

# Real-World Burden of Infection Among Triple-Class-Exposed Patients With Relapsed/Refractory Multiple Myeloma

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### Key Takeaways

- Real-world data from the KRD and APCD demonstrate that patients with TCE RRMM and at least 4 prior LOTs have high rates of infections
- The rate of severe infections among these patients was 46.1%, with the most common infections being bacterial (42.5%), followed by viral (17.1%) and fungal (4.9%). Infection rates increased over time

### Conclusion

These real-world data highlight the substantial burden of infection in patients with TCE RRMM who received conventional, non-T-cell-redirecting therapies after at least 4 prior LOTs, with a high rate of any infection (>60%) and severe infections (>45%), emphasizing the importance of proactive infection management in this vulnerable patient population

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## Introduction

- Patients with triple-class-exposed (TCE) relapsed/refractory multiple myeloma (RRMM; defined as exposure to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 monoclonal antibody) often receive multiple lines of therapy (LOTs) and subsequently go on to receive additional LOTs due to the challenging nature of managing RRMM<sup>1,2</sup>
- The cumulative immunosuppressive effect of these multiple LOTs across all prior and future regimens may contribute to an elevated risk of infection<sup>1</sup>
- Infections are a significant concern in the management of RRMM as they can lead to severe complications that affect the overall survival and quality of life of patients with RRMM<sup>3</sup>
- Based on findings from pivotal clinical studies, including the phase 1/2 MonumenTAL-1 and phase 1/2 MajesTEC-1 studies, bispecific antibodies (BsAbs) have emerged as a key treatment option in later LOTs<sup>4,5</sup>
- Although clinical studies of BsAbs have explored infection rates,<sup>6-8</sup> real-world data on the infection burden associated with conventional therapies (as opposed to T-cell-redirecting therapies such as B-cell maturation antigen [BCMA]-targeted therapy, G protein-coupled receptor family C group 5 member D [GPCR5D]-targeted therapy, and chimeric antigen receptor T-cell therapy) remain limited
- Infection rates among patients with multiple myeloma were comparable, irrespective of the specific type of therapeutic regimen administered<sup>9,10</sup>
- This retrospective, observational study aimed to assess the infection risk in patients with TCE RRMM who received conventional, non-T-cell-redirecting therapies

## Results

### Patient demographic and baseline characteristics

- The study included 2702 patients from the KRD and 1755 patients from the APCD
- Demographic and clinical characteristics are summarized in **Table 2**
  - The median (interquartile range) follow-up period was 9.5 (4.1-19.4) months for patients from the KRD and 14.9 (6.2-31.6) months for patients from the APCD
  - The mean (standard deviation [SD]) age was 67.2 (10.6) years for patients from the KRD and 69.3 (9.5) years for patients from the APCD
  - 54.0% of patients from the KRD and 52.4% of patients from the APCD were male, and 53.2% and 64.2% were White, respectively
  - In terms of insurance coverage, 29.3% of patients from the KRD and 17.4% of patients from the APCD had a commercial payer, 9.0% and 6.6% had Medicaid, and 61.5% and 75.0% had Medicare, respectively
  - The mean (SD) Quan-Charlson Comorbidity Index score was 3.2 (3.1) for patients from the KRD and 2.3 (2.8) for patients from the APCD

**Table 2: Demographic and clinical characteristics**

Characteristic	KRD (n=2702)	APCD (n=1755)
<b>Age at index, years</b>		
Mean (SD)	67.2 (10.6)	69.3 (9.5)
Median (IQR)	67.0 (60-75)	71.0 (64-77)
<b>Age group, n (%)</b>		
<65 years	1130 (41.8)	466 (26.6)
65-69 years	395 (14.6)	307 (17.5)
70-74 years	420 (15.5)	374 (21.3)
≥75 years	757 (28.0)	608 (34.6)
<b>Sex, n (%)</b>		
Male	1458 (54.0)	919 (52.4)
Female	1244 (46.0)	836 (47.6)
<b>Race/ethnicity, n (%)</b>		
White	1438 (53.2)	1126 (64.2)
Other/unknown	602 (22.3)	410 (23.4)
Black or African American	596 (22.1)	194 (11.1)
Asian or Pacific Islander	66 (2.4)	25 (1.4)
<b>Region, n (%)</b>		
Northeast	882 (32.6)	269 (15.3)
South	813 (30.1)	674 (38.4)
Midwest	565 (20.9)	442 (25.2)
West	434 (16.1)	370 (21.1)
Unknown	8 (0.3)	0
<b>Payer, n (%)</b>		
Commercial	792 (29.3)	306 (17.4)
Medicare	1662 (61.5)	1316 (75.0)
Medicaid	244 (9.0)	116 (6.6)
Unknown	4 (0.1)	17 (1.0)
<b>Mean (SD) QCCI score excluding MM diagnosis</b>	3.2 (3.1)	2.3 (2.8)
<b>Comorbidities, n (%)</b>		
Any CRAB symptoms <sup>a</sup>	1425 (52.7)	637 (36.3)
Peripheral neuropathy	1064 (39.4)	483 (27.5)
Renal impairment	914 (33.8)	231 (13.2)
Bone lesion	407 (15.1)	179 (10.2)
Diabetes	722 (26.7)	351 (20.0)
Anemia	703 (26.0)	350 (19.9)
Hypercalcemia	268 (9.9)	142 (8.1)
<b>Mean (SD) follow-up, months</b>	13.5 (12.9)	21.3 (19.6)
<b>Median (IQR) follow-up, months</b>	9.5 (4.1-19.4)	14.9 (6.2-31.6)

