

New study finds bortezomib improves survival in children with newly diagnosed Tcell lymphoblastic lymphoma

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A Wright's stained bone marrow aspirate smear of patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikimedia/CC BY-SA 3.0

Adding the proteasome inhibitor bortezomib to chemotherapy



significantly improved overall survival in children and young adults with newly diagnosed T-cell lymphoblastic lymphoma (T-LL), according to a Children's Oncology Group (COG) study led by researchers at Children's Hospital of Philadelphia (CHOP). This international phase 3 clinical trial also found that radiation could be eliminated in 90% of children with Tcell acute lymphoblastic leukemia (T-ALL) when the chemotherapy regimen was intensified.

The findings were published in the Journal of Clinical Oncology.

"The results of this trial have the potential to change the standard of care for patients with T-cell lymphoblastic lymphoma and T-cell acute lymphoblastic leukemia," said study chair and first author David T. Teachey, MD, an attending physician and Director of Clinical Research at the Center for Childhood Cancer Research at Children's Hospital of Philadelphia. "The data show that most patients with T-ALL no longer need cranial radiation for cure and also suggest bortezomib should be considered as part of the new standard of care for newly diagnosed patients with T-cell lymphoblastic lymphoma."

With advances in treatment, overall survival for <u>children</u> with T-ALL and T-LL approximates that of B-cell acute lymphoblastic <u>leukemia</u> (B-ALL) and B-cell lymphoblastic <u>lymphoma</u> (B-LL), with a 5-year survival rate of approximately 85%. However, less than 35% of patients with relapsed T-ALL and T-LL survive. To improve outcomes in these patients, COG trials have focused on different strategies to prevent relapse in newly diagnosed patients, including refining risk stratification, introducing new drugs and treatments, and intensifying <u>chemotherapy</u>.

While outcomes were excellent on the prior COG phase 3 clinical trial AALL0434, the majority of children with T-ALL received cranial radiotherapy (CRT), which can have significant long-term side effects, including second cancers, brain tumors, and neurocognitive decline that



can significantly affect school performance and employability.

Therefore, in the AALL1231 (NCT02112916) trial, the investigators modified the treatment further, utilizing the steroid dexamethasone instead of prednisone during chemotherapy and adding two extra doses of pegaspargase with a goal of eliminating CRT in most patients with T-ALL. Of the 824 patients enrolled in the trial between 2014 and 2017, half also received proteosome inhibitor bortezomib, based on strong preclinical data for its use in relapsed T-LL and T-ALL.

For patients with T-LL, both the 4-year event-free survival and overall survival were significantly improved for patients on bortezomib plus chemotherapy versus chemotherapy alone: 86.4% and 89.5% vs. 76.5% and 78.3%, respectively. The researchers also did not observe any excess toxicity with bortezomib.

"This is the first trial demonstrating an overall survival benefit for newly diagnosed pediatric T-LL with a small molecule inhibitor," said senior study author Stephen P. Hunger, MD, Chief of the Division of Oncology, Director of the Center for Childhood Cancer Research, and holder of the Jeffrey E. Perelman Distinguished Chair in the Department of Pediatrics at Children's Hospital of Philadelphia. "Before this study, the only drugs that have improved survival for newly diagnosed T-ALL/T-LL patients have been cytotoxic chemotherapeutics. The success of bortezomib in this trial could potentially change the approach to frontline treatment of T-LL."

Although overall outcomes in patients with T-ALL were not statistically significantly improved by bortezomib, the researchers were able to eliminate CRT in nearly all T-ALL patients on <u>bortezomib</u> and still achieve excellent outcomes for most patients. Indeed, whereas 90.8% of T-ALL patients in the earlier trial received CRT, less than 10% received it in this trial, and yet patients who did not receive CRT had no statistical



differences in outcomes.

The COG trial involved 212 sites around the world.

More information: David T. Teachey et al, Children's Oncology Group Trial AALL1231: A Phase III Clinical Trial Testing Bortezomib in Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia and Lymphoma, *Journal of Clinical Oncology* (2022). DOI: 10.1200/JCO.21.02678

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