

Plain language summary of the CheckMate 816 study results: nivolumab plus chemotherapy given before surgery for non-small-cell lung cancer

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Summary

What is this summary about?

In this article, we summarize results from the ongoing phase 3 CheckMate 816 clinical study that were published in *The New England Journal of Medicine* in 2022. The goal of CheckMate 816 was to find out if **nivolumab**, an immunotherapy that activates a person's immune system (the body's natural defense system) to fight cancer, **plus chemotherapy** works better than **chemotherapy alone** when given before surgery in people with non-small-cell lung cancer (NSCLC) that can be removed surgically (resectable NSCLC).

What happened in the study?

- Adults who had not previously taken medications to treat NSCLC and whose cancer could be removed with surgery were included in CheckMate 816.
- During this study, a computer randomly assigned the treatment each person would receive before surgery for NSCLC.
 - In total, 179 people were randomly assigned to receive **nivolumab plus chemotherapy**, and 179 people were randomly assigned to receive **chemotherapy alone**.
- The researchers assessed whether people who received **nivolumab plus chemotherapy** lived longer without the cancer getting worse or coming back and whether there were any cancer cells left in the tumor and lymph nodes removed by surgery.
- The researchers also assessed how adding nivolumab to chemotherapy affected the timing and outcomes of surgery and whether the combination of these drugs was safe.

How to say (double-click on the icon to play sound)...

- **Nivolumab:** nih-VOL-yoo-mab
- **Neoadjuvant:** nee-oh-AD-juh-vnt
- **Adjuvant:** AD-juh-vnt
- **Chemotherapy:** kee-mo-THEH-ruh-pee
- **Immunotherapy:** im-mew-no-THEH-ruh-pee

What were the results?

- Researchers found that people who took **nivolumab plus chemotherapy** lived longer without the cancer getting worse or coming back compared with those who took **chemotherapy alone**.
 - More people in the **nivolumab plus chemotherapy** group had no cancer cells left in the tumor and lymph nodes removed by surgery.
- Most people went on to have surgery in both treatment groups; the people who took **nivolumab plus chemotherapy** instead of **chemotherapy alone** had less extensive surgeries and were more likely to have good outcomes after less extensive surgeries.
- **Adding nivolumab to chemotherapy** did not lead to an increase in the rate of side effects compared with **chemotherapy alone**, and side effects were generally mild and manageable.

What do the results of the study mean?

Results from CheckMate 816 support the benefit of using **nivolumab plus chemotherapy** before surgery for people with resectable NSCLC.

Where can I find the original article on which this summary is based?

The original article, titled “Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer,” was published in *The New England Journal of Medicine* in 2022. You can read the full article at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2202170>.

More information about the CheckMate 816 study can also be found at: <https://clinicaltrials.gov/ct2/show/NCT02998528>.

What is the study looking at and why is it important?

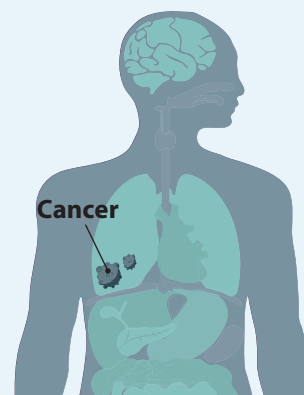
What is NSCLC and what are the different stages?

- NSCLC is a common type of cancer that starts in the lungs.
- Some NSCLC can be removed by surgery (resectable NSCLC).
- Staging is the process, including imaging scans and other tests, performed to find out how large the tumor is and how far it has spread inside and outside of the lungs; the stage is a summary of these results, with higher numbers and letters representing bigger tumors and/or more spreading.
- In this study, American Joint Committee on Cancer 7th edition staging categories were used to determine the disease stage for each person.

Smaller tumors/
less spreading

IB
IIA
IIB
IIIA

Larger tumors/
more spreading



How are people diagnosed and treated for resectable NSCLC?

Example of a person's journey through treatment



First suspicions of cancer

A primary care provider may think that a person has lung cancer based on that person's symptoms or the results of a test performed for other reasons.



Referral

The person may be referred to a lung specialist (also called a pulmonologist) or a doctor who specializes in treating cancer (also called an oncologist), who performs an exam and works with other specialists who may perform additional tests for evidence of cancer.

What are the current treatments for resectable NSCLC?

- Some people with NSCLC have tumors that can be removed surgically; however, the cancer often recurs or comes back in the lungs and surrounding areas and/or in other parts of the body, which may lead to a poor outcome for that person.
- Taking chemotherapy before or after surgery can reduce the risk of cancer coming back and may help people to live longer, but this only works for a few people.



