Poster SA7

Outcomes With Novel Therapies for Relapsed or Refractory Follicular Lymphoma: A Targeted Literature Review

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INTRODUCTION

- Follicular lymphoma (FL) is a common indolent non-Hodgkin lymphoma that often relapses or becomes refractory to current therapy
- Relapsed/refractory (R/R) FL treatments have evolved with the availability of novel agents

OBJECTIVE

- This targeted literature review aimed to review outcomes associated with novel therapies in R/R FL

METHODS

- A targeted literature review was conducted in Embase, PubMed, and conference databases to identify abstracts and manuscripts published from Jan 1, 2022, to Nov 15, 2023
- Studies were screened for all the following inclusion criteria:
  - R/R FL;
  - Use of ≥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
  - Clinical trials, real-world evidence (RWE) studies, comparative effectiveness research (CER), or pharmacoeconomic models
- Non–English language 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,[1-28] 8 CER models,[29-38] 2 RWE studies,[39,40] and 3 pharmacoeconomic models[41-43]) were included
- Three BTKis (ibrutinib, pirtobrutinib, and zanubrutinib), 3 CAR-Ts (axicabtagene ciloleucel [axi-cel], tisagenlecleucel [tisa-cel], and lisocabtagene maraleucel [liso-cel]), 3 bispecifics (mosunetuzumab, odronextamab, and epcoritamab), 1 EZH2 inhibitor (tazemetostat), and 1 antibody-drug conjugate (ADC) (loncastuximab tesirine) were identified

Clinical Trials

- The included trials by class of treatment and regimen, as well as key characteristics, are summarized in **Figure 1**
- In 12 trials, ORRs were 86.2% to 97% with CAR-Ts, 78.9% to 97% with bispecifics, 36.4% to 69% with BTKis, and 95.2% with ADC. Among CAR-Ts, ORR was highest (97%) with liso-cel in patients in the third-line and later setting in the TRANSCEND-FL study[6]
- Among bispecifics, epcoritamab + rituximab-lenalidomide (R2) produced an ORR of 97% in a group of patients with R/R FL, the majority of whom had received only 1 prior line of treatment. ORR was highest (69%) with zanubrutinib + obinutuzumab within the BTKi class[23,25,26]
- Median PFS was 15.4 to 24 months with bispecifics, 5.8 to 38.4 months with BTKis, and 40.2 months in a CAR-T trial (**Figure 2**)
- Estimated 12-month PFS ranged from 77.5% with axi-cel[1] to 91.3% with liso-cel[7] in second-line patients with high-risk features
- PROs were reported in 3 trials (TRANSCEND-FL [liso-cel], ELM-2 [odronextamab], and ROSEWOOD [zanubrutinib + obinutuzumab])[8,15,27]
- The ROSEWOOD trial was the only comparative study to report PROs and found that improvements in fatigue, pain symptoms, and role function were greater with zanubrutinib + obinutuzumab than obinutuzumab monotherapy[27]
- Liso-cel was the only CAR-T with reported PROs, which showed transient deterioration in physical and role functioning within 15 days of infusion. However, most domains showed improvement in overall least-squares mean change from baseline[8]
- In the ELM-2 study of odronextamab, the median time to definitive deterioration (22.41 months) generally corresponded to median PFS (20.2 months)[14,15]

Comparative Effectiveness Research

- Eight comparative effectiveness studies were included (**Table 1**)[29-38]
- Comparison of efficacy of CAR-T in clinical trials and standard of care in external control cohorts showed that CAR-T generally had improved efficacy.[29-31,33,34] The study by Kambhampati et al. compared real-world patients receiving axi-cel in the Center for International Blood and Marrow Transplant Research (CIBMTR) registry to the SCHOLAR-5 cohort receiving standard of care and found that efficacy outcomes favored axi-cel in the real-world setting[32]
- CAR-Ts were also found to have a favorable efficacy profile compared to mosunetuzumab in CER using clinical trial data[35,38]
- Tazemetostat demonstrated similar efficacy but an improved safety profile vs PI3Ks[34]

Real-World Evidence

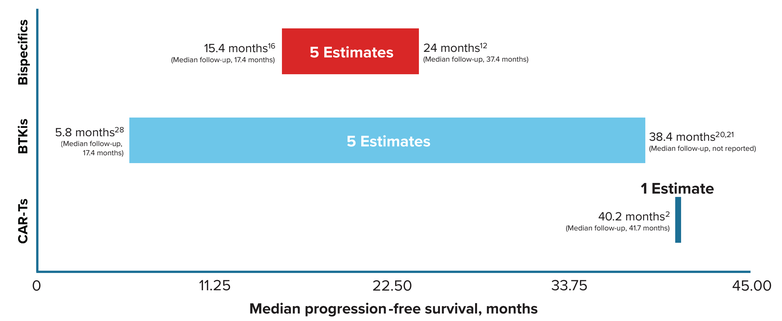
- Both real-world studies evaluated CAR-T in patients with R/R FL.[39,40] The study by Jacobson et al. included 230 patients with R/R FL across 72 US centers in the CIBMTR registry.[39] The efficacy analysis included 151 patients, with a median follow-up of 6.2 months. ORR was 93%, and 6-month rates of PFS and OS were 88% and 96%, respectively

