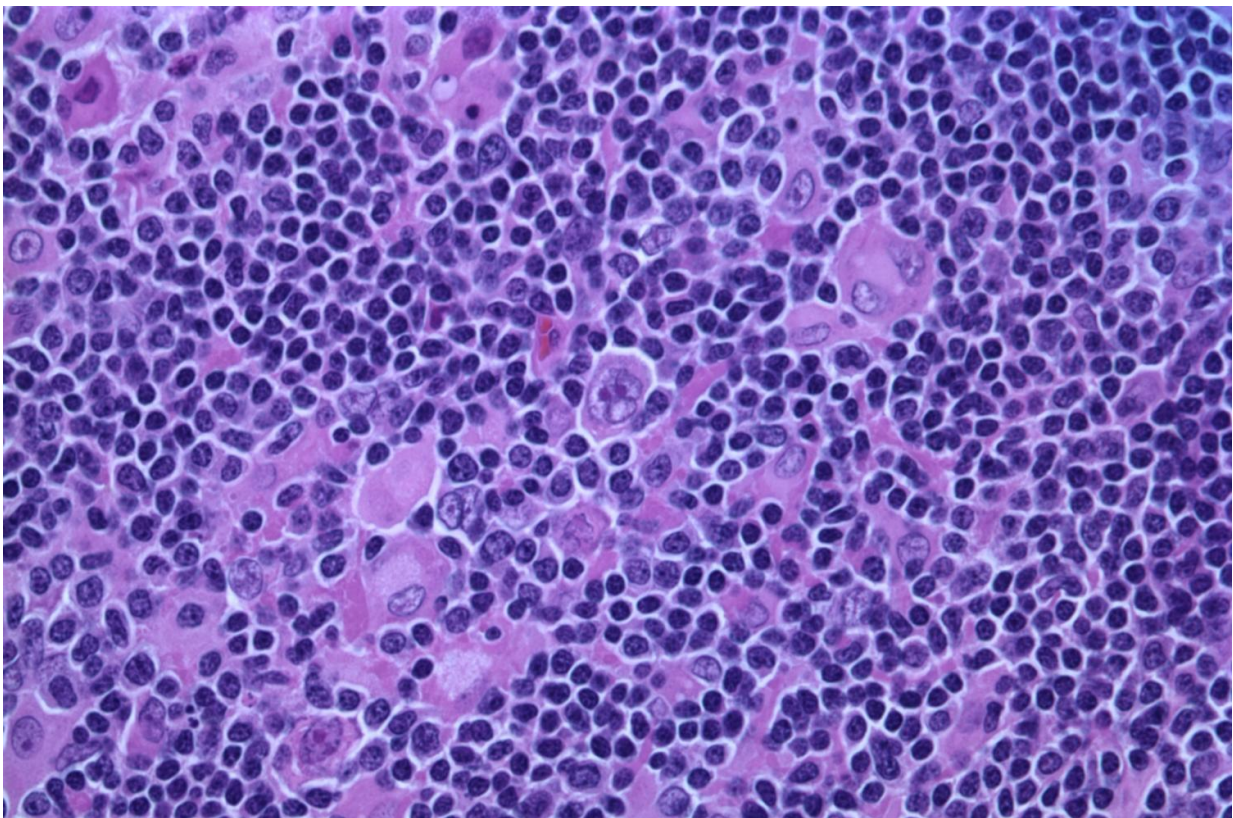


# Pediatric multicenter study shows targeted therapy for high-risk Hodgkin lymphoma reduces relapse

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Hodgkin lymphoma, nodular lymphocyte predominant (high-power view) Credit: Gabriel Caponetti, MD./Wikipedia/CC BY-SA 3.0

A targeted therapy for children with high-risk Hodgkin lymphoma (HL)

was shown to significantly reduce relapse rates when tested in a large multicenter clinical trial conducted by the Children's Oncology Group (COG) and led by pediatric oncologists at Roswell Park Comprehensive Cancer Center, Children's Healthcare of Atlanta and Winship Cancer Institute of Emory University. By combining the targeted antibody-drug conjugate (ADC) brentuximab vedotin (BV) with the standard chemotherapy regimen, children were 10% less likely to relapse. The findings were published today in the *New England Journal of Medicine* (NEJM).

"We saw a 10% improvement in event-free survival—a real breakthrough," says study senior author Kara Kelly, MD, Chair of the Roswell Park Oishei Children's Cancer and Blood Disorders Program, and also Division Chief of Hematology/Oncology in the Department of Pediatrics at the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo. "That's quite a big gain, especially in this field. We expect that this [treatment regimen](#) will soon become standard of care for [pediatric patients](#) with high-risk Hodgkin lymphoma."

