Simple blood protein tests predict which lymphoma patients are most likely to have poor CAR T outcomes

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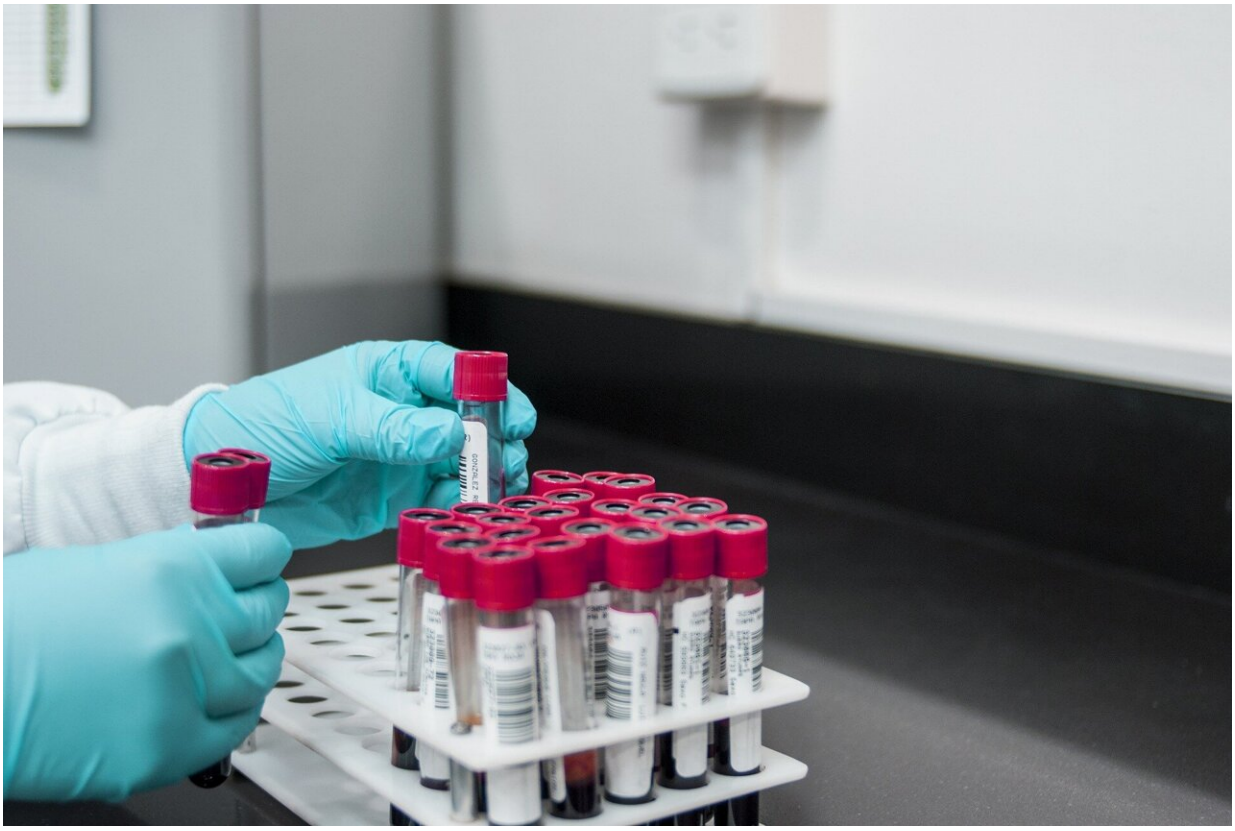

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As new cancer treatments become available, some of the most important ongoing research must look at ways to optimize those new approaches so

that more patients can benefit from groundbreaking therapies. In work published in *Blood Cancer Discovery* a team of collaborators from Roswell Park Comprehensive Cancer Center and Moffitt Cancer Center report the first strategy for identifying before treatment which patients are at risk for poor outcomes from CAR T-cell therapy—pointing to opportunities to improve the safety and efficacy of this new and fast-growing class of cancer immunotherapies.

"We determined that two common and easily measured blood tests can identify in advance which patients are at high risk for poor outcomes after treatment with CD19-targeted CAR T cells," says co-senior author Marco Davila, MD, Ph.D., Senior Vice President and Associate Director for Translational Research at Roswell Park.

"We're excited because these findings not only help us to make CAR T-cell therapies work for more patients with hard-to-treat cancers, they also help us spare some patients from additional medications they don't need."

"Despite encouraging outcomes with CAR T-cell therapy for hard-to-treat B-cell lymphoma, some patients experience toxicity and poor outcomes. Our work determined that readily available lab tests for c-reactive protein and ferritin can identify which patients, pre-treatment, are at high risk for side effects and not responding to CD19-targeted CAR T-cell therapy," adds study first author Rawan Faramand, MD, Assistant Member of the Blood and Marrow Transplant and Cellular Immunotherapy Department at Moffitt Cancer Center.

CAR T, or chimeric antigen receptor T-cell therapy, has been FDA-approved for the treatment of many blood cancers, including some forms of lymphoma, leukemia and multiple myeloma. But these groundbreaking treatments, which enable a patient's immune cells to better target and eradicate cancer cells, can be associated with significant

and sometimes-severe side effects.

The new publication reports findings from a study of 146 patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) treated with the CAR T immunotherapy axicabtagene ciloleucel (also known as axi-cel, and sold under the brand name Yescarta)—all of whom had already received at least two prior lines of therapy for lymphoma.

Nearly all the patients (93%) experienced cytokine release syndrome (CRS) following CAR T, and the majority (61%) developed immune effector cell-associated neurotoxicity syndrome (ICANS).

"Chimeric antigen receptor T-cell therapy has changed the treatment paradigm for patients with relapsed/refractory hematologic malignancies," the authors write.

"Despite encouraging efficacy, a subset of patients have poor clinical outcomes. We show that a simple clinically applicable model using pre-lymphodepletion CRP and ferritin"—two tests that measure key blood proteins—"can identify patients at high risk of poor outcomes."

The team determined that patients with baseline serum blood levels of c-reactive protein (CRP) of at least 4 mg/dL and of ferritin of 400 ng/mL or higher represent those at highest risk for poor outcomes, including reduced progression-free and overall survival as well as higher rates of severe toxicities.

While several studies have explored ways to characterize and measure the effectiveness of CAR T therapy following treatment, there was previously no widely available lab test or biomarker to rapidly identify patients at high risk for poor outcomes prior to CAR T-cell infusion.

All 146 patients in the study were treated at a single center, Moffitt

Cancer Center. The authors document two independent international cohorts that validate the approach, demonstrating that patients classified as low risk have excellent efficacy and safety outcomes.

"Our algorithm allows us to identify patients who would be good candidates for prophylaxis, or additional therapies to control and prevent side effects, or for clinical studies to improve their outcomes," notes Dr. Davila. "It's an important tool that will help us personalize treatment for each patient."

"Our group has previously shown that systemic inflammation and suppressive myeloid cells are associated with decreased efficacy in CAR T-cell therapy for lymphoma. Here we demonstrate that simple, and widely available, laboratory tests can similarly predict those patients with a decreased chance for success with CAR T. New strategies are needed for these patients, although CAR T remains the best therapeutic option for most patients we studied," says Frederick Locke, MD, Chair of the Blood and Marrow Transplant and Cellular Immunotherapy Department at Moffitt Cancer Center.

More information: Rawan G. Faramand et al, Baseline serum inflammatory proteins predict poor CAR T outcomes in diffuse large B-cell lymphoma, *Blood Cancer Discovery* (2024). DOI: 10.1158/2643-3230.BCD-23-0056

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