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Maximizing the possibilities in the evolving treatment paradigm for R/R follicular lymphoma: From optimal sequencing to shared decision-making

Practice aid for R/R follicular lymphoma

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There is now a wide range of approved therapeutic options for patients with R/R FL

	Drug name	Indication	FDA approval date	NCCN guidance[8]
CAR T-cell therapy	**Axicabtagene ciloleucel**	Adults with R/R FL; ≥2 lines of systemic therapy[1–3]	March 2021[1]	Preferred regimen (≥ third-line)
	Lisocabtagene maraleucel		May 2024[2]	
	Tisagenlecleucel		May 2022[3]	
CD20/CD3 BsAb	**Epcoritamab (SC)**	Adults with R/R FL; ≥2 lines of systemic therapy[4,5]	June 2024[4]	Preferred regimen (≥ third-line)
	Mosunetuzumab		December 2022[5]	
EZH2 inhibitor	**Tazemetostat**	• Adults with *EZH2*mut positive R/R FL; ≥2 prior systemic therapies • Adults with R/R FL with no satisfactory alternative treatment options[6]	June 2020[6]	Other recommended regimen (≥ third-line)
BTK inhibitor	**Zanubrutinib + obinutuzumab**	R/R FL; ≥2 lines of systemic therapy[7]	March 2024[7]	Other recommended regimen (≥ third-line)

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Recent evidence supports the use of approved therapies in patients with R/R FL

	Drug name	Efficacy	Safety
CAR T-cell therapy	**Axicabtagene ciloleucel**[9]	ZUMA-5 study (n=127); mFU: ≥3 years **ORR:** 94%; Estimated 36-month **PFS:** 54%	**Grade ≥3 SAEs** after 18-months (n=124): 8%
	Lisocabtagene maraleucel[10]	TRANSCEND FL (n=130); mFU: 19 months **Bridging therapy** (n=45) **ORR:** 93% **No bridging therapy** (n=79) **ORR:** 99%	**Bridging therapy:** (n=49) **Grade 3 CRS:** 0; **Grade 3 NE:** 6% **No bridging therapy:** (n=81) **Grade 3 CRS:** 1%; **Grade 3 NE:** 0
	Tisagenlecleucel[11]	ELARA study (N=97); FU: ≥3 years **ORR:** 86%	Most common **grade ≥3 AEs:** Neutropenia and anaemia
CD20/CD3 BsAb	**Epcoritamab (SC)**[12]	FL-dose expansion cohort from EPCORE™ NHL-1 trial (n=128); mFU: 17 months **ORR:** 82%; **mPFS:** 15.4 months	Most common **TEAEs:** CRS, injection-site reaction, COVID-19
	Mosunetuzumab[13]	Subgroup analysis of high-risk patients* (N=90); FU: ≥3 years 36-month **PFS:** 43%; 36-month **OS:** 83%	**Rate of CRS:** 44%
EZH2 inhibitor	**Tazemetostat**[14]	Open-label, single-arm trial (N=99); mFU: 22.0 (*EZH2*mut) and 35.9 months (*EZH2*wt)† ***EZH2*mut** (n=45) **ORR:** 69%; **mPFS:** 13.8 months ***EZH2*wt** (n=54) **ORR:** 35%; **mPFS:** 11.1 months	Most common **grade ≥3 TRAEs:** thrombocytopenia, neutropenia, anaemia
BTK inhibitor	**Zanubrutinib + obinutuzumab**[15]	ROSEWOOD study; ZO vs O; (N=217; R, 2:1); mFU: 20.2 months **ZO** - **ORR:** 69%; **mPFS:** 28.0 months **O** - **ORR:** 46%; **mPFS:** 10.4 months	Most common **AEs with ZO:** thrombocytopenia, neutropenia, diarrhoea

*POD24, ≥4th line of therapy, aged ≥65 years (NCT02500407), figures for overall population; †NCT01897571.

Multiple factors influence treatment decisions in R/R FL

Factors influencing optimal treatment sequencing in R/R FL[16,17]

- Disease burden
- Patient performance status
- Duration of response after first therapy
- Potential presence of high-grade transformation
- Anticipated depth and duration of response
- Patient preference
- Prior treatment regimens
- Potential need for future lines of therapy

Risk/benefit ratio of each option should be assessed in the context of the patients' overall condition and their individual goals for therapy[16]

Key factors influencing a patient's treatment decision in R/R FL[16–18]

- Preservation of patient QoL
- Availability of psychosocial/caregiver support
- Distance from treatment centre
- Short-term treatment-related side effects: e.g. CRS or ICANS
- Long-term and cumulative toxicities
- Administration schedule: e.g. repeat doses vs 'one and done'
- Convenience of administration
- Speed of access to therapy: e.g. off-the-shelf or bespoke
- Ability of the patient to tolerate therapy e.g. due to advanced age, frailty, comorbidities

Shared decision-making and equity of access is important in R/R FL

Shared decision-making in R/R FL

What does shared decision-making mean for patients?[16,17,19]

- Better identification of patients' needs, individual goals for therapy, perceptions and expectations
- Identification of patient-specific issues, e.g. need for travel or preference for less intrusive treatment regimens

How does shared decision-making impact outcomes?[19,20]

- Increased adherence to treatment
- Increased patient satisfaction
- Increased patient wellbeing and QoL

Improving access for patients from all backgrounds[21–25]

- **Practising equity-based communication** and using preferred languages to improve health outcomes and build stronger patient–provider relationships
- **Tailoring information for minority populations** to improve decision-quality and patient-provider communication
- Use of **telemedicine or virtual visits**
- Improved **community engagement** strategies
- Enhanced **patient education** to empower self-referral
- **Introducing measures to improve access** e.g. transportation to treatment centre

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Abbreviations and references

Abbreviations

AE, adverse event; BsAb, bispecific antibody; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; FU, follow-up; ICANS, immune effector cell-associated neurotoxicity syndrome; mFU, median FU; mPFS, median PFS; mut, mutant; NE, neurological event; O, obinutuzumab; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; POD24, progression of disease within 24 months; QoL, quality of life; R, randomization; R/R FL, relapsed/refractory follicular lymphoma; SAE, serious AE; SC, subcutaneous; TEAE, treatment-emergent AE; TRAE, treatment-related AE; wt, wildtype; ZO, zanubrutinib + obinutuzumab.

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The guidance provided by this practice aid is not intended to directly influence patient care. Clinicians should always evaluate their patients' conditions and potential contraindications and review any relevant manufacturer product information or recommendations of other authorities prior to consideration of procedures, medications, or other courses of diagnosis or therapy included here.

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