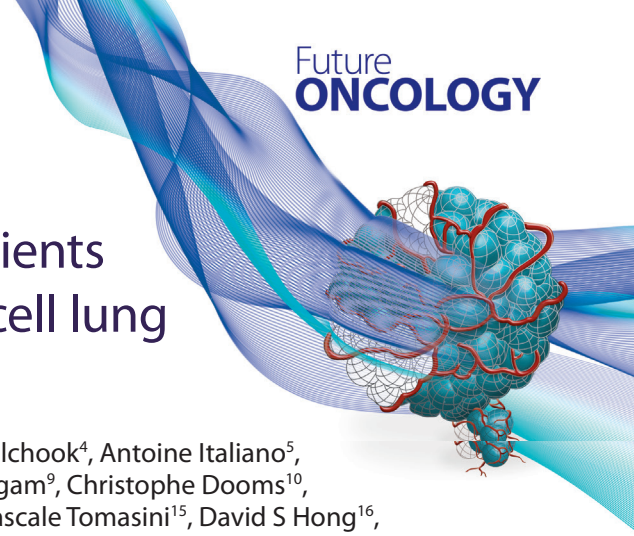
Plain Language Summary of Publication



Long-term benefit of sotorasib in patients with *KRAS* G12C-mutated non-small-cell lung cancer: plain language summary

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Summary

How to say (double click sound icon to play sound)...

Chemotherapy:
KEE-moh-THAYR-uh-pee
Immunotherapy:
IH-myoo-noh-THAYR-uh-pee
Sotorasib: SOH-toh-RA-sib

What is this summary about?
This is a plain language summary of a study called CodeBreaK 100. The CodeBreaK 100 study included patients with non-small-cell lung cancer that had spread outside the lung (advanced). Lung cancer is one of the most common forms of cancer.
CodeBreaK 100 specifically looked at patients with a particular change (mutation) in the *KRAS* gene resulting in the mutated protein called KRAS G12C. The *KRAS* G12C mutation can lead to development and growth of lung cancer.

Patients received a treatment called sotorasib, which has **accelerated approval** or full approval in over 50 countries for patients with non-small-cell lung cancer with the *KRAS* G12C mutation.
The CodeBreaK 100 study looked at whether sotorasib is a safe and effective treatment for advanced non-small-cell lung cancer. Sotorasib is designed to specifically target and lock the mutated KRAS protein in the inactive state to treat non-small-cell lung cancer.

Accelerated approval: This type of approval allows for earlier approval of drugs that treat serious conditions and fill an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a measurable indicator that can help us know what the real result is.

Treatment-related side effects: Treatment-related side effects are the negative effects that can happen when a patient receives a medical treatment. While a medicine is meant to help the patient, it is important to be aware of these potential side effects to manage them correctly.

What were the results?
In total, 174 adults were treated with sotorasib. **Treatment-related side effects** were seen in 70% of patients and were severe in 21% of patients. The most common side effects included diarrhea, increased liver enzymes, nausea and tiredness. 70 (41%) patients responded to sotorasib and 144 (84%) patients had tumors that either remained stable or shrunk in size. 29 (41%) patients who responded to sotorasib responded for over 12 months. After 2 years, 9 patients with a response remained on sotorasib; there were no notable increases in tumor size or development of new tumors over this time. There were 5 patients who received sotorasib for more than 2 years and continued to respond. Long-term benefit was seen for some patients. Patients also benefitted from treatment when the tumor expressed different amounts of a protein called PD-L1. In total, 33% of patients were still alive after 2 years.

What do the results mean?
Results show the long-term benefit of sotorasib therapy for people with advanced *KRAS* G12C-mutated non-small-cell lung cancer.

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

The original article discussed in this summary titled 'Long-term outcomes and molecular correlates of sotorasib efficacy in patients with pretreated *KRAS* G12C-mutated non-small-cell lung cancer: 2-year analysis of CodeBreaK 100' was published in the *Journal of Clinical Oncology* in April 2023.
You can read the original article at: https://ascopubs.org/doi/full/10.1200/JCO.22.02524

Who sponsored the study?

This study was sponsored by Amgen Inc.

Who is this article for?

This article may be helpful for doctors or healthcare professionals who treat patients with non-small-cell lung cancer. It may also be helpful for patients with non-small-cell lung cancer and their family members or caregivers.

Why was the study carried out?

Mutation: Mutations are changes in the genetic code of a cell. These changes can happen when cells divide and make mistakes, or when they come into contact with damaging factors in the environment like cigarette smoke.

Non-small-cell lung cancer is the most common form of lung cancer.
Advanced cancer is the term for cancer that has spread to other parts of the body and cannot be removed with surgery.

