

E4412 Clinical Trial Results Summary

A Study of the Combination of Immunotherapy and Targeted Chemotherapy in Relapsed Hodgkin Lymphoma

What did this trial involve and who was it for?

This trial was for people with Hodgkin lymphoma (HL) whose cancer had either stopped responding to treatment (refractory) or returned after treatment (relapsed). Refractory or relapsed HL is challenging to treat, and the cure rate is only about 50%. More research is needed to find better options for these patients.

E4412 tested different doses and combinations of three drugs for treating relapsed or refractory HL: brentuximab vedotin, nivolumab, and ipilimumab. Brentuximab vedotin is a targeted chemotherapy, and nivolumab and ipilimumab are immunotherapy drugs. (Immunotherapy drugs train your own body's immune system to find and destroy harmful cells, such as cancer.)

E4412 was conducted in two phases, from January 2014 to October 2024: a phase 1 trial to establish safe doses for the drugs, and a phase 2 trial to compare two different combinations of drugs.

- Phase 1 included 64 adults (18 years of age or older). During phase 1, researchers determined that the drugs were safe and effective. They also established dose levels for phase 2.
- Phase 2 included 147 patients (12 years of age or older) who were randomly assigned by a computer to receive either:
 - Brentuximab vedotin and nivolumab (BV/N), or
 - Brentuximab vedotin, nivolumab, and ipilimumab (BV/N/I)

Patients are followed for up to 10 years.

What are the results?

Published results for the phase 1 portion of the trial showed no long-term safety concerns for any of the 3 drugs used. In both the BV/N and BV/N/I arms, there was a substantial improvement over chemotherapy alone.

Early phase 2 results were published in 2023:

- At the end of study treatment, 60.7% of patients who received BV/N had a complete response, meaning their cancer was completely undetectable after treatment; 66.7% of patients who received BV/N/I had a complete response.
- Patients who received BV/N/I were more likely to have rash as a side effect, but no significant differences in other side effects were observed between the two treatment groups. In all cases, the rash was treatable with steroids.

Additional [phase 2](#) results were published in 2026:

- After treatment with the study drugs was completed, some patients in both groups chose to receive a stem cell transplant (SCT). Both study groups showed excellent outcomes after SCT.
 - These patients had a 3-year progression-free survival rate of more than 90%, meaning their cancer did not worsen or spread.
- For patients who did not choose SCT, 73% of those who received BV/N/I did not experience worsening or return of their cancer at 3 years after the end of treatment. Only 45.8% of patients who received BV/N had these same results.

What do the results mean for patients?

- Both drug combinations were proven safe and effective as initial treatments for relapsed or refractory Hodgkin lymphoma.
 - Patients in both groups were equally likely to have their cancer become undetectable by the end of treatment.
- Receiving a stem cell transplant after initial treatment with immunotherapy drugs significantly improves patients' long-term outcomes.
 - For patients who do not choose to receive a stem cell transplant, the combination of brentuximab vedotin, nivolumab, and ipilimumab may improve long-term treatment outcomes.

For more information, go to:

- United States National Institutes of Health (NIH) Library of Medicine: <https://clinicaltrials.gov/study/NCT01896999>
- *Journal of Clinical Oncology* (initial Phase 1 results, 2015): https://doi.org/10.1200/jco.2015.33.15_suppl.tps8602
- *HemaSphere* (Phase 1 long-term follow-up results, 2022): <https://doi.org/10.1097/01.HS9.0000890968.53519.f4>
- *Blood* (initial Phase 2 results, 2023): <https://doi.org/10.1182/blood-2023-184531>
- *Blood* (Phase 2 long-term follow-up results, 2026): <https://doi.org/10.1182/blood.2025029546>

About ECOG-ACRIN

This trial was led by the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN). ECOG-ACRIN is a membership-based scientific organization that designs and conducts cancer research involving adults who have or are at risk of developing cancer. ECOG-ACRIN is a component of the National Cancer Institute's National Clinical Trials Network. Learn more at www.ecog-acrin.org.

To all the patients that participated in this trial, thank you. Your participation, and that of other patients like you, made this research possible.