Diagnosis and staging

Based on the exams, the pulmonologist or oncologist confirms the diagnosis and also assesses the extent (stage) of cancer.



Treatment plan

A multidisciplinary team, which may include pulmonologists, surgeons, medical oncologists, and/or radiation oncologists, works with each person to choose a treatment plan, which can include surgery, radiation, and/or medications. For some people, the standard treatment is surgery that could cure them of the cancer.



Pre-surgery (neoadjuvant) treatment

Some people receive medications and/or radiation before surgery to reduce the risk of cancer coming back or to prevent new tumors from appearing after surgery.



Surgery

People have surgery to remove the tumor and surrounding tissue.



Post-surgery (adjuvant) treatment

After surgery, people may receive radiation and/or medications to treat any cancer left and to reduce the risk of cancer coming back or to prevent new tumors from appearing.

Immunotherapy is a type of treatment that works by activating a person's immune system (the body's natural defense system) to fight cancer cells.

Nivolumab is an immunotherapy that stops PD-L1 (a protein made by cancer cells in some tumors that helps the cancer hide from the immune system) from working, which can help the body's immune system fight the cancer cells again.

Immunotherapy in combination with chemotherapy can be used before surgery (as a neoadjuvant treatment) or alone after surgery (as an adjuvant treatment).

What was the goal of the study?

The goal of CheckMate 816 was to find out if **adding nivolumab to chemotherapy** works better than **chemotherapy alone** when given before surgery to people with resectable NSCLC.

Who took part in this study?

This study took place at hospitals in 14 countries across the world.








358 people took part in the study:

- All had lung tumors (4 cm or larger, or any size if extending to the nearby lymph nodes and/or the surrounding areas) that could be removed with surgery (resectable NSCLC at stages IB, IIA, IIB, or IIIA).
- All were fully active or able to complete light daily activities.
- None had previous anticancer therapy.




People could not take part in the study if they had:

- Lung cancer that had spread to nearby tissues and could not be removed by surgery.
- Cancer that had spread to other parts of the body.
- Known changes (mutations) in genes called *EGFR* or *ALK* that are involved in cell growth.

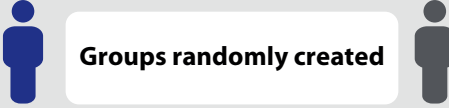
Sex		7 in 10 were men, and 3 in 10 were women.
Age		5 in 10 were younger than 65 years old.
Stage		6 in 10 had stage IIIA NSCLC, and 4 in 10 had stage IB-II NSCLC.
Region		5 in 10 were located in Asia, and 5 in 10 were located in North America, Europe, or the rest of the world.
Smoking history		9 in 10 were current or former smokers.
Histology (how cancer cells look under a microscope)		5 in 10 had a type of tumor called squamous cell lung cancer, and 5 in 10 had a type of tumor called non-squamous cell lung cancer.
PD-L1 (a protein made by cancer cells in some tumors that helps the cancer hide from the immune system)		5 in 10 had PD-L1 on at least 1% of their cancer cells, and 5 in 10 had no PD-L1 or an unknown amount of PD-L1 on their cancer cells.

What treatments were used and what did the researchers look at?


179 people in the nivolumab plus platinum-doublet chemotherapy group



Groups randomly created



179 people in the platinum-doublet chemotherapy alone group



Each treatment was taken **once every 3 weeks** for a total of **3 times**.
Surgery was planned to happen **within 6 weeks** of the last dose.

People knew which treatment they received. This study began in March 2017, with the first main results collected on or before October 2021. This study is still ongoing.

What did the researchers look at?

- Primary assessments:**
 - **Event-free survival:** How long did each person live without the cancer getting worse or coming back?
 - **Pathological complete response:** How many people had no cancer cells left in the tumor and lymph nodes removed by surgery?
- Additional assessments:**
 - **Major pathological response:** How many people had less than or equal to 10% of cancer cells left in the tumor and lymph nodes removed by surgery?
 - **Time to death or distant metastases:** How much time did each person have
 - without the cancer coming back outside of the lungs or surrounding areas or
 - before they died without the cancer coming back

- **Overall survival:** How long did each person live after being given treatment?
- **Surgical outcomes:** How many people could have surgery to remove NSCLC after receiving study treatment, what kind of surgery did they have, and what were the results of the surgery?
- What **side effects** did people have?

What were the main results as of October 2021?

People who took **nivolumab plus chemotherapy** lived longer without the cancer getting worse or coming back (event-free survival) than those who took chemotherapy alone.