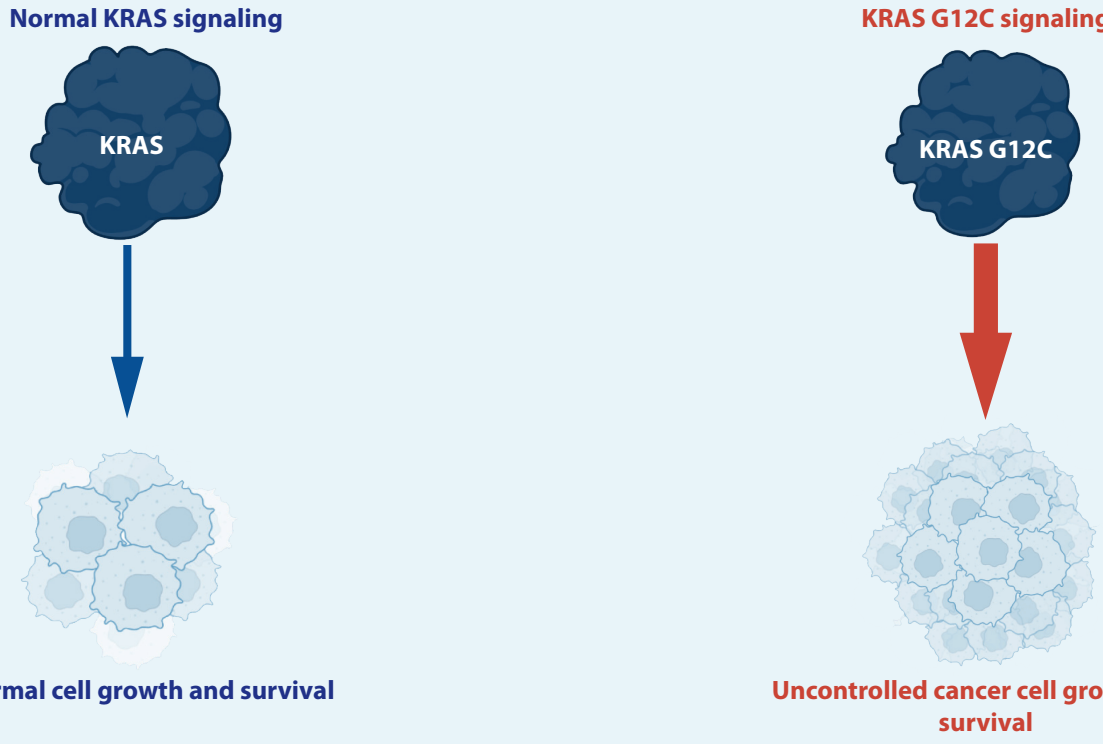
The *KRAS* G12C gene **mutation** is the most common *KRAS* mutation found in patients with non-small-cell lung cancer, occurring in about 13% of these patients.

Patients do not have many options if chemotherapy does not fully treat the cancer.

- Patients with advanced non-small-cell lung cancer typically have worsening of cancer after approximately 2–5 months of treatment
- Only about 14% of patients with this form of cancer survive for 2 years

What medicine was tested?

Sotorasib is a medicine that targets the mutated KRAS protein made from the mutated *KRAS* G12C gene. The *KRAS* G12C gene is found in some patients with non-small-cell lung cancer.



What was the aim of the study?

The aim of this study was to see if sotorasib was safe and if sotorasib could help patients by:

- Reducing the size of their tumors and/or preventing their cancer from worsening
- Improving survival

Who took part in the study?

All patients had non-small-cell lung cancer with a change (mutation) in the *KRAS* gene called *KRAS* G12C.
Patients who took part in the study had growing tumors despite previous treatment with systemic therapy (chemotherapy and/or anti-PD-(L)1 immunotherapy).

- Systemic therapy is treatment that travels through the bloodstream and reaches and affects cells all over the body
- Systemic therapy can be a tablet that is swallowed, a treatment injected through a needle, or a treatment infused through a needle over a longer amount of time
- Chemotherapy is a treatment that uses drugs to attack rapidly growing cells such as cancer cells
- PD-(L)1 immunotherapy is a type of treatment that boosts the immune system to identify and kill cancer cells

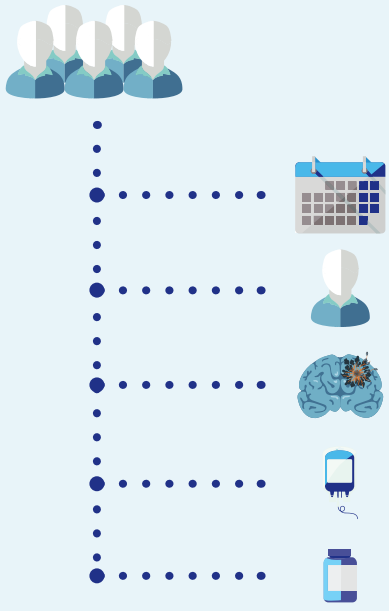
All patients in this study had **advanced *KRAS* G12C-mutated non-small-cell lung cancer**.

