Bendamustine prior to CAR T-cell therapy in patients with refractory large B-cell lymphoma: Poorer treatment outcomes

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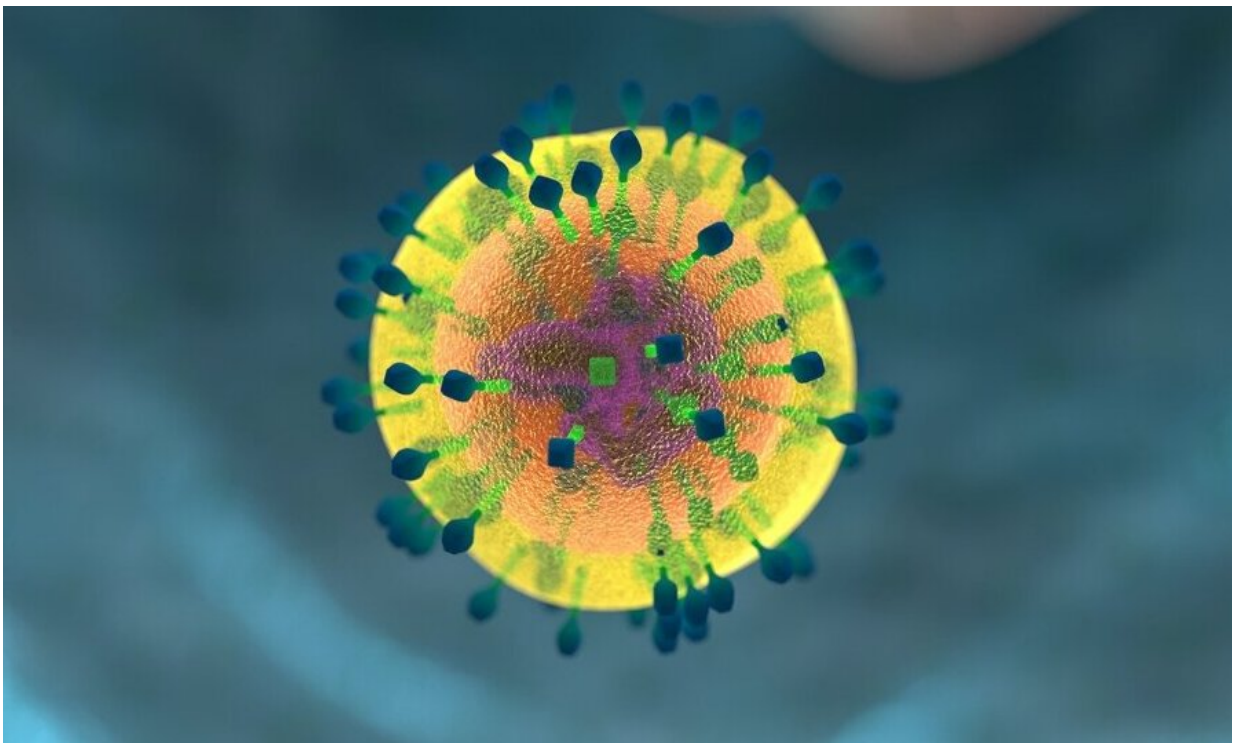

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Treatment with bendamustine prior to CAR T-cell therapy in patients with refractory large B-cell lymphoma associates with poorer treatment outcomes, finds a recent study.

Led by investigators of the Vall d'Hebron Institute of Oncology's (VHIO) Experimental Hematology Group and the Advanced Therapies Program of the Vall d'Hebron University Hospital's (HUVH) Hematology Service, results of a study show that patients with refractory large B-cell lymphoma (LBCL) who had received chimeric antigen receptor (CAR) T-cell therapy and treatment with bendamustine before apheresis had a shorter progression-free survival and overall response rate in comparison with the bendamustine-naïve group, irrespective of patient characteristics and dose received.

Bendamustine is a type of chemotherapy called an alkylating drug and is used in the treatment of chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), and myeloma. While clinical consensus guidelines exist on the limitations of using bendamustine due to its toxic effect on patient lymphocytes, this multicenter study—results of which recently published in the Journal of Clinical Oncology—is the first to report on the impact of recent exposure (9 months) to this agent as an independent factor of poorer outcomes of CAR-T cell therapy in patients with LBCL.

"While the advent of CAR T-Cell therapy has undoubtedly revolutionized the treatment landscape of patients with relapsed or refractory large B-cell lymphoma, only between 30% and 40% of patients infused with CAR T-cells achieve a durable remission," says Gloria Iacoboni, Hematologist at HUVH, Clinical Investigator of VHIO's Experimental Hematology Group and first author of this Original Report.

"Patients who progress after this therapy have low response rates to salvage regimens, and long-term outcomes are dismal. Advancing insights into factors associated with treatment success will ultimately help us to improve outcomes for more of our patients," adds Pere Barba, Director of the Advanced Therapies Program of HUVH's Hematology

Service, Clinical Investigator of the same VHIO Group and corresponding author of this article.

This retrospective study included clinical data of 439 patients who had received CAR T-cell therapy in the third or later line of treatment at 7 European sites. These patients were divided into two different cohorts based on whether they had been exposed to bendamustine prior to T-lymphocyte apheresis. Eighty (18%) patients had been exposed to this agent at a median of 6 months before T cell collection with a median of four cycles of treatment.

After statistically equating baseline characteristics to rule out that the results were perhaps influenced by the fact that those patients who had received bendamustine had more aggressive disease, the investigators identified previous exposure as an independent factor associated with poorer outcomes following CAR T-cell therapy.

In a second analysis, they sought to confirm if recent exposure (9 months before apheresis) to bendamustine led to worse results. Recent exposure to this agent correlated with poorer outcomes, irrespective of patient characteristics and dose received. The 42 patients who had received this agent nine months before apheresis had a median overall survival of 4.6 months compared to 23.5 months in the bendamustine-naïve group.

"On the basis of our results, the use of bendamustine should be avoided when possible in patients with refractory large B-cell lymphoma who are potential candidates for CAR T-cell therapy," observes Pere Barba.

"Our findings should be considered in future clinical guidelines, not only for these lymphomas but also for other types of lymphoma that may eventually progress and require CAR-T therapies, as we collectively seek to anticipate all treatment scenarios and improve patient outcomes."

More information: Gloria Iacoboni et al, Recent Bendamustine Treatment Before Apheresis Has a Negative Impact on Outcomes in Patients With Large B-Cell Lymphoma Receiving Chimeric Antigen Receptor T-Cell Therapy, *Journal of Clinical Oncology* (2023). DOI: 10.1200/JCO.23.01097

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