SECONDARY PRIMARY MALIGNANCIES ASSOCIATED WITH CD20×CD3 BISPECIFIC T-CELL ENGAGING ANTIBODIES IN PATIENTS WITH B-CELL NON-HODGKIN'S LYMPHOMA

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INTRODUCTION

CD20×CD3 bispecific antibodies—mosunetuzumab, epcoritamab, and glofitamab—are approved for relapsed/refractory B-cell lymphoma.

Long-term safety regarding second primary malignancies (SPM) is incompletely defined in a population already exposed to cytotoxic therapy, T-cell dysfunction, and cumulative immunosuppression.

No published study has systematically evaluated SPM risk across this class.

AIM

To evaluate the frequency, characteristics, and disproportionality safety signals of second primary malignancies (SPMs) associated with the three FDA-approved CD20×CD3 bispecific antibodies, using real-world FAERS pharmacovigilance data, including comparison with CAR-T therapy.

METHOD

Retrospective pharmacovigilance analysis using FAERS, Q4 2022–Q4 2025 (13 quarters)

- Reports of mosunetuzumab, epcoritamab, or glofitamab in lymphoma patients were screened for SPM via MedDRA preferred terms
- Cases were clinically adjudicated (certain/probable vs. uncertain) and deduplicated
- Reporting Odds Ratios (ROR) with 95% CI calculated overall and against CAR-T comparators; signal defined as lower 95% CI limit >1.0
- Case fatality rates (CFR) computed overall and by SPM status

CONCLUSIONS

SPM events associated with CD20×CD3 bispecific antibodies were rare (pooled rate, 0.68%), with no disproportionality signal detected at the class or individual-drug level and significantly lower SPM reporting versus CAR-T therapy. Hematologic malignancies (predominantly AML/MDS) were the most common SPM subtype, consistent with known therapy-related myeloid neoplasm risk in a heavily pretreated lymphoma cohort. These findings provide reassuring real-world safety data for the CD20×CD3 bispecific class; ongoing surveillance with longer follow-up is warranted as post-marketing exposure accumulates.

RESULTS

Among 4,237 lymphoma reports (epcoritamab 2,368; glofitamab 1,138; mosunetuzumab 731), 29 unique SPM cases were adjudicated (12 certain/probable; 17 uncertain); pooled SPM rate was 0.68%.

Per-drug crude SPM rates were highest with glofitamab (1.14–1.23%) and lower with epcoritamab (0.51%) and mosunetuzumab (0.41%); no disproportionality signal was detected at the individual-drug level.

The underlying lymphoma was predominantly DLBCL (53.6%) and follicular lymphoma (17.9%); median age of SPM patients was 70 years (range, 29–90), and 73.7% were ≥65 years.

Hematologic malignancies accounted for 42.9% of SPMs (AML/MDS, n=7; leukemia NOS, n=3; ALL, n=1; multiple myeloma, n=1); solid tumors accounted for 39.3% (skin 14.3%, GI 14.3%, breast 10.7%).

Median time to SPM onset was 515 days (range, 1–1,096). Case fatality was 21.4% (6/28), highest with glofitamab (28.6%) and lowest with mosunetuzumab (0%).

At the class level, SPM reporting was significantly lower than for other lymphoma drugs (ROR 0.47; 95% CI 0.26–0.86) and for CAR-T therapy (ROR 0.11; 95% CI 0.06–0.23).

4,237
FAERS lymphoma reports analyzed (mosunetuzumab, epcoritamab, glofitamab)

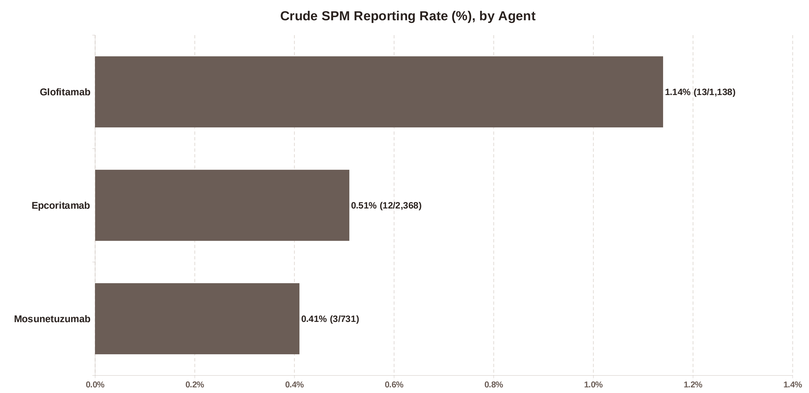
29 (0.68%)
Adjudicated SPM cases (12 certain/probable; 17 uncertain)

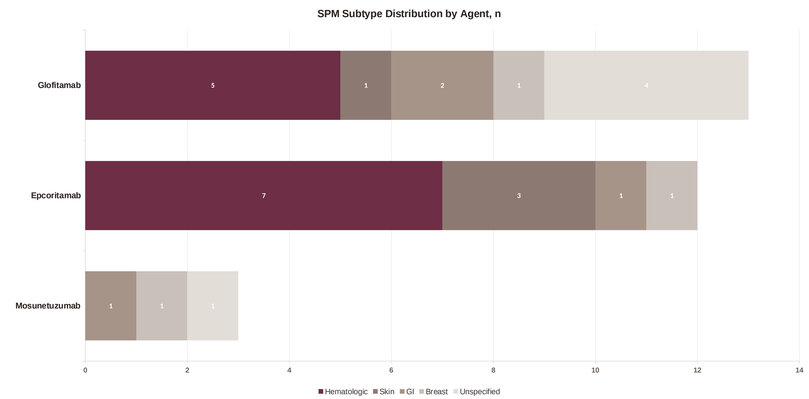
21.4%
Case fatality rate among SPM cases (6/28)

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; NHL = non-Hodgkin lymphoma.

Characteristic	Pooled Class	Mosunetuzumab	Epcoritamab	Glofitamab
Lymphoma reports, n	4,237	731	2,368	1,138
SPM cases, n	28	3	12	13
Crude SPM rate, %	0.66%	0.41%	0.51%	1.14%
Case fatality, %	25.0% (7/28)	0% (0/3)	25.0% (3/12)	30.8% (4/13)
ROR vs other lymphoma drugs	0.47 (0.26–0.86); p=0.009	—	—	—
ROR vs CAR-T	0.11 (0.06–0.23); p<0.001	—	—	—

Bold = statistically significant disproportionality signal (95% CI excludes 1.0); black = decreased risk. Table reflects the de-duplicated B-cell NHL analytic cohort (n=28); one additional glofitamab-associated SPM case in a Hodgkin lymphoma patient (included in the abstract's overall count of n=29) was excluded from this cohort. Dashes denote comparisons not computed at the single-agent level.





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