KRD, Komodo Research Dataset; APCD, All-Payer Claims Data; SD, standard deviation; IQR, interquartile range; QCCI, Quan-Charlson Comorbidity Index; MM, multiple myeloma; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification. <sup>a</sup>Evaluated based on ICD-9-CM and ICD-10-CM diagnosis codes for hypercalcemia, renal impairment, anemia, and bone lesions.

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## Methods

### Study design and patients

- Patients with TCE RRMM and at least 4 prior LOTs who started a subsequent LOT (defined as the index LOT) during the study period from January 1, 2016, to October 31, 2024, were identified from the US Komodo Research Dataset (KRD) and All-Payer Claims Data (APCD)
  - Data from both the KRD and the APCD were used to ensure valid, generalizable evidence across diverse populations, enhancing confidence in the findings and broadening their applicability
- Patients enrolled in a clinical trial up to 6 months prior to the index date (defined as the index LOT start date) or who received T-cell-redirecting therapies on or after the index date were excluded
- Patient characteristics were collected during the 6-month baseline period, which was defined as the 6-month continuous enrollment period prior to the index date
- Patients were followed from the index date to the end of continuous enrollment for insurance coverage, death, data cutoff, or the end of the study period, whichever occurred first

- Overall, patients were heavily pretreated, with a median index LOT number of 5 in both datasets (**Table 3**)

**Table 3: Treatment history**

Pretreatment	KRD (n=2702)	APCD (n=1755)
<b>Prior PI, n (%)</b>	2702 (100)	1755 (100)
Bortezomib	2148 (79.5)	1432 (81.6)
Carfilzomib	1584 (58.6)	926 (52.8)
Ixazomib	763 (28.2)	339 (19.3)
<b>Prior IMiD, n (%)</b>	2702 (100)	1755 (100)
Lenalidomide	2263 (83.8)	1578 (89.9)
Pomalidomide	1879 (69.5)	686 (39.1)
Thalidomide	132 (4.9)	83 (4.7)
<b>Prior anti-CD38, n (%)</b>	2702 (100)	1755 (100)
Daratumumab	2683 (99.3)	1739 (99.1)
Isatuximab	67 (2.5)	46 (2.6)
<b>Prior BCMA, n (%)</b>	46 (1.7)	20 (1.1)
Ciltacabtagene autoleucl	3 (0.1)	0
Idecabtagene vicleucl	5 (0.2)	3 (0.2)
Teclistamab	8 (0.3)	6 (0.3)
Belantamab mafodotin-blmf	32 (1.2)	13 (0.7)
Eiranatamab	0	0
<b>Prior GPRC5D therapy, n (%)</b>		
Talquetamab	0	2 (0.1)
<b>Prior quad-exposed, n (%)</b>	891 (33.0)	312 (17.8)
<b>Index LOT number, median (IQR)</b>	5.0 (5-5)	5.0 (5-6)

KRD, Komodo Research Dataset; APCD, All-Payer Claims Data; PI, proteasome inhibitor; IMiD, immunomodulatory drug; BCMA, B-cell maturation antigen; GPRC5D, G protein-coupled receptor family C group 5 member D; LOT, line of therapy; IQR, interquartile range. <sup>a</sup>Defined as exposure to ≥2 PI and ≥2 IMiD.

