Bispecific Antibodies in FL: EHA 2026 Explores Advancing Outcomes

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> The management of relapsed/refractory follicular lymphoma (FL) presents a persistent challenge, with patients often experiencing multiple lines of therapy and diminishing response durability. The EHA 2026 interactive session, "Interactive, Case-Based Journey Through Follicular Lymphoma (FL): Choosing the Path for Bispecific Antibodies in Advancing Outcomes," aims to delineate the current and future role of bispecific antibodies in this evolving treatment landscape.

KEY TAKEAWAYS

- The Pivot: Bispecific antibodies offer a novel mechanism of action for FL, particularly in later lines of therapy.
- The Data: Complete response rates for approved bispecific antibodies in relapsed/refractory FL typically range from 60% to 80%.
- The Action: Clinicians should consider patient-specific factors, prior therapies, and disease burden when evaluating bispecific antibodies for FL.

Follicular lymphoma, an indolent non-Hodgkin lymphoma, is characterized by a relapsing and remitting course. While initial therapies often achieve high response rates, the disease is generally incurable, and patients frequently require subsequent lines of treatment.1 The cumulative toxicity of multiple regimens and the development of resistance mechanisms necessitate the continuous exploration of new therapeutic strategies. Bispecific antibodies, which simultaneously engage CD3 on T-cells and a tumor-associated antigen (e.g., CD20 or CD19) on lymphoma cells, represent a significant advancement in this context.2 These agents redirect T-cells to lyse malignant B-cells, offering a chemotherapy-free option with a distinct mechanism of action.3

The EHA 2026 session focused on a case-based approach to illustrate the practical application of bispecific antibodies in various clinical scenarios within FL. This format allowed for a detailed examination of patient selection, management of potential toxicities, and sequencing considerations. The discussion highlighted the importance of understanding the patient's prior treatment history, including exposure to rituximab, alkylating agents, and PI3K inhibitors, as these factors can influence the efficacy and safety profile of subsequent therapies.4 Follicular lymphoma is the second most common type of non-Hodgkin lymphoma, accounting for approximately 20-30% of all cases. Its incidence increases with age, with a median age at diagnosis typically in the sixth decade of life. The disease often presents with widespread lymphadenopathy and can involve the bone marrow, spleen, and other extranodal sites. The indolent nature of FL means that some patients may be managed with a "watch and wait" approach, particularly in asymptomatic early stages. However, progression or symptomatic disease necessitates active treatment, which has evolved significantly over the past

decades from chemotherapy to chemoimmunotherapy and now to targeted agents. The relapsing nature of FL underscores the need for therapies that can maintain disease control and improve quality of life over extended periods.1

What the session covered

The interactive cases presented at EHA 2026 explored the integration of currently approved and emerging bispecific antibodies for FL. Key agents discussed included mosunetuzumab and glofitamab, both targeting CD20 and CD3. Mosunetuzumab, administered as a fixed-duration intravenous regimen, has demonstrated durable responses in patients with relapsed/refractory FL. In a pivotal phase 2 study (NCT02500498), mosunetuzumab achieved a complete response (CR) rate of 60% (95% CI, 49-70) in patients who had received at least two prior lines of therapy.5 The median duration of response was 22.8 months. Glofitamab, also a CD20xCD3 bispecific antibody, has shown similar efficacy, with a CR rate of 68.8% (95% CI, 56.9-79.0) in a phase 2 study (NCT03075696) involving patients with heavily pretreated relapsed/refractory FL.6 Both agents are associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), requiring careful monitoring and management.5,6

The session emphasized the importance of patient characteristics, such as age, comorbidities, and performance status, in determining suitability for bispecific antibody therapy. For instance, patients with a high tumor burden may experience a higher incidence or severity of CRS, necessitating proactive management strategies.7 The discussion also touched upon the sequencing of bispecific antibodies relative to other novel agents, such as CAR T-cell therapy. While CAR T-cells offer deep and durable responses, their logistical complexities and potential for severe toxicities may position bispecific antibodies as an earlier, more accessible option for some patients.8 The session did not present new trial data but rather synthesized existing evidence through a practical, case-based lens, allowing clinicians to apply the information directly to patient care scenarios. The absence of head-to-head trials comparing different bispecific antibodies or bispecific antibodies with CAR T-cell therapy means that treatment decisions currently rely on indirect comparisons and expert consensus.9 The session also explored the potential for resistance mechanisms to bispecific antibodies, similar to those observed with other targeted therapies. These may include antigen escape, impaired T-cell function, or alterations in the tumor microenvironment. Future research will likely focus on strategies to overcome these challenges, such as combination therapies or novel bispecific antibody designs. The discussion acknowledged that while bispecific antibodies offer a promising avenue, their optimal integration into the evolving treatment landscape for FL requires ongoing investigation and real-world data collection. The long-term safety and efficacy profiles, particularly in diverse patient populations and across multiple lines of therapy, remain areas of active study.9

> **CLINICAL IMPLICATIONS**
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> The EHA 2026 session on bispecific antibodies in follicular lymphoma underscores a critical shift in the treatment paradigm for relapsed/refractory disease. For clinicians, the immediate takeaway is the necessity of integrating these novel agents into their therapeutic armamentarium, particularly for patients who have exhausted conventional options. The impressive complete response rates, often exceeding 60%, cannot be ignored, even if they come with the caveat of managing cytokine release syndrome and ICANS. The interactive case-based format was a welcome approach, providing practical guidance on patient selection and toxicity management, which is far more useful than simply presenting raw data.
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> The industry, particularly companies like Roche with mosunetuzumab and glofitamab, is clearly pushing for

broader adoption. The fixed-duration nature of mosunetuzumab and the potential for outpatient administration for some bispecifics could significantly improve patient access compared to the logistical hurdles of CAR T-cell therapy. However, the lack of direct comparative trials means that treatment choices remain largely empirical, guided by individual drug profiles and institutional experience. This gap in evidence will need to be addressed to optimize sequencing and combination strategies, potentially through real-world data collection or pragmatic trials.

For patients, the availability of bispecific antibodies offers renewed hope for durable responses in a disease characterized by its relapsing nature. These therapies provide a chemotherapy-free option, which can significantly improve quality of life for those who have endured multiple lines of cytotoxic agents. However, patients must be thoroughly counselled on the potential for acute toxicities, particularly CRS, and the need for close monitoring during the initial treatment phase. The ongoing evolution of this field means that what constitutes 'standard of care' for relapsed FL is a moving target, demanding continuous education and adaptation from both prescribers and patients.

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