Number of months half of the people were estimated to have lived without the cancer getting worse or coming back (median event-free survival)



People alive at 2 years without the cancer getting worse or coming back



Number of months half of the people were estimated to have lived without the cancer getting worse or coming back (median event-free survival)

People with stage IB-II cancer



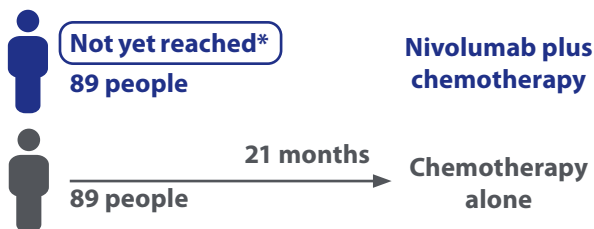
Nivolumab plus chemotherapy

Chemotherapy alone

People with stage IIIA cancer



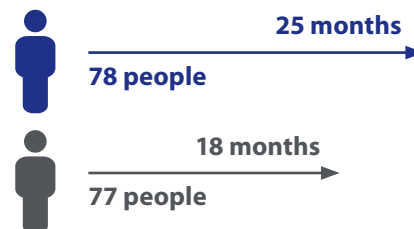
People with PD-L1** on at least 1% of their cancer cells



Nivolumab plus chemotherapy

Chemotherapy alone

People without PD-L1** on their cancer cells



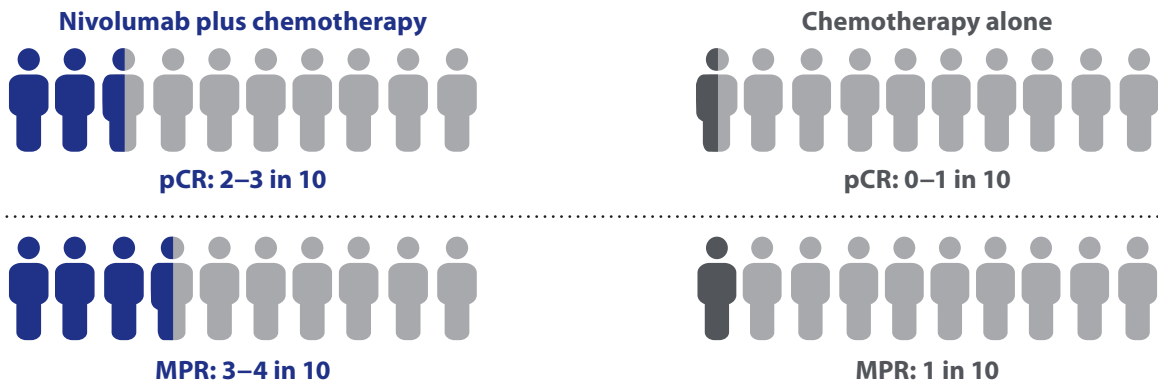
*When these data were collected in October 2021 (minimum follow-up, 21 months), more than half of these people were estimated to be alive without their cancer getting worse or coming back.

**PD-L1 is a protein made by cancer cells in some tumors that helps the cancer hide from the immune system.



*When these data were collected in October 2021 (minimum follow-up, 21 months), more than half of these people were estimated to be alive without their cancer getting worse or coming back.

More people who took nivolumab plus chemotherapy than those who took chemotherapy alone had no cancer cells left (pathological complete response [pCR]) or less than or equal to 10% of cancer cells left (major pathological response [MPR]) in the tumor and lymph nodes removed by surgery.



People who took **nivolumab plus chemotherapy** and had no cancer cells left in the tumor and lymph nodes removed by surgery lived longer without the cancer getting worse or coming back than those who still had some cancer cells left in the tumor and lymph nodes removed by surgery.

People who took nivolumab plus chemotherapy had a longer period of time without the cancer coming back outside of the lungs or surrounding areas or before they died without the cancer coming back (time to death or distant metastases) than those who took chemotherapy alone.

Number of months half of the people were estimated to have lived without the cancer coming back outside of the lungs or surrounding areas or before they died without the cancer coming back (median time to death or distant metastases)

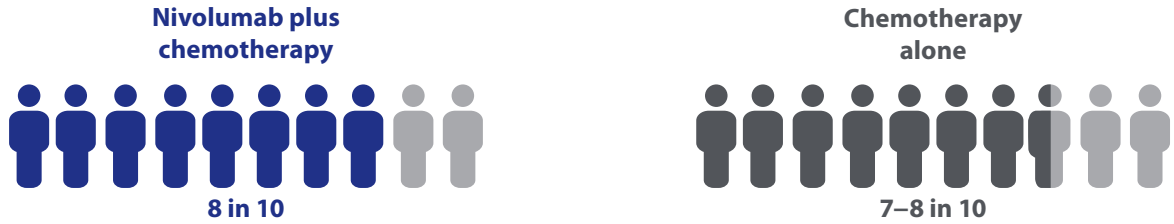
People alive at 2 years without the cancer coming back outside of the lungs or surrounding areas



*When these data were collected in October 2021 (minimum follow-up, 21 months), more than half of these people were estimated to be alive without their cancer coming back outside of the lungs or surrounding areas.

