Chemo-Free Regimens Show Promise, Could Redefine Care for B-Cell Lymphomas

Dana-Farber studies of chemo-free targeted therapy and immunotherapy combinations show rapid, deep responses and potential for time-limited care.

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Researchers at Dana-Farber Cancer Institute are advancing chemo-free regimens that pair immunotherapy with targeted therapies to treat common B cell lymphomas. In two investigator initiated studies, these approaches produced rapid, deep responses in follicular lymphoma and mantle cell lymphoma, moving care toward less chemotherapy and, for some patients, time limited treatment.

The findings were presented at the 67th American Society for Hematology Annual Meeting and Exposition from December 6–9 in Orlando, FL.

Current standard treatment for follicular lymphoma and mantle cell lymphoma involves chemotherapy plus immunotherapy. Dana-Farber investigators, however, are testing regimens that involve combinations of immunotherapies and targeted therapies in Phase I/II and Phase II clinical trials. Early results from those trials are showing impressive rates and depths of response.

Immunotherapy with bispecific antibody therapy for follicular lymphoma

Dr. Reid Merryman, a lymphoma specialist and clinical investigator at Dana-Farber, presented findings from an investigator-initiated, multi-center, open-label Phase II clinical trial testing a combination of rituximab [Rituxan] and epcoritamab [Epkinly] as first-line therapy for patients with high-tumor burden follicular lymphoma.

Epcoritamab is a novel type of immunotherapy called a bispecific antibody. It binds two targets – CD3 on immune cells called T cells and CD20 on the surface of the follicular lymphoma tumor cells – to mediate immune destruction of the cancer cell. Rituximab, another immunotherapy agent that is a standard part of follicular lymphoma treatment, is given first to lower the burden of lymphoma. The goal is that rituximab can both deepen responses and also lower the risk of an

immune side effect, called cytokine release syndrome, that is observed with epcoritamab.

Epcoritamab was approved in 2024 for treatment of patients who have already received two or more treatments for their follicular lymphoma. This trial, based on the success of epcoritamab in the relapsed disease setting, investigates replacement of first-line chemotherapy with the drug.

Results so far, reports Merryman, show that the combination therapy is very active, with 97% of patients achieving an objective response. The responses occurred rapidly, with 34 of 35 patients responding within the first two of nine cycles. Only one patient has progressed, and the 9-month progression free response rate is 97%. Merrymen also reports that pre-treatment with rituximab appears to lower the risk of cytokine release syndrome (CRS), a potential side effect of epcoritamab. Only six percent of patients experienced grade 2 or higher CRS, lower than expected in this setting.

“Based on the encouraging results seen in the initial cohort of 35 patients, the trial has been expanded with plans to enroll an additional 65 patients,” says Merryman. “The expansion cohort is enrolling rapidly with approximately 35 of 65 planned patients enrolled in the last five months.”

Targeted therapy plus immunotherapy for mantle cell lymphoma

Dr. Austin Kim, a lymphoma specialist and clinical investigator at Dana-Farber, presented results from the investigator-initiated, multi-center MAVO Phase I/II study of a chemotherapy-free, triplet regimen in mantle cell lymphoma (MCL). The triplet regimen includes acalabrutinib [Calquence], an oral Bruton tyrosine kinase (BTK) inhibitor, venetoclax [Venclexta], an oral BCL2 inhibitor, and obinutuzumab [Gazyva], an anti-CD20 monoclonal antibody.

This study included patients with previously treated and treatment naïve mantle cell lymphoma. Patients were grouped into three cohorts: (A) previously treated patients; (B) treatment naïve patients who are ineligible for aggressive therapy or have TP53 aberrant MCL; and (C) treatment naive patients who are eligible for aggressive therapy without TP53 aberrant MCL. Patients with TP53 mutated mantle cell lymphoma typically have aggressive disease and poorer outcomes.

The triplet regimen had a high complete remission rate in all three cohorts with manageable side effects. Kim reports that cohort B had a complete remission rate of 83% after a median 20-months of follow-up, meeting its primary endpoint. In the subset of 17 patients in cohort B with a TP53 mutation, the complete remission rate was 82%, with an estimated 2-year progression free survival of 82%.

In cohorts B and C, treatment naive patients who achieved a complete remission and had no microscopic disease detected in the blood using a test called minimal residual disease (MRD), were able to discontinue acalabrutinib and venetoclax while completing 2 years of maintenance obinutuzumab, allowing for time-limited therapy. Of the 19 patients with evaluable MRD in cohort B, 15 patients achieved MRD complete remission and discontinued acalabrutinib and venetoclax,

with only one patient relapsing after treatment discontinuation.

“This study adds to the current literature in mantle cell lymphoma supporting the use of triplet chemotherapy-free regimens in mantle cell lymphoma, especially in patients with a TP53 mutation,” says Kim. “Based on the encouraging results of this study, a 16-patient expansion cohort is now open and enrolling for untreated mantle cell lymphoma with a TP53 mutation.”

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