

# Chemotherapy and blinatumomab improves survival for patients with B-cell acute lymphoblastic leukemia

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A study led by The University of Texas MD Anderson Cancer Center showed that first-line treatment with a regimen of chemotherapy

combined with the monoclonal antibody blinatumomab resulted in increased survival and achieved a high rate of measurable residual disease (MRD) negativity for patients who were newly diagnosed with a high-risk form of acute lymphoblastic leukemia (ALL) known as Philadelphia chromosome-negative B-cell ALL (Ph-negative B-ALL).

Findings from the study were presented by Nicholas Short, M.D., assistant professor of Leukemia, at the virtual 2020 Annual Meeting of the American Society of Hematology. The study was led by Elias Jabbour, M.D., professor of Leukemia.

"The best opportunity to cure any acute leukemia is by giving the most effective therapy in the front-line setting," Short said. "We are very encouraged that every patient on the study achieved a complete remission and 97% achieved MRD negativity, which is highly associated with better outcomes."

### **Advancing treatment options and improving quality of life for ALL patients**

Standard treatment for patients with Ph-negative B-ALL is combination chemotherapy, which has a high rate of treatment failure and complications. Current therapies for ALL have high remission rates of up to about 90%. However, many patients relapse, leading to long-term survival rates of 50% or less. Finding new treatment options that can improve response and survival for these patients is critical.

Immunotherapy using monoclonal antibodies, such as [blinatumomab](#), encourages changes in the body's immune system and interferes with the ability of tumor cells to grow and spread. Blinatumomab has two components, one targets CD3, on the T-cells, and one targets CD19, which is overexpressed in most cases of B-cell ALL. Previous clinical trials have shown blinatumomab to be effective in improving overall

survival in the relapsed or refractory setting and it has been proven to clear up MRD, as well.

"Although the survival data is early, it is promising, with a two-year survival of 80%. This is particularly important as about a third of these patients had high-risk features," Jabbour said. "We are encouraged that we can decrease the amount and duration of chemotherapy for patients and hope that these results will translate to long-term survival and increased cure compared to standard chemotherapy regimens."

### **Evaluating patient response and adding a new study arm**

The trial enrolled 38 patients, ages 14 to 59, with newly diagnosed Ph-negative B-ALL, 34 of whom were able to be evaluated in the study. Patients could not have received more than one prior cycle of chemotherapy and were required to have a performance status of  $\leq 3$ , total bilirubin  $\leq 2$  mg/dl and creatinine  $\leq 2$  mg/dl.

Trial participants were 55% Caucasian, 32% Hispanic, 5% Black, 3% Asian and 5% other. At least one high-risk feature was present in 19 patients (56%), including TP53 mutation in 10 patients (17%), CRLF2+ in 6 patients (19%), and an adverse-risk karyotype in 12 patients (32%).

Patients received two cycles of hyperfractionated cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride, and dexamethasone (hyper-CVAD) chemotherapy alternating with two cycles of high-dose methotrexate and cytarabine, followed by four cycles of blinatumomab at standard doses. The maintenance phase consisted of 12 monthly cycles of daily mercaptopurine, monthly vincristine, weekly methotrexate, and monthly pulses of prednisone (POMP) with three additional cycles of blinatumomab.

All patients in the study experienced at least one adverse event, which

was expected with the hyper-CVAD regimen. Four patients developed cytokine release syndrome, which resolved with corticosteroids and interruption of blinatumomab.

Thirty-one percent of patients had a blinatumomab-related neurological event, including a grade 2 seizure in one patient, a grade 1 tremor in two patients, a grade 3 ataxia in one patient and a grade 2 encephalopathy and dysphasia in one patient. All other neurological events were easily manageable, reversible and did not alter the planned treatment.

Relapses occurred in 13% of patients, but no relapses were observed in patients without baseline high-risk features or in any patients beyond two years. Twelve patients underwent an allogenic stem cell transplant and 17 patients remain in continuous remission.

The next stage of this study will incorporate inotuzumab ozogamicin into the regimen for the next 40 patients enrolled in the trial. Inotuzumab ozogamicin is an anti-CD22 antibody drug that attaches to the CD22, which is highly expressed in B lymphoblasts, and then delivers the toxin directly to the ALL cells. While these findings need to be confirmed in larger studies, the data suggests that blinatumomab can improve treatment response for Ph-negative B-ALL patients.

"Our goal now is to see if we can do hyper-CVAD with blinatumomab and adding inotuzumab ozogamicin to get even better results," Short said. "We believe this will decrease chemotherapy-related toxicity, minimize MRD, further decrease reliance on stem cell transplants and improve long-term outcomes for these [patients](#)."

**More information:** [ash.confex.com/ash/2020/webpro ... ram/Paper138565.html](https://ash.confex.com/ash/2020/webprogram/Paper138565.html)

Provided by University of Texas M. D. Anderson Cancer Center

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