Early results suggest that people who took **nivolumab plus chemotherapy** might live longer overall (overall survival) than those who took chemotherapy alone. This result remains to be confirmed as the study continues.

After treatment with **nivolumab plus chemotherapy** or chemotherapy alone, most people went on to have surgery.



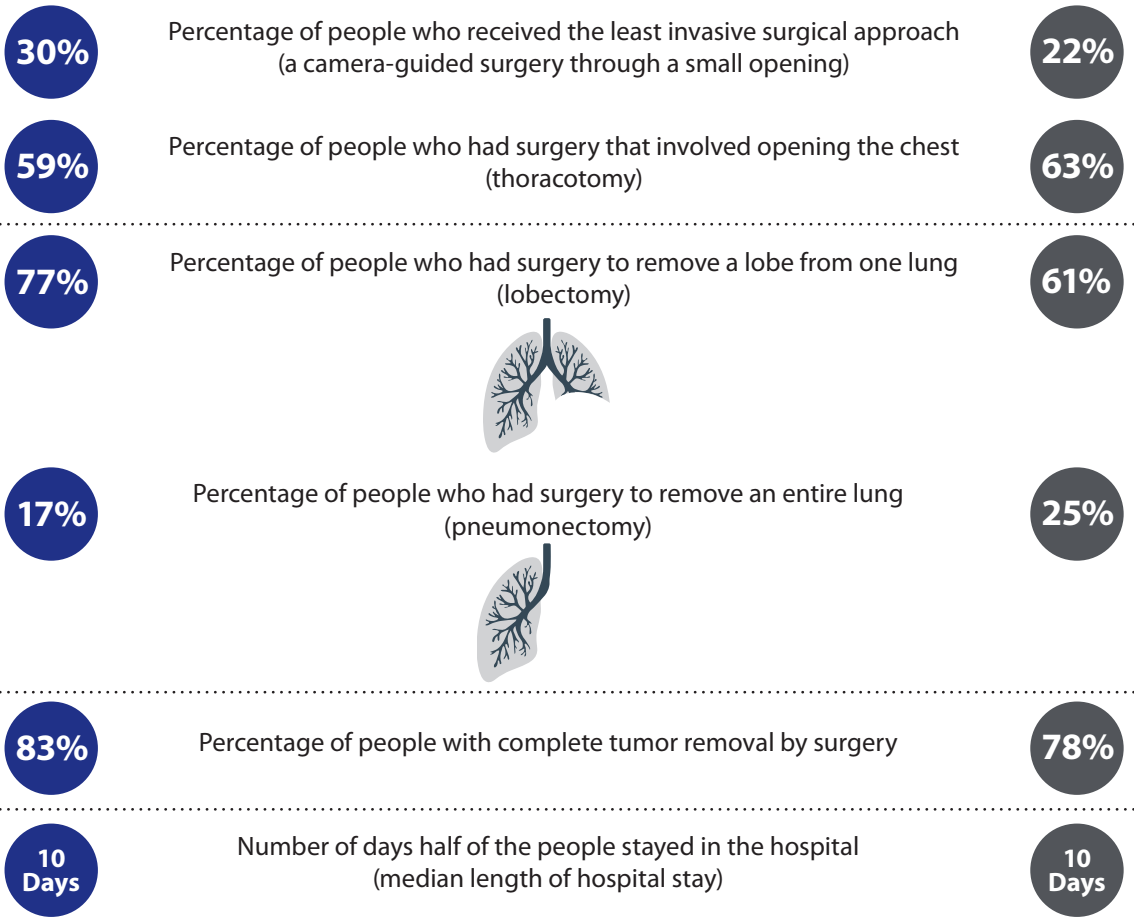
Why did some people not have surgery?

- Disease spread: **7%** versus **10%**
- Side effects: **1%** versus **1%**
- Other reasons (including the person’s decision, their lungs not working well enough, or the tumor could no longer be removed surgically): **8%** versus **11%**

People who took **nivolumab plus chemotherapy** had less extensive surgeries and better surgical outcomes than people who took chemotherapy alone.

