**Outcomes with novel therapies for relapsed or refractory follicular lymphoma: a targeted literature review**

**Authors:** Bijal Shah[1], Wesley Furnback[2], Mei Xue[3], Kaitlyn Esselman[2], Erlene K. Seymour[3], Keri Yang[3]

**Affiliations:** [1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [2]Real Chemistry, New York, NY, USA; [3]BeiGene USA, Inc, San Mateo, CA, USA

**ABSTRACT**

**Objective:** Relapsed/refractory (R/R) follicular lymphoma (FL) treatments have evolved with the availability of novel agents. This targeted literature review (TLR) aimed to review outcomes associated with novel therapies in R/R FL.

**Methods:** A TLR was conducted in Embase, PubMed, and conference databases to identify abstracts and manuscripts published from 1/1/2022-11/15/2023 that met inclusion criteria: (1) R/R FL; (2) ≥1 novel therapy, including chimeric antigen receptor T-cell therapy (CAR-T), enhancer of zeste homolog 2 (EZH2) inhibitors, bispecifics, or Bruton tyrosine kinase inhibitors (BTKis); and (3) clinical trials, real-world evidence (RWE) studies, comparative effectiveness research (CER), or pharmacoeconomic models. Non-English and phase 1b and earlier studies were excluded. Outcomes of interest were overall response rate (ORR), progression-free survival (PFS), overall survival, costs, and patient-reported outcomes (PROs).

**Results:** Forty-three publications (12 trials, 8 CER, 2 RWE, and 3 models) were included. Three BTKis, 3 CAR-Ts, 3 bispecifics, 1 EZH2 inhibitor, and 1 antibody-drug conjugate (ADC) were identified. In 12 trials, ORRs were 86.2%-97% with CAR-Ts, 78.9%-97% with bispecifics, 36.4%-91.6% with BTKis, and 95.2% with ADC. Median PFS was 15.4-24 months with bispecifics, 5.8-40.5 months with BTKis, and 40.2 months in a CAR-T trial. PROs were reported in 3 trials. Improvements in fatigue, pain symptoms, and role function were greater with zanubrutinib + obinutuzumab than obinutuzumab monotherapy. CAR-Ts had improved efficacy vs controls and mosunetuzumab. A study of axicabtagene ciloleucel (axi-cel) vs tisagenlecleucel (tisa-cel) reported no difference in efficacy but an improved safety profile for tisa-cel. Tazemetostat demonstrated similar efficacy but an improved safety profile vs PI3Ks. In the third line, axi-cel was cost-effective vs standard of care, while another model favored mosunetuzumab over both axi-cel and tisa-cel.

**Conclusions:** Novel therapies have demonstrated promising efficacy results. Future research is needed to understand real-world long-term outcomes, impact on PROs, and treatment sequencing for R/R FL.