REAL-WORLD OUTCOMES OF BREXUCABTAGENE AUTOLEUCEL (BREXU-CEL) IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY (R/R) MANTLE CELL LYMPHOMA (MCL): A SYSTEMATIC LITERATURE REVIEW (SLR) AND META-ANALYSIS

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

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Abstract

Background:

Brexu-cel is a chimeric antigen receptor (CAR) T-cell therapy approved in Europe and the United States (US) in 2020 for patients with R/R MCL (after a Bruton tyrosine kinase inhibitor in Europe) based on the ZUMA-2 Phase 2 study results. Real-world studies published since approval have evaluated the safety and effectiveness of brexu-cel in broader, more diverse patient populations.

Aims:

To report results of an SLR examining the real-world evidence of brexu-cel safety and effectiveness in pts with R/R MCL, quantifying evidence through a meta-analysis of global published studies.

Methods:

Systematic searches were conducted in Embase and Medline to identify observational studies reporting clinical outcomes for the use of brexu-cel in pts with R/R MCL published from 2020 onward. Hand searches included relevant conference abstracts. Safety and effectiveness profiles were assessed, including key outcomes: cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), secondary malignancies, infections, treatments to mitigate these adverse events, overall response rate (ORR), and complete response (CR) rate. Study selection and data extraction were conducted independently in duplicate. Cohort quality was evaluated using the Newcastle-Ottawa Scale. Random-effects models were used to compare outcomes across Europe and the US.

Results:

The SLR identified 613 records. After screening, 38 publications on R/R MCL, representing 19 unique cohorts were included in the analysis. Geographically, 12 cohorts were from US and 6 from Europe, with 1 international cohort. The European cohorts encompassed multiple countries including Germany, France, Italy, the Netherlands, Spain, and Switzerland.

Any Grade CRS was reported in 66%-96% of pts, with a pooled estimate of 88% (95% CI, 85-90; estimates provided in Table). Grade ≥3 CRS was estimated at 12% (95% CI, 10-14) overall, 13% (95% CI, 10-17) in Europe, and 11% (95% CI, 8-14) in the US. Any Grade ICANS occurred at a mean proportion of 54% (95% CI, 48-59), with Grade ≥3 ICANS estimated at 20% (95% CI, 14-

28). US cohorts reported 29% (95% CI, 25-33) Grade ≥3 ICANS compared to 17% (95% CI, 12-23) in European cohorts. Any grade infections occurred in an estimated 35% (95% CI, 23-49) of pts, being more common in the US (41%; 95% CI, 36-46) versus Europe (28%; 95% CI, 20-37). Secondary malignancies were reported at a pooled estimate of 5% (95% CI, 2-10).

Effectiveness outcomes showed an ORR estimated at 88% (95% CI, 85-91), with high variability across European cohorts with an estimate of 86% (95% CI, 82-90) and 91% (95% CI, 88-94) for the CIBMTR US cohort. Similarly, high variability was observed in Europe for CR rates with an estimate of 73% (95% CI, 65-80), versus CIBMTR US cohort at 81% (95% CI, 77-85). The overall pooled estimated CR rate was 76% (95% CI, 68-82).

Table

		RWE Meta-Analysis			Pivotal Trial
Outcome type	Outcome	Overall	Europe	US	ZUMA-2[1]
Adverse events	Any Grade CRS, % (95% CI), n	88% (85-90) n=460	88% (83-91) n=282	88% (84-91) n=178	91% n=68
	Grade ≥3 CRS, % (95% CI), n	12% (10-14) n=844	13% (10-17) n=388	11% (8- 14)[a] n=456	15% n=68
	Any Grade ICANS,[b] % (95% CI), n	54% (48-59) n=775	52%(47-57) n=395	60%(55-65)[a] n=380	63% n=68
	Grade ≥3 ICANS, % (95% CI), n	20% (14-28) n=808	17% (12-23) n=352	29% (25-33)[a] n=456	31% n=68
	Any Grade infections,[c] % (95% CI), n	35% (23-49) n=491	28% (20-37)[a] n=111	41% (36-46)[a] n=380	56% n=68
	Secondary malignancies, % (95% CI), n	5% (2-10) n=466	2% (0-8)[a] n=86	6% (4-9)[a] n=380	NA
Response	ORR, % (95% CI), n	88% (85-91) n=769	86% (82-90) n=343	91% (88-94)[a] n=426	93% (84–98) n=60
	CR, % (95% CI), n	76% (68–82) n=769	73% (65–80) n=343	81% (77-85)[a] n=426	67% (53–78) n=60

[a] Only 1 cohort contributed to the estimate. [b] In ZUMA-2 reported as neurologic events. [c] Infections Grade ≥3 not enough data sources available for meta-analysis. CR, complete response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, objective response rate; NA, not available; NR, not reached; NE, not estimable; N/A, not applicable. 1. Wang et al. NEJM 2020.

Summary/Conclusion:

The growing availability of real-world evidence, particularly from European registries, has improved the understanding of the safety and effectiveness outcomes of brexu-cel in real-world settings, offering valuable insights into its use in a broader population. Response outcomes were largely similar to ZUMA-2 and among US and European cohorts. Rates of Grade ≥3 ICANS and any Grade infections were lower in the European cohort than the US, but overall, a numerically more favorable safety profile was observed in the real-world setting, which may lead to improved safety and management over time.

Keyword(s):

Real world data | Mantle cell lymphoma | Systematic review | CAR-T