Novel Approaches in R/R MM: Expert Perspectives from EHA 2026

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> Relapsed/refractory multiple myeloma (R/R MM) presents a significant clinical challenge, with patients often exhausting established treatment options and facing poor prognoses.1 The European Hematology Association (EHA) 2026 congress provided updates on novel therapeutic strategies, including B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell therapies and bispecific antibodies, offering new avenues for disease control in this difficult-to-treat population.

KEY TAKEAWAYS

- The Pivot: Novel immunotherapies, specifically CAR T-cells and bispecific antibodies, are demonstrating efficacy in heavily pretreated R/R MM.
- The Data: Objective response rates (ORRs) for these agents often exceed 60% in late-line settings, with some studies reporting complete response (CR) rates over 30%.
- The Action: Clinicians should consider these emerging therapeutic classes for eligible R/R MM patients, particularly those with multiple prior lines of therapy.

Multiple myeloma remains an incurable hematological malignancy, with nearly all patients eventually experiencing relapse. For those with relapsed/refractory multiple myeloma (R/R MM), defined by disease progression on or within 60 days of their last therapy, treatment options become increasingly limited and outcomes diminish with each subsequent line of therapy.1 The median overall survival for patients refractory to at least a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody is historically poor, underscoring the urgent need for effective novel agents.2 The incidence of multiple myeloma is approximately 7.1 per 100,000 persons per year, with an estimated 35,730 new cases diagnosed in the United States in 2024. Despite significant advances in frontline therapy, including proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies, a substantial proportion of patients will ultimately progress to R/R MM. This patient population often presents with high-risk cytogenetics, extramedullary disease, and a history of multiple prior treatment regimens, further complicating management and necessitating highly effective salvage therapies.1,2

Emerging Therapeutic Strategies

The EHA 2026 congress featured several presentations on investigational agents targeting B-cell maturation antigen (BCMA), a protein highly expressed on multiple myeloma cells. These included updates on CAR T-cell therapies and bispecific antibodies. CAR T-cell therapy involves genetically modifying a patient's T-cells to express a chimeric antigen receptor that recognizes and binds to specific antigens on cancer cells, leading to their destruction. Bispecific antibodies,

conversely, are engineered to bind simultaneously to two different antigens, typically one on the T-cell (e.g., CD3) and one on the myeloma cell (e.g., BCMA), thereby redirecting T-cells to kill myeloma cells.3

Data presented on BCMA-directed CAR T-cell therapies, such as idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel), continue to demonstrate substantial efficacy in heavily pretreated R/R MM patients. For instance, in a cohort of patients who had received a median of six prior lines of therapy, ide-cel achieved an objective response rate (ORR) of 73% (95% CI, 65-81) and a complete response (CR) rate of 33% (95% CI, 25-42). The median progression-free survival (PFS) was 8.8 months (95% CI, 6.2-11.8).4 Cilta-cel, in a similarly advanced patient population, showed an ORR of 97.9% (95% CI, 92.1-99.7) and a stringent complete response (sCR) rate of 80.4% (95% CI, 70.2-88.2), with a median PFS not yet reached at the time of analysis.5 These studies typically enrolled patients with an ECOG performance status of 0 or 1, adequate organ function, and measurable disease, reflecting a patient population capable of tolerating intensive cellular therapies. The manufacturing process for CAR T-cells involves leukapheresis, T-cell enrichment, genetic modification with a viral vector, expansion, and cryopreservation, followed by lymphodepleting chemotherapy prior to infusion.4,5

Bispecific antibodies also showed promising activity. Teclistamab, a BCMA-CD3 bispecific antibody, demonstrated an ORR of 63% (95% CI, 56.6-69.0) in patients who had received a median of five prior lines of therapy, including triple-class exposed patients. The median duration of response (DoR) was 18.4 months (95% CI, 14.9-not estimable).6 Elranatamab, another BCMA-CD3 bispecific, reported an ORR of 61% (95% CI, 50.8-70.5) in a cohort of patients refractory to at least one proteasome inhibitor, one immunomodulatory drug, and one anti-CD38 antibody. The median DoR was 15.6 months (95% CI, 9.7-not estimable).7 These agents are administered intravenously or subcutaneously, often with step-up dosing to mitigate initial cytokine release syndrome. The patient populations in these bispecific antibody trials were also heavily pretreated, often having received prior autologous stem cell transplantation and multiple lines of conventional and novel therapies.6,7

Common adverse events associated with CAR T-cell therapies included cytokine release syndrome (CRS) and neurotoxicity (ICANS), which were generally manageable with established protocols. For bispecific antibodies, CRS was also a frequent adverse event, typically low grade and reversible. Infections remain a concern with both classes of agents, requiring proactive monitoring and management.4,5,6,7

While these data are encouraging, direct comparisons between studies are challenging due to differences in patient populations, prior therapies, and study designs. The long-term durability of responses and the optimal sequencing of these novel agents within the R/R MM treatment paradigm require further investigation. Ongoing trials are exploring these agents in earlier lines of therapy and in combination with other anti-myeloma drugs, which may further improve outcomes. The logistical complexities and resource intensity associated with CAR T-cell therapy, including apheresis, manufacturing, and specialized inpatient care, also represent practical considerations for broader implementation. Bispecific antibodies, being off-the-shelf products, offer a potentially more accessible alternative, though they also require careful management of initial adverse events, often in an inpatient setting.8 Further research is needed to identify biomarkers that predict response and resistance to these therapies, and to understand the mechanisms of relapse following BCMA-directed treatments, which can include antigen escape or T-cell exhaustion. The cost-effectiveness of these advanced therapies also warrants consideration in healthcare systems globally.8

CLINICAL IMPLICATIONS

The data presented at EHA 2026 confirm that BCMA-directed immunotherapies are transforming the landscape for relapsed/refractory multiple myeloma. For clinicians, the availability of these agents means that patients who have exhausted traditional therapies now have viable, effective options. The high response rates, even in heavily pretreated populations, necessitate a shift in how we approach late-line therapy, moving beyond palliative care to active disease management with curative intent for some. The choice between CAR T-cells and bispecific antibodies will increasingly depend on institutional capabilities, patient fitness, and the urgency of treatment, given the logistical differences in their administration.

From a patient perspective, these advancements offer renewed hope. The prospect of achieving deep and durable responses after multiple relapses is significant, potentially extending life and improving quality of life. However, patients must be counselled on the unique toxicity profiles, particularly cytokine release syndrome and neurotoxicity, and the intensive monitoring required. The financial burden and access issues, especially for CAR T-cell therapies, remain substantial challenges that healthcare systems and payers will need to address to ensure equitable access to these transformative treatments.

For the pharmaceutical industry, the continued success of agents like ide-cel, cilta-cel, teclistamab, and elranatamab reinforces the value of targeted immunotherapy in hematologic malignancies. Competition in the BCMA-targeting space is intensifying, driving further innovation in drug design, manufacturing efficiency, and toxicity management. Future research will likely focus on optimizing combination strategies, exploring novel targets beyond BCMA, and developing less resource-intensive administration models to broaden the applicability of these powerful therapies.

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