### Prior therapies

- The most common prior therapies in the TCE category for patients from the KRD and APCD, respectively, were daratumumab (99.3% and 99.1%), lenalidomide (83.8% and 89.9%), and bortezomib (79.5% and 81.6%)
  - Notably, the most frequent index LOTs for patients from the KRD were elotuzumab+pomalidomide±dexamethasone (5.1%), daratumumab+pomalidomide±dexamethasone (6.3%), carfilzomib±dexamethasone (5.2%), daratumumab+carfilzomib±dexamethasone (4.4%), and carfilzomib+pomalidomide±dexamethasone (3.9%)

### Infection rates

- The weighted average infection rate for any infection across patients from the KRD and APCD was 63.5% (95% confidence interval [CI], 61.2-65.8), including 58.2% (95% CI, 55.9-60.4) for bacterial infections, 27.4% (95% CI, 25.9-28.9) for viral infections, and 8.2% (95% CI, 7.4-9.0) for fungal infections (**Figure 1**)
- Weighted average cumulative infection rates trended high across patients from the KRD and APCD (**Figure 2**)
  - At 26 and 52 weeks, the weighted average cumulative infection rate for any infection was 49.5% and 66.4%, respectively

### Severe infection rates

- The weighted average rate of any severe infection across patients from the KRD and APCD was 46.1% (95% CI, 44.1-48.1), including 42.5% (95% CI, 40.6-44.4) for bacterial infections, 17.1% (95% CI, 18.4-25.9) for viral infections, and 4.9% (95% CI, 4.3-5.6) for fungal infections (**Figure 1**)
- Weighted average cumulative severe infection rates trended high across patients from the KRD and APCD (**Figure 3**)
  - At 26 and 52 weeks, the weighted average cumulative rate for any severe infection was 31.5% and 44.9%, respectively

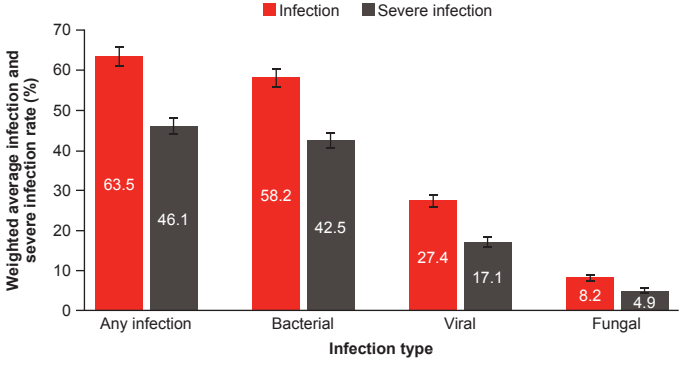
## Statistical analysis

- The algorithm developed to define infection episodes required a 30-day washout period with no record of infection prior to the index date
  - Infections that led to hospitalization or emergency room visits were considered severe
- A 2-stage meta-analysis was used to synthesize data between the KRD and the APCD and provide weighted averages of estimates from both datasets<sup>11</sup>
- Censored data included patients without an infection episode from the index date to the earliest of the following events: the end of continuous enrollment, death, data cutoff, or the end of the study period
- Infectious disease outcomes were assessed (**Table 1**)

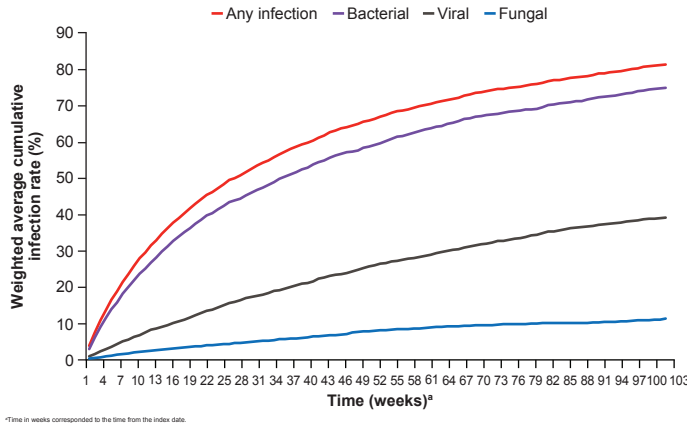
**Table 1: Infectious disease outcome definitions**

Term	Definition
Infection rate	Ratio of the average number of patients with an infection and the total number of patients at risk
Severe infection rate	Ratio of the average number of patients with a severe infection and the total number of patients at risk
Cumulative infection rate	Proportion of patients with an infection over time, while accounting for censored data
Cumulative severe infection rate	Proportion of patients with a severe infection over time, while accounting for censored data

**Figure 1: Weighted average infection and severe infection rates\***



**Figure 2: Weighted average cumulative infection rates**



**Figure 3: Weighted average cumulative severe infection rates**

