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# Clinical Trial Results: Plain Language Summary

## **S1826:** Comparing Nivolumab and Brentuximab Vedotin with Standard Chemotherapy in People with Newly Diagnosed, Advanced Classical Hodgkin Lymphoma

### Overview

S1826 compared 2 treatment approaches in people with advanced classical Hodgkin lymphoma:

- Brentuximab vedotin plus standard chemotherapy (the usual approach)
- Nivolumab plus standard chemotherapy (the study approach)

**The study asked which approach helped people live longer without the cancer getting worse.**

#### Key study takeaways

Compared to people who received brentuximab vedotin plus standard chemotherapy, **people who received nivolumab plus standard chemotherapy**:

- Were less likely to have the cancer come back or get worse within 2 years of starting treatment
- Were less likely to die within 2 years of starting treatment
- Had fewer side effects — and less serious side effects

#### Why this study matters

It's common for doctors to treat classical Hodgkin lymphoma with brentuximab vedotin plus standard chemotherapy. But this treatment combination doesn't work for everyone, and it can cause many side effects.

S1826 found that nivolumab plus standard chemotherapy worked for more people — and caused fewer side effects. This could give more people with classical Hodgkin lymphoma a treatment option that works for them.

#### What's next

People in the study will keep having visits with the study team for 10 years total. This way the study team can learn about patients' health beyond the 2-year mark.

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# Detailed Trial Results

## What was the trial about?

The S1826 clinical trial compared 2 treatment approaches for adults and adolescents with advanced classical Hodgkin lymphoma ("advanced" means the lymphoma has spread). Both approaches used a chemotherapy base called **AVD**, which combines 3 drugs: adriamycin (also known as doxorubicin), vinblastine, and dacarbazine.

For classical Hodgkin lymphoma, doctors usually add the drug **brentuximab vedotin** to AVD. The S1826 trial asked if replacing brentuximab vedotin with **nivolumab** could improve the treatment. The study aimed to find out which drug combination is better for patients.

| **usual approach:** BV-AVD | **vs.** | **study approach:** N-AVD |
|---|---|---|
| brentuximab vedotin<br>+<br>AVD | | nivolumab<br>+<br>AVD |

## Why was the research important?

Brentuximab vedotin is a monoclonal antibody drug that targets lymphoma cells and then releases a chemotherapy drug inside the cells to attack the cancer. When combined with AVD, it can work well to cure patients with classical Hodgkin lymphoma.

But for about 1 in 5 patients, this standard treatment doesn't work. Side effects can also be a problem for many people. The S1826 trial was an important step in seeking better treatments that work for more newly diagnosed patients.

**Nivolumab** is an immunotherapy drug that helps the immune system attack cancer by targeting a protein in white blood cells called PD-1. Before the S1826 trial, nivolumab was approved by the Food and Drug Administration (FDA) to treat classical Hodgkin lymphoma that came back or got worse after other treatments.

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## What were the goals of the study?

The study was set up to find out:


Which treatment (BV-AVD or N-AVD) controls classical Hodgkin lymphoma longer


Which treatment helps patients stay free of major problems from cancer for longer


Which treatment helps patients live longer


What side effects BV-AVD and N-AVD can cause

## Who took part in the study?

970 people joined the study at 256 hospitals in the United States and Canada. All were newly diagnosed with stage 3 or 4 classical Hodgkin lymphoma. They had not received treatment yet.

**Age**

The study was for adults and adolescents, age 12 or older.

To learn how the study treatments affect people of different ages, the researchers looked at 3 age groups. The chart below shows how many participants were in each age group.

| | |
|---|---|
| **Ages 12-17** | 236 |
| **Ages 18-60** | 639 |
| **Ages 61-83** | 95 |

**Sex**

- 56% of all participants were male.
- 44% were female.

