 2500 clinicians across 280 community oncology practices and academic medical centers in the United States, which enables comprehensive real-world data analysis
  - A previously reported algorithm was used to derive LOTs[11]
- Patients were followed from the index date (defined as the index LOT start date) until the earliest of last activity date, death, or end of the study period (January 31, 2025)
  - For index LOTs that contained chimeric antigen receptor T-cell (CAR-T) therapies, the LOT start date may have been the start of bridging therapy while the patient was waiting for a CAR-T infusion; thus, the index date was the CAR-T infusion date instead of the LOT start date
- Patients were categorized into 2 cohorts based on the presence or absence of soft-tissue EMD[12] (ie, arising from soft tissue; EMD arising from bone and extending into soft tissue was not included) documented prior to or on the index date
  - EMD cohort: soft-tissue EMD confirmed via chart review
  - Non-EMD cohort: no evidence of soft-tissue EMD via chart review; served as a descriptive benchmark for the EMD cohort

Data analysis

- Study variables included patient demographic and clinical characteristics, treatment history, and treatment patterns
- Time-to-event outcomes included progression-free survival (PFS), overall survival (OS), time to treatment discontinuation or death (TTD), and time to next treatment or death (TTNT)
- All study variables were reported descriptively
- Time-to-event outcomes were estimated using the Kaplan–Meier method
  - Progression events were derived by Flatiron Health's algorithm based on M protein and structured free light chain measures. Incident or growing plasmacytomas were not considered in the progression algorithm, which may have resulted in the undercapture of progression events
  - TTD was not applicable to CAR-T therapy, thus patients with CAR-T therapy in their index regimen were excluded from TTD calculations

Results

Patient characteristics

- Overall, 175 patients with EMD and 2259 patients without EMD were included in this study
- Key patient demographic and clinical characteristics are summarized in **Table 1**
  - The median age at index was 66.0 years for patients with EMD and 69.0 years for patients without EMD
  - Patients with EMD were more likely to have high-risk cytogenetics compared with patients without EMD
- The median duration of follow-up was 10.2 months for patients with EMD and 16.9 months for patients without EMD

Table 1: Demographic and clinical characteristics

Characteristic	EMD (n=175)	Non-EMD (n=2259)
Age at index, years		
Mean (SD)	66.0 (9.9)	67.9 (10.4)
Median	66.0	69.0
Sex, n (%)		
Male	89 (50.9)	1234 (54.6)
Female	86 (49.1)	1025 (45.4)
Race, n (%)		
White	114 (65.1)	1431 (63.3)
Black or African American	29 (16.6)	394 (17.4)
Other race	15 (8.6)	225 (10.0)
Unknown	17 (9.7)	209 (9.3)
Ethnicity, n (%)		
Hispanic or Latino	17 (9.7)	178 (7.9)
Not Hispanic or Latino	127 (72.6)	1745 (77.2)
Unknown	31 (17.7)	336 (14.9)
Insurance type at index,[a] n (%)		
Commercial	112 (64.0)	1245 (55.1)
Medicare[b]	68 (38.9)	986 (43.6)
Practice type, n (%)		
Academic	83 (47.4)	830 (36.7)
Community	82 (46.9)	1314 (58.2)
Both	10 (5.7)	115 (5.1)
CCI score,[c] mean (SD)	3.5 (3.5)	2.5 (3.0)
High-risk cytogenetics,[d] n (%)	61/148 (41.2)	550/1868 (29.4)
Time from first evidence of EMD to index date, months		
Mean (SD)	15.0 (22.2)	–
Median	7.2	–

EMD, extramedullary disease; SD, standard deviation; CCI, Charlson Comorbidity Index; FISH, fluorescence in situ hybridization.
[a]Patients may be included in multiple categories. The most common insurance types are listed.
[b]Medicare included both Fee-for-Service and Medicare Advantage plans.
[c]Measured during the entire preindex period.
[d]High-risk cytogenetics were defined by the presence of del(17p), t(4;14), or t(14;16) and measured from the study start date through 7 days after the index date. The denominator indicates the number of patients with ≥1 FISH test record.

- A total of 34.3% of patients with EMD and 39.2% of patients without EMD had received 3 to 4 prior LOTs before the index date (**Table 2**)
  - Penta-exposure was observed in 19.4% of patients with EMD and 13.9% of patients without EMD
  - Prior stem cell transplant was received by nearly half of all patients (EMD, 49.7%; non-EMD, 44.6%)

Table 2: Prior treatment exposure

	EMD (n=175)	Non-EMD (n=2259)
Number of prior LOTs before the index date		
Mean (SD)	2.6 (1.2)	2.7 (1.2)
Median	2.0	2.0
1-2, n (%)	100 (57.1)	1176 (52.1)
3-4, n (%)	60 (34.3)	886 (39.2)
≥5, n (%)	15 (8.6)	197 (8.7)
Prior treatment type, n (%)		
PI		
Bortezomib	168 (96.0)	2143 (94.9)
IMiD		
Lenalidomide	168 (96.0)	2191 (97.0)
Anti-CD38 mAb		
Daratumumab	175 (100)	2219 (98.2)
Penta-exposed[a]	34 (19.4)	314 (13.9)
Prior stem cell transplant	87 (49.7)	1008 (44.6)

EMD, extramedullary disease; LOT, line of therapy; SD, standard deviation; PI, proteasome inhibitor; IMiD, immunomodulatory drug; mAb, monoclonal antibody.
[a]Exposed to ≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb.

