

# Results 'encouraging' from phase II trial for relapsed acute myeloid leukemia

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Bone marrow aspirate showing acute myeloid leukemia. Several blasts have Auer rods. Credit: Wikipedia

There is a significant need for new treatments for patients with relapsed acute myeloid leukemia, a rare cancer of the blood that is more common

in older adults. UNC Lineberger Comprehensive Cancer Center researchers recently reported encouraging findings from a clinical trial that leverages the immune system to fight the disease. Now they are working to find genetic signatures to try to predict which patients will respond best to the treatment.

UNC Lineberger's Joshua Zeidner, MD, reported preliminary data at the 60th American Society of Hematology Annual Meeting from a phase II clinical trial for administering high-dose of the chemotherapy [treatment](#) cytarabine followed by an [immune checkpoint inhibitor](#), pembrolizumab, in patients with [acute myeloid leukemia](#) that had relapsed or no longer responded to other treatment.

Acute myeloid leukemia has a low survival rate; just 27 percent of patients live five years after being diagnosed. Of the patients who do not respond to therapy or whose [cancer](#) comes back, there is a need for new therapies, said Zeidner, who is an assistant professor in the UNC School of Medicine Division of Hematology/Oncology.

"Relapsed and refractory AML have dismal outcomes, with response rates in the 20 to 30 percent range for salvage chemotherapy, and targeted agents," Zeidner said. "Although we have had eight new drug approvals for AML in the past two years, there remains a significant unmet need for the majority of patients with relapsed and refractory AML."

In the new UNC Lineberger study, researchers reported that in 29 patients, 12 people, or 41 percent, had an overall response, and 10, or 35 percent, had a complete remission. The median amount of time that patients responded to the treatment without progression of their cancer was 5.7 months. Zeidner said that while it is difficult to compare this to other treatments, conventional treatments for relapsed or refractory AML typically generate a remission lasting less than six months.

"We are encouraged by the safety profile and clinical activity of high-dose cytarabine followed by pembrolizumab to date," Zeidner said.

Zeidner said the phase II study is ongoing. Once they complete it, the researchers plan to analyze their results to determine whether there is a genetic signature that might indicate which patients will respond to pembrolizumab. Their preliminary analysis of six patients reveals a potential predictive gene signature, and they are planning to continue their work to see if the signature can help predict response in the other patients in the trial.

"Checkpoint inhibitors work by repressing an immune brake on activated T-cells, therapy stimulating an immune-mediated attack against cancer cells," Zeidner said. "Although these agents have activity against a multitude of cancer subtypes, the majority of patients do not respond. However, patients that do respond can have a long-lasting, durable response. It is, therefore, critical to ascertain predictive biomarkers of response so that these agents are administered to patients that have the highest predilection for response."

Zeidner is leading other trials to try to improve responses in patients with AML. He presented findings from a phase I study at the ASH Annual Meeting that showed that adding an oral small molecule immunomodulatory agent, pomalidomide, to chemotherapy for patients with newly diagnosed AML, or high-risk myelodysplastic syndrome, was safe, and that the overall complete response rate was 74 percent.

"Notably, we found that pomalidomide led to significant changes in T-cell differentiation, suggesting that pomalidomide may be enhancing an immune response against leukemia after chemotherapy," said Zeidner.

Zeidner is also the lead investigator of Zella 201. He presented findings from this study at the ASH Annual Meeting. Zella 201 is a biomarker

guided phase II study of alvocidib followed by cytarabine and mitoxantrone (ACM) in patients who overexpress MCL-1, a gene that regulates survival of cancer cells, in relapsed/refractory AML. This treatment strategy led to a complete [response](#) rate of 57 percent in 23 MCL-1 dependent [patients](#).

**More information:** 4054 Genomics Reveal Potential Biomarkers of Response to Pembrolizumab after High Dose Cytarabine in an Ongoing Phase II Trial in Relapsed/Refractory AML.

[ash.confex.com/ash/2018/webpro...ram/Paper116608.html](http://ash.confex.com/ash/2018/webpro...ram/Paper116608.html)

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