Tumor samples of each patient were examined in a laboratory to confirm the presence of the *KRAS* G12C mutation.

The patients in this study were **18 years or older**. Patients must previously have been **treated with at least 1 systemic therapy** and have either not responded to treatment or responded but the tumor started growing again.

174

Patients with *KRAS* G12C-mutated non-small-cell lung cancer received sotorasib.



Among the **174** included patients

The average (median) age was **65**

81% were White

23% of patients had a history of tumor spread to the brain

Patients generally had **2** or more previous treatments

83% of patients had received previous chemotherapy and PD-(L)1 immunotherapy

How was this study carried out?

Sotorasib 960 mg was given orally (by mouth) once a day.

Safety
Side effects were checked throughout the study for all patients who received at least 1 dose of sotorasib.

Anti-cancer effects of treatment
Tumors were scanned every 6 weeks for the first 8 scans, then every 12 weeks. The size of the tumor after treatment was compared with the size of the tumor before treatment started using the standard 'RECIST' approach.

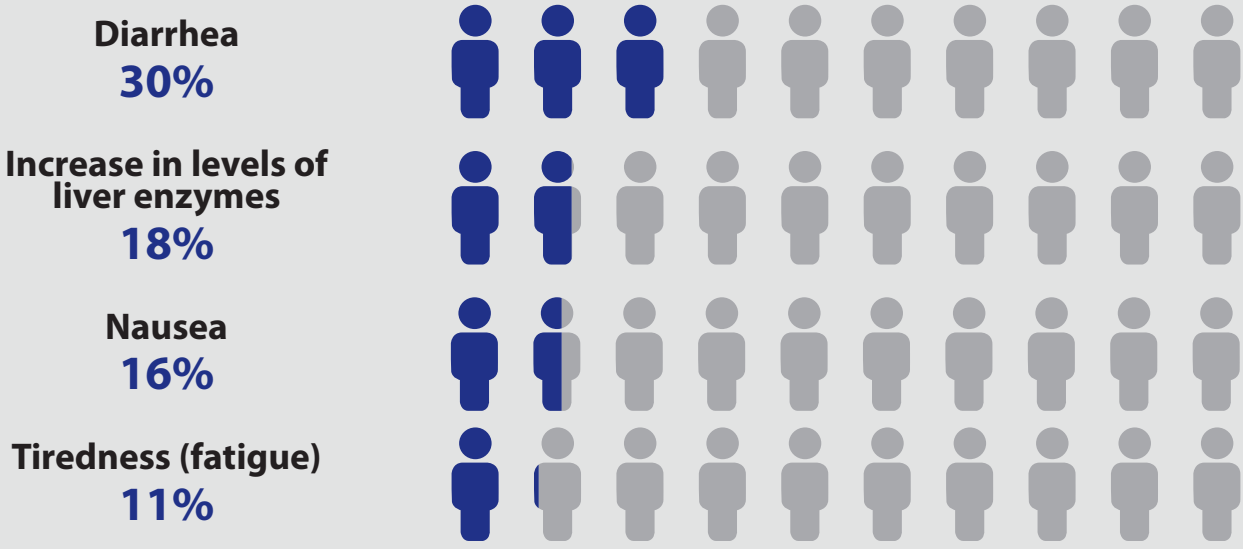
RECIST stands for Response Evaluation Criteria In Solid Tumors and is a system to measure how a tumor responds to treatment.

- First, the tumor must be able to be measured when scanned using medical scans before and after treatment
- RECIST testing then identifies patients who have:
  - Complete response: the tumor is no longer detectable
  - Partial response: the tumor has shrunk but is still detectable
  - Stable disease: there is no change in tumor size
  - Progressive disease: the tumor has grown

What were the overall results of the study?

What were the side effects?
Treatment-related side effects were seen in 70% of patients.
The most common side effects included diarrhea and increases in liver enzymes.