Nivolumab plus chemotherapy
(149 people had surgery)

Chemotherapy alone
(135 people had surgery)



What were the side effects?



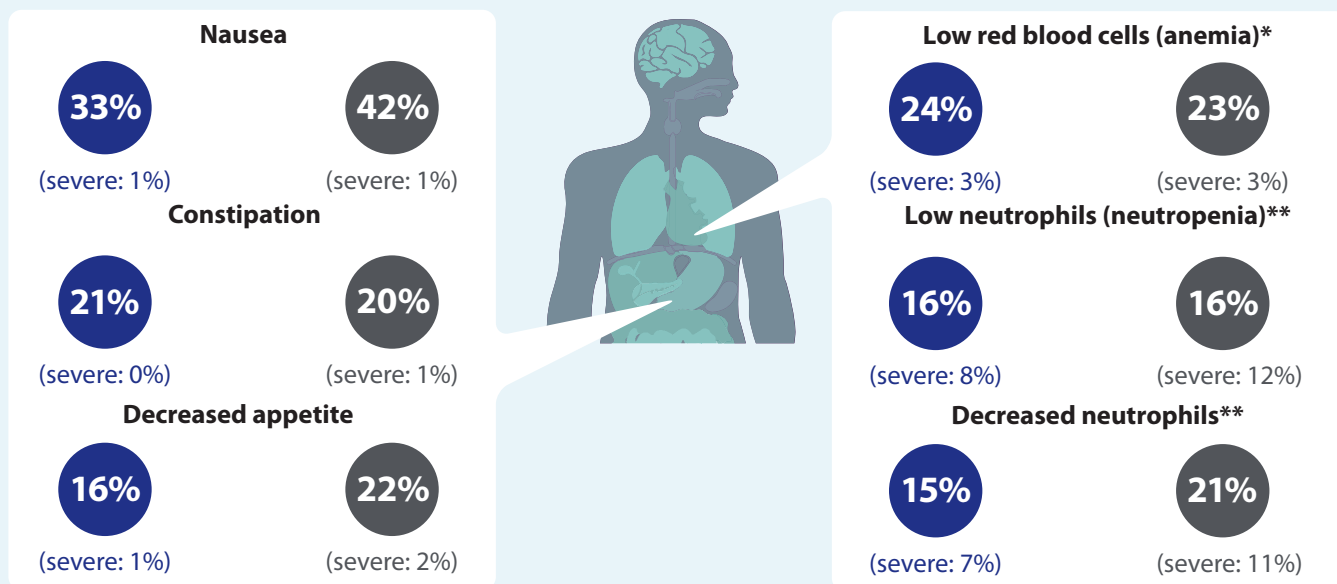
Most side effects from treatment were mild or moderate in both groups.



About 1 in 10 people in each group had a serious side effect from treatment.

A serious side effect from treatment is one that is life-threatening, requires going to the hospital, or results in death.

Most common side effects from treatment



- All side effects from **nivolumab plus chemotherapy**
- All side effects from **chemotherapy alone**

No people died because of side effects from nivolumab plus chemotherapy, and 3 people died because of side effects from chemotherapy alone.

*Low red blood cells (anemia) can cause weakness and tiredness.






**Low/decreased neutrophils refers to a condition in which a person has reduced neutrophils (a type of white blood cell), which can increase the chance of getting an infection. Researchers could have used either “neutropenia” or “decreased neutrophils” to refer to this condition during this study.

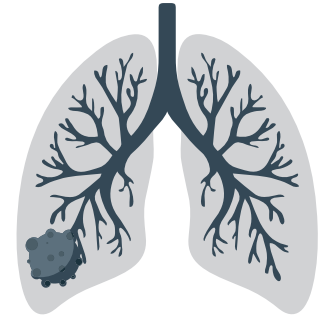
Few people had severe side effects from surgery; there was no increase in the rate of side effects from surgery with nivolumab plus chemotherapy versus chemotherapy alone.



What do the results of the CheckMate 816 study mean?

Compared with those who took **chemotherapy alone**, people who took **nivolumab plus chemotherapy** before their surgery:

-  Lived longer without the cancer getting worse or coming back.
-  More often had no cancer cells left in the tumor and lymph nodes removed by surgery.
-  Might live longer in general, although this result needs more time to be confirmed.
-  Had no impact on their chance of having surgery.
Were more likely to have good outcomes after surgery.
-  Had manageable side effects.



Nivolumab plus chemotherapy before surgery is now an approved treatment in the USA and other countries for adults with resectable NSCLC whose tumors are 4 cm or larger or have spread to nearby lymph nodes and/or the surrounding areas.

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