**Race and Ethnicity**

- 124 participants reported their ethnicity as Hispanic or Latino.
- The chart below shows what is known about the study participants' races.

| | |
|---|---|
| **Asian** | 28 |
| **Black** | 114 |
| **White** | 733 |
| **Unknown or not reported** | 95 |

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## What happened during the study?

Study participants were randomly assigned to one of 2 treatment groups:

**Treatment with BV-AVD**
(usual treatment)

Participants received 6 cycles of BV-AVD (about 6 months of treatment).

483 participants

**Treatment with N-AVD**
(study treatment)

Participants received 6 cycles of N-AVD (about 6 months of treatment).

487 participants

If their doctor recommended it, participants received radiation treatment after finishing BV-AVD or N-AVD treatment.

The study doctors monitored patients' health and how the cancer responded to treatment. They tracked if the cancer got better, worse, or stayed the same. They also tracked side effects and health problems that occurred.

## Study results

**N-AVD was better than BV-AVD at controlling classical Hodgkin lymphoma.**

After 2 years, the study team compared how many participants in each treatment group did not experience the cancer getting worse.

| BV-AVD | N-AVD |
|---|---|
| The cancer did not get worse for **83%** of participants. | The cancer did not get worse for **92%** of participants. |

**N-AVD helped patients avoid problems for longer than BV-AVD did.**

In all patients in the study, the study team watched to see if:

- The cancer came back or got worse
- They received treatment that was not part of the study's treatment plan even though the cancer did not get worse
- They died without the cancer getting worse

These things were less likely to happen to people who received N-AVD than people who received BV-AVD.

| BV-AVD | N-AVD |
|---|---|
| After 2 years, **about 8 out of 10** patients did not have major health problems from cancer.  | After 2 years, **about 9 out of 10** participants did not have major health problems from cancer.  |

**Overall, people who received N-AVD had fewer side effects — and less serious side effects — than people who received BV-AVD.**

In the BV-AVD treatment group, more patients had to stop treatment early because of side effects.

| BV-AVD | N-AVD |
|---|---|
| 58 out of 483 patients **(about 12%)** had to stop treatment early. | 37 out of 487 patients **(about 7%)** had to stop treatment early. |

Age was an important factor in the BV-AVD treatment group. Participants who were older than 60 and received BV-AVD were more likely to stop treatment because of side effects.
In the N-AVD group, side effects were similar across all ages.

**2 years after starting treatment, fewer patients in the N-AVD treatment group had died.**

| BV-AVD | N-AVD |
|---|---|
| 14 people had died after 2 years (**2%** of all patients in the BV-AVD group) | 7 people had died after 2 years (**1%** of all patients in the N-AVD group) |

Infection was the most common cause of death in both groups. 3 study participants died from lymphoma.

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## How has this study helped patients and researchers?

The S1826 trial showed that adolescents and adults benefited more from using nivolumab with AVD chemotherapy than brentuximab vedotin with AVD chemotherapy. After 2 years, N-AVD controlled the cancer better, helped patients live longer without major problems from cancer, and caused fewer side effects.

BV-AVD has worked well for many people with classical Hodgkin lymphoma, so finding a treatment with even better results is encouraging for patients and doctors. With fewer side effects, N-AVD could allow more patients to finish treatment. This may be especially important for older patients, who were more likely to stop treatment early from BV-AVD.

The study team will follow how people in the study are doing for up to 10 years in total. The longer follow-up will help them learn about patients' health beyond the 2-year mark. This may lead to other important study results about N-AVD and BV-AVD.

### How to learn more

- Visit **ClinicalTrials.gov** and search **S1826** or the national clinical trial number, **NCT03907488**
- Check out the report in the New England Journal of Medicine at nejm.org/doi/full/10.1056/NEJMoa2405888

*The S1826 clinical trial was sponsored by SWOG Cancer Research Network.*

### Thank you!

Thank you to all the participants who joined this trial and made it possible. Your courage helps answer important questions that will make cancer care better for future patients.