SECONDARY PRIMARY MALIGNANCIES ASSOCIATED WITH BCMA-DIRECTED BISPECIFIC ANTIBODIES IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: A FAERS PHARMACOVIGILANCE ANALYSIS

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INTRODUCTION

Four BCMA-directed bispecific antibodies (BsAbs)—teclistamab, talquetamab, elranatamab, and linvoseltamab—are FDA-approved for relapsed/refractory multiple myeloma (RRMM) after ≥4 prior lines of therapy.

Immune-related toxicities and infections with these T-cell redirecting agents have been studied, but the risk of second primary malignancies (SPMs) is not well defined.

AIM

To evaluate the frequency, characteristics, and disproportionality safety signals of second primary malignancies (SPMs) associated with the four FDA-approved BCMA-directed BsAbs, using real-world FAERS pharmacovigilance data.

METHOD

Retrospective pharmacovigilance analysis using FAERS, Q4 2022–Q4 2025

- Cases reporting exposure to teclistamab, talquetamab, elranatamab, or linvoseltamab were identified and classified by SPM status
- SPMs categorized as hematologic, skin, lung/pleural, solid tumor, or other
- Reporting Odds Ratios (ROR) with 95% CI calculated for each drug vs. pooled data from the other three agents
- Case fatality rates (CFR) computed overall and stratified by SPM status

CONCLUSIONS

These findings provide a baseline estimate of SPM burden with BsAbs in RRMM. Teclistamab is associated with a significant SPM signal, mostly skin cancers, while elranatamab and talquetamab show lower signals with mostly hematologic SPMs. This pattern suggests heterogeneity within the class rather than a uniform class-wide risk. Linvoseltamab data are too limited for any meaningful assessment. Continued pharmacovigilance, inclusion of SPM endpoints in clinical trials, and prospective long-term studies are warranted.

RESULTS

Of 5,419 cases (teclistamab 2,436; talquetamab 1,531; elranatamab 1,435; linvoseltamab 17), 143 SPMs were identified (2.6%).

Teclistamab showed a significant disproportionality signal (ROR 2.00; 95% CI 1.42–2.81), with skin cancers as the most common subtype (36.4%).

Elranatamab (ROR 0.64; 95% CI 0.42–0.98) and talquetamab (ROR 0.61; 95% CI 0.40–0.93) had significantly lower SPM reporting, with hematologic malignancies most common (48.1% and 42.9%, respectively).

Linvoseltamab had zero SPM reports among 17 cases, reflecting limited post-marketing data.

Overall case fatality rate (CFR) was 19.4% (1,053/5,419), with variation across drugs (teclistamab 24.8%; elranatamab 21.3%; talquetamab 9.3%; linvoseltamab 0%). Pooled CFR for SPM cases was 22.4% (32/143).

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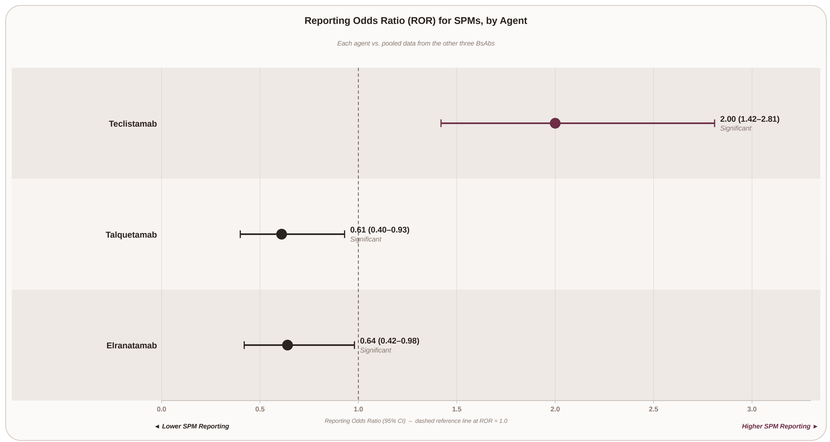
5,419
FAERS cases analyzed
(teclistamab, talquetamab, elranatamab, linvoseltamab)

143 (2.6%)
Cases were SPM-positive

19.4%
Overall case fatality rate

Agent	Cases, N	ROR (95% CI)	Predominant SPM Subtype (%)	CFR, %
Teclistamab	2,436	2.00 (1.42–2.81)	Skin cancers (36.4%)	24.8%
Talquetamab	1,531	0.61 (0.40–0.93)	Hematologic (42.9%)	9.3%
Elranatamab	1,435	0.64 (0.42–0.98)	Hematologic (48.1%)	21.3%
Linvoseltamab	17	No SPM reports	—	0%
All 4 BsAbs (overall)	5,419	—	143/5,419 SPM-positive (2.6%)	19.4%

Bold = statistically significant disproportionality signal (95% CI excludes 1.0); burgundy = increased risk, dark = decreased risk. RORs calculated for each drug vs. pooled data from the other three agents. Dashes denote comparisons not applicable at the pooled/overall level.



SPM Category Distribution by Agent, n

Agent	Hematologic	Skin	Lung/ Pleural	Solid tumor	Other
Teclistamab	33	13	7	19	13
Elranatamab	16	3	2	2	7
Talquetamab	12	2	–	2	3
Linvoseltamab	–	–	–	–	–

Fewer — More
cases (n)

Data source: FDA Adverse Event Reporting System (FAERS), Q4 2022–Q4 2025. ROR = reporting odds ratio; CI = confidence interval; CFR = case fatality rate; SPM = second primary malignancy; RRMM = relapsed/refractory multiple myeloma. Figure 2 category totals are drawn from a supplementary case-level analysis (n=5,298 deduplicated cases; 130 SPM-positive) and are not mutually exclusive per case, so per-drug totals may exceed each drug's SPM count.