The clinical trial, AHOD1331 ([NCT02166463](#)), was funded by the National Cancer Institute (NCI) of the National Institutes of Health and conducted at 153 COG sites. The study was also supported by Seagen, formerly known as Seattle Genetics, and the St. Baldrick's Foundation. The study was sponsored by the Division of Cancer Treatment and Diagnosis, NCI, and the brentuximab vedotin was provided by Seagen under a Cooperative Research and Development Agreement with NCI.

"This trial reflects a paradigm shift for advanced-stage Hodgkin lymphoma in children, and an introduction of the first targeted approach for initial therapy in pediatric Hodgkin lymphoma and the first new regimen in two decades," says study first author Sharon Castellino, MD, MSc, Director of the Leukemia and Lymphoma Program at the Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta,

Professor of Pediatrics at Emory University School of Medicine, and a research member at Winship Cancer Institute of Emory University. Dr. Castellino succeeded Dr. Kelly this year as COG Hodgkin Committee Chair. "We are optimistic that this trial will set the stage for FDA approval of this targeted antibody drug conjugate for children and adolescents."

Study Vice Chair and Co-Author Frank Keller, MD, Pediatric Hematologist/Oncologist at the Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta and Professor of Pediatrics at Emory University School of Medicine, adds: "The demonstration of the effectiveness of a highly targeted treatment directed against the malignant cell population in newly diagnosed pediatric and young adult patients with high-risk Hodgkin lymphoma is a significant step forward toward improving cure rates and may do so without adding significant long-term toxicity for this young population with many years of life remaining."

HL is the most common cancer in patients 12-29 years old. Although it has a high five-year survival rate—97% of those under 19 are alive five years after diagnosis—about one-third of survivors are classified as high risk; of those, approximately 15-20% will relapse.

The COG study—the largest and only randomized phase 3 trial with the CD-30 targeted ADC ever conducted with newly diagnosed high-risk HL pediatric patients—involved 587 patients ages 2-21 with previously untreated disease.

Patients were randomized to one of two arms, both arms receiving treatment over five 21-day cycles. Those in the [control group](#) received the standard pediatric chemotherapy regimen.

The second group received the standard pediatric chemotherapy

regimen, plus brentuximab vedotin. Brentuximab vedotin (BV) is an antibody-drug conjugate that specifically targets the CD30 protein on the surface of HL cancer cells, destroying them while mostly sparing healthy cells.

Both groups received site radiation therapy based on responses assessed after two cycles of treatment.

Follow-up at about three and a half years after treatment showed 92.1% event free survival in the brentuximab vedotin group, compared with 82.5% for the control group—an overall risk reduction of 59% of relapse, death or a second malignant neoplasm.

Lower risk of relapse could possibly eliminate the need for re-treatment with additional toxic therapies. Over the long term, treatment toxicity puts HL survivors at very high risk of breast cancer, stroke, myocardial infarction, restrictive pulmonary disease, infertility and shortened lifespan.

"Brentuximab vedotin is not anticipated to have long-term toxicity," says Dr. Kelly, noting that during the treatment phase of the clinical trial, less than 10% of patients who received it needed a dose reduction. "Because the drug could be given more consistently, its efficacy improved with no increase in neuropathy or serious infection."

Dr. Kelly, Dr. Castellino and colleagues will build on these findings in a new clinical trial set to open in early 2023 with support from the National Cancer Institute. The phase 3 randomized study will enroll approximately 1,900 children and adults ages 5-60 with medium- and low-risk HL. The goal: to determine whether the combination of the CD30 targeted ADC brentuximab vedotin and immunotherapy agent nivolumab can prolong progression-free survival and further reduce patients' exposure to standard chemotherapy and radiation. Patients will

be followed for 12 years to monitor their progress and gauge the results.

Allison Brashear, MD, Vice President for Health Sciences at the University at Buffalo and Dean of the Jacobs School of Medicine and Biomedical Sciences, says results of the study "mean a greatly improved quality of life for the most vulnerable and courageous patients—children with cancer.

"As one of the largest demonstrations of a successful immuno-oncologic approach in children with cancer," Dr. Brashear notes, "it is a powerful example of what happens when extraordinary institutions decide that collaboration is key to their success."

Lucky Jain, MD, MBA, Pediatrician-in-Chief for Children's Healthcare of Atlanta, and Chair of the Department of Pediatrics for Emory University School of Medicine, says, "A 10 percent reduction in relapse among children with high-risk Hodgkin lymphoma is a significant milestone for the field of pediatric [cancer](#). Children's Healthcare of Atlanta and Emory University are proud of this incredible leap forward led by our physicians, Dr. Sharon Castellino and Dr. Frank Keller, along with their collaborators and the Children's Oncology Group."

**More information:** Sharon M. Castellino et al, Brentuximab Vedotin with Chemotherapy in Pediatric High-Risk Hodgkin's Lymphoma, *New England Journal of Medicine* (2022). [DOI: 10.1056/NEJMoa2206660](https://doi.org/10.1056/NEJMoa2206660)

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