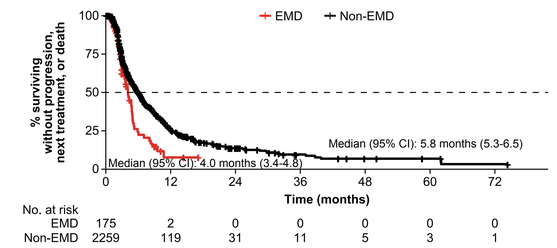
Treatment patterns

- Among patients with ≥3 months of follow-up or follow-up ending in death (EMD, n=149; non-EMD, n=2081), the most common index regimens, excluding corticosteroids, were daratumumab + pomalidomide (n=11; 7.4%), carfilzomib + pomalidomide (n=10; 6.7%), and carfilzomib + cyclophosphamide (n=8; 5.4%) for patients with EMD and daratumumab + pomalidomide (n=235; 11.3%), daratumumab + carfilzomib (n=154; 7.4%), and carfilzomib + pomalidomide (n=150; 7.2%) for patients without EMD
  - The most common drugs within index regimens included carfilzomib (n=59; 39.6%), pomalidomide (n=49; 32.9%), and daratumumab (n=37; 24.8%) for patients with EMD and daratumumab (n=926; 44.5%), carfilzomib (n=799; 38.4%), and pomalidomide (n=790; 38.0%) for patients without EMD

Outcomes

- The median PFS was 4.0 months (95% confidence interval [CI], 3.4-4.8) for patients with EMD and 5.8 months (95% CI, 5.3-6.5) for patients without EMD (**Figure 1**)
  - These results are similar to results from the LocoMMotion study, in which median PFS was 2.7 months versus 5.1 months among patients with TCE RRMM with EMD versus without EMD, respectively[9]

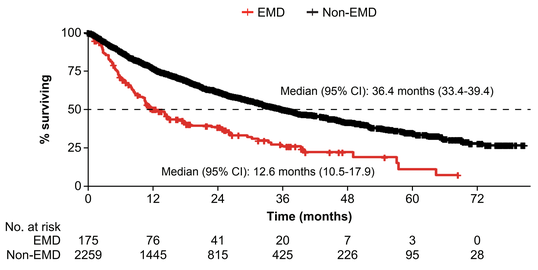
Figure 1: Progression-free survival



EMD, extramedullary disease; CI, confidence interval.

- The median OS was 12.6 months (95% CI, 10.5-17.9) for patients with EMD and 36.4 months (95% CI, 33.4-39.4) for patients without EMD (**Figure 2**)

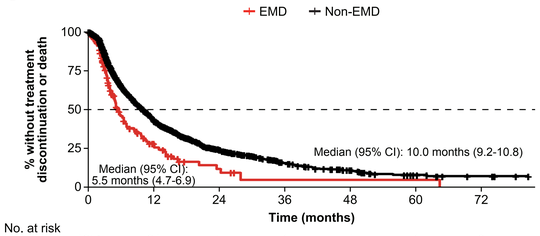
Figure 2: Overall survival



EMD, extramedullary disease; CI, confidence interval.

- Excluding patients with CAR-T index regimens, the median TTD was 5.5 months (95% CI, 4.7-6.9) for patients with EMD and 10.0 months (95% CI, 9.2-10.8) for patients without EMD (**Figure 3**)

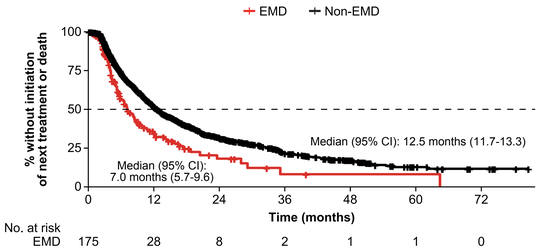
Figure 3: Time to treatment discontinuation or death



EMD, extramedullary disease; CI, confidence interval; CAR-T, chimeric antigen receptor T cell; TTD, time to treatment discontinuation or death.
[a]A total of 10 patients with EMD and 30 patients without EMD received CAR-T–containing index regimens and were therefore excluded from the TTD analysis.

- The median TTNT was 7.0 months (95% CI, 5.7-9.6) for patients with EMD and 12.5 months (95% CI, 11.7-13.3) for patients without EMD (**Figure 4**)

Figure 4: Time to next treatment or death



EMD, extramedullary disease; CI, confidence interval.

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