Figure 1. Clinical Trials

		Trial name	Sample, n	Prior therapies[a]	Follow-up, mo[b]
ADCs	Loncastuximab tesirine[19]	NCT04998669	26	1 (1-6)	NA
Bispecifics	Mosunetuzumab[9-13]	GO29781	90	3 (2-4)	37.4
	Odronextamab[14,15]	ELM-2	96	3 (2-13)	17.3
	Epcoritamab[16]	EPCORE NHL-1	128	3 (2-9)	17.4
	Epcoritamab + R2[17,18]	EPCORE NHL-2	109	1	8.8
BTKis	Ibrutinib + BR/R-CHOP[20,21]	SELENE	174	NA	NA
	Pirtobrutinib[28]	BRUIN	48	3 (1-12)	18.4
	Zanubrutinib[22]	BGB-3111-AU-003	33	3 (1-8)	32.8
	Zanubrutinib + obinutuzumab[23-27]	ROSEWOOD	145	3 (2-11)	20.2
CAR-Ts	Axi-cel[1,2]	ZUMA-5	124	3 (2-4)	41.7
	Tisa-cel[3,5]	ELARA	97	4 (2-13)	28.9
	Liso-cel[6-8]	TRANSCEND-FL[c]	130	3 (2-10)/1	18.9/18.1

[a] Median (range) number of prior therapies.
[b] Median follow-up in months.
[c] The TRANSCEND-FL trial included separate analyses of the third-line and later (3L+) and second-line (2L) with high-risk features cohorts. The median follow-up in the 3L+ and 2L with high-risk features cohorts was 18.9 months and 18.1 months, respectively.
ADC, antibody-drug conjugate; BR, bendamustine-rituximab; BTKi, Bruton tyrosine kinase inhibitor; CAR-T, chimeric antigen receptor T-cell therapy; NA, not available; R2, rituximab-lenalidomide; R-CHOP, cyclophosphamide, doxorubicin, prednisone, rituximab + vincristine.

Figure 2. Median Progression-Free Survival Range by Class of Treatment



- The study by Ysabaert et al. included 70 total patients (62 tisa-cel and 8 axi-cel) receiving CAR-T in the DESCAR-T registry, part of the French early access program.[40] Included patients had a median of 3 (range, 2-9) prior lines of therapy
- After a median follow-up of 5.4 months, ORR was 97.5% and estimated 6-month PFS and OS rates were 71.8% and 97.4%, respectively

CONCLUSIONS

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

Pharmacoeconomics

- This study included 3 pharmacoeconomic models,[41-43] 2 cost-effectiveness models,[41,42] and 1 cost-minimization model.[43] All included studies were set in the US
- Axi-cel was found to be cost-effective in the third-line setting compared with the standard of care, with an incremental cost-effectiveness ratio of $182,127 per quality-adjusted life-year (QALY) gained[41]
- Mosunetuzumab was found to be the dominant strategy (lower costs and higher QALYs) compared with both axi-cel and tisa-cel[42]
- The cost-minimization study compared axi-cel and tisa-cel while considering drug, administration, serious adverse event, and relapse costs. The study reported a lower total cost per patient with tisa-cel ($450,885) vs axi-cel ($512,021)[43]

Table 1. Comparative Effectiveness Outcomes

Comparators	Data Sources	Results Summary
Axi-cel vs standard of care[29-31]	ZUMA-5 (axi-cel) and SCHOLAR-5 (standard of care)	Efficacy favors axi-cel
Axi-cel vs standard of care[32]	CIBMTR (axi-cel and standard of care)	Efficacy favors axi-cel
Axi-cel vs tisa-cel[36]	ZUMA-5 (axi-cel) and ELARA (tisa-cel)	No significant difference in efficacy; safety advantage with tisa-cel
Tisa-cel vs standard of care[33]	ELARA (tisa-cel) and RECORD-FL (standard of care)	Efficacy favors tisa-cel
Tisa-cel vs standard of care[34]	ELARA (tisa-cel) and Flatiron Health Research Database (standard of care)	Efficacy favors tisa-cel
Tisa-cel vs mosunetuzumab[35]	ELARA (tisa-cel) and GO29781 (mosunetuzumab)	Efficacy favors tisa-cel
Liso-cel vs mosunetuzumab[38]	TRANSCEND-FL (liso-cel) and GO29781 (mosunetuzumab)	Efficacy favors liso-cel
Tazemetostat vs PI3Ks[34]	E7438-G000-101 (tazemetostat), DELTA (idelalisib), DYNAMO (duvelisib), CHRONOS-1 Part B (copanlisib), and UNITY-NHL (umbralisib)	No significant difference in efficacy; safety advantage with tazemetostat
Tazemetostat + R2 vs R2[35]	SYMPHONY-1 (tazemetostat) and the Flatiron Health Research Database (R2)	Efficacy favors tazemetostat + R2

PI3K, phosphoinositide 3-kinase; R2, rituximab-lenalidomide.

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