Bispecific Antibodies Show Promise in Relapsed/Refractory Haematological Malignancies

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Managing relapsed or refractory non-Hodgkin lymphoma (NHL) and multiple myeloma (MM) presents a significant clinical challenge, with limited effective options for patients who have exhausted standard therapies. Emerging data on bispecific antibodies presented at EHA 2026 indicate these agents may provide a novel and effective treatment strategy for these difficult-to-treat haematological malignancies.12

KEY TAKEAWAYS

- The Pivot: Bispecific antibodies are moving beyond early-phase trials, showing consistent efficacy signals in heavily pretreated patient populations.
- The Data: Objective response rates (ORR) for specific bispecific agents in relapsed/refractory NHL and MM have been reported in the range of 60% to 80%.
- The Action: Clinicians should consider bispecific antibodies as a potential therapeutic option for patients with relapsed/refractory NHL and MM, particularly those with limited alternative treatments.

Patients with relapsed or refractory non-Hodgkin lymphoma (NHL) and multiple myeloma (MM) face a poor prognosis, often having received multiple prior lines of therapy including chemotherapy, targeted agents, and autologous stem cell transplantation. The development of novel immunotherapies capable of redirecting T-cells to malignant cells represents a critical area of unmet need. Bispecific antibodies, designed to simultaneously bind to a T-cell surface antigen (typically CD3) and a tumour-associated antigen, facilitate direct T-cell mediated cytotoxicity against cancer cells. This mechanism offers a distinct advantage over conventional monoclonal antibodies by engaging the host's immune system more directly.1

Early clinical investigations into bispecific antibodies have focused on their safety profile and preliminary efficacy in heavily pretreated patient cohorts. Common tumour targets for bispecific antibodies in NHL include CD20 and CD19, while in MM, B-cell maturation antigen (BCMA) is a primary target. The rationale for targeting these antigens is their high expression on malignant cells and limited expression on healthy tissues, aiming to maximise therapeutic effect while minimising off-target toxicity.2

Relapsed/refractory NHL encompasses a heterogeneous group of lymphoid malignancies, with DLBCL being the most common aggressive subtype. Despite advances in front-line therapy, a significant proportion of patients with DLBCL will relapse or become refractory, necessitating further treatment options. Similarly, MM, a plasma cell malignancy, remains largely incurable, with patients experiencing multiple relapses and developing resistance to successive lines of therapy. The median overall survival for patients with triple-class refractory MM is typically less than one year, underscoring the

urgent need for effective new treatments. Bispecific antibodies offer a novel approach by harnessing the patient's own immune system to overcome resistance mechanisms often encountered with conventional therapies.

Emerging Clinical Data from EHA 2026

Data presented at EHA 2026 highlighted several bispecific antibody programmes across NHL and MM. In relapsed/refractory diffuse large B-cell lymphoma (DLBCL), a bispecific CD20xCD3 antibody demonstrated an objective response rate (ORR) of 62% (95% CI, 55%-69%) in a cohort of 150 patients who had received a median of 3 prior lines of therapy. Complete responses (CR) were observed in 38% of these patients. The median duration of response (DoR) had not yet been reached at the time of data cut-off, with a median follow-up of 12.5 months.3

For multiple myeloma, a BCMAxCD3 bispecific antibody was evaluated in 180 patients with relapsed/refractory disease, all of whom were triple-class refractory (refractory to an immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 antibody). The ORR was 75% (95% CI, 69%-81%), with a very good partial response (VGPR) or better achieved in 50% of patients. Stringent complete responses (sCR) were observed in 20% of the cohort. The median progression-free survival (PFS) was 11.8 months (95% CI, 9.5-14.2 months).4

The safety profiles across these trials were generally consistent with the known mechanism of action of T-cell engaging therapies. Cytokine release syndrome (CRS) was the most frequently reported adverse event, occurring in 65% to 80% of patients, predominantly grade 1 or 2. Grade 3 or higher CRS was reported in 5% to 10% of patients and was manageable with corticosteroids and tocilizumab. Neurotoxicity, specifically immune effector cell-associated neurotoxicity syndrome (ICANS), was observed in 15% to 25% of patients, with grade 3 or higher ICANS in less than 5%. These events typically occurred early in the treatment course and were reversible.3,4

Limitations of the presented data include the single-arm, open-label design of most studies, which inherently limits direct comparisons to standard therapies. The follow-up duration, while sufficient for initial efficacy and safety assessment, is still relatively short, meaning long-term durability of response and overall survival benefits remain to be fully elucidated. Furthermore, patient populations were highly selected, often comprising those with extensive prior treatment, which may not fully represent the broader patient population in earlier lines of therapy. The lack of a control arm also makes it challenging to definitively attribute observed benefits solely to the bispecific antibody, as natural disease course variability or prior treatments could confound results. Future research will need to address these limitations through larger, randomised controlled trials and longer-term follow-up. Investigation into optimal dosing schedules, combination therapies, and strategies to mitigate toxicity are also ongoing.5

> **CLINICAL IMPLICATIONS**
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> The consistent efficacy signals from bispecific antibodies in heavily pretreated relapsed/refractory non-Hodgkin lymphoma and multiple myeloma patients are compelling. For clinicians managing these challenging populations, these agents represent a genuine expansion of therapeutic options beyond the current standard of care, which often includes salvage chemotherapy or CAR T-cell therapy with its own logistical and toxicity burdens. The observed objective response rates, particularly the complete responses, in patients who have exhausted multiple prior lines of therapy, suggest a meaningful clinical benefit that warrants careful consideration.
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> However, the toxicity profile, particularly cytokine release syndrome and neurotoxicity, necessitates careful

patient selection and proactive management. The need for hospitalisation for initial dosing and monitoring, as seen with CAR T-cell therapies, will impact treatment accessibility and resource allocation. Pharmaceutical companies developing these agents, such as Genentech, Amgen, and Johnson & Johnson, will need to provide robust educational programmes for clinicians and support staff to ensure safe administration and management of adverse events. The cost-effectiveness of these novel therapies will also be a significant factor in their integration into national guidelines and formularies.

From a patient perspective, the availability of effective new treatments offers renewed hope in situations where prognosis has historically been very poor. While the initial treatment period may involve intensive monitoring, the potential for durable responses and improved quality of life in a population with limited alternatives is substantial. The ongoing development of these bispecific antibodies, and their potential application in earlier lines of therapy or in combination with other agents, could further redefine treatment paradigms for these haematological malignancies, moving beyond incremental gains to more transformative outcomes.

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