- An increase in liver enzymes can be a sign of liver problems

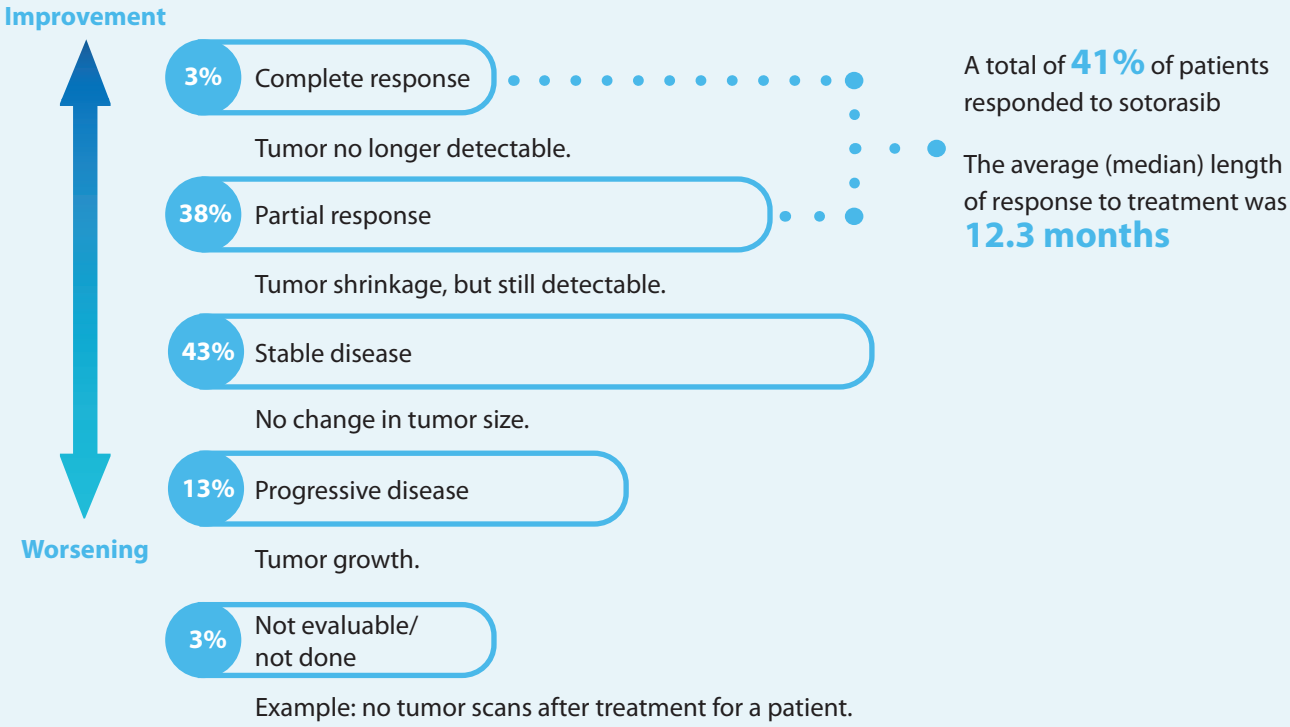


21% of patients had severe side effects.

- Severe side effects are those that limit patients' ability to look after themselves, require medical attention, or have a risk of death

22% of patients had treatment stopped for a short time or reduced, and 6% of patients stopped treatment due to side effects.
No patients died because of sotorasib or its associated side effects.

Tumor responses as measured by RECIST



On average (median), patients receiving sotorasib stayed on treatment without worsening of disease or death for:

6.3 months

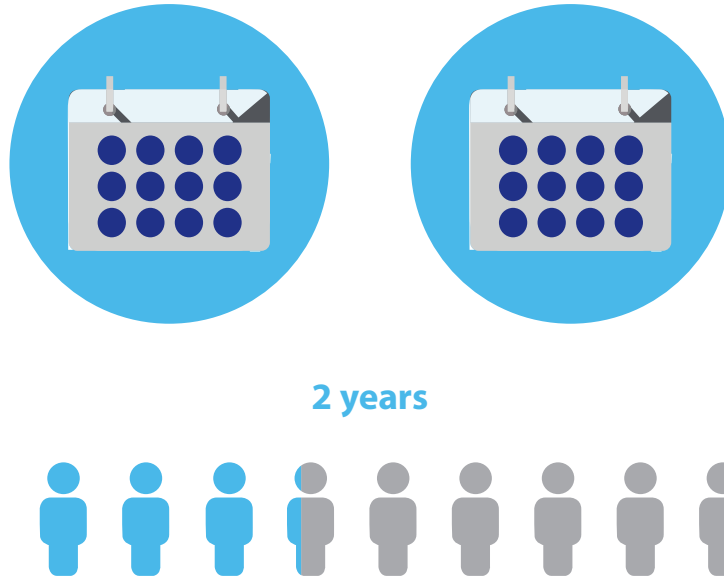
On average (median), patients receiving sotorasib survived for:

12.5 months

Long-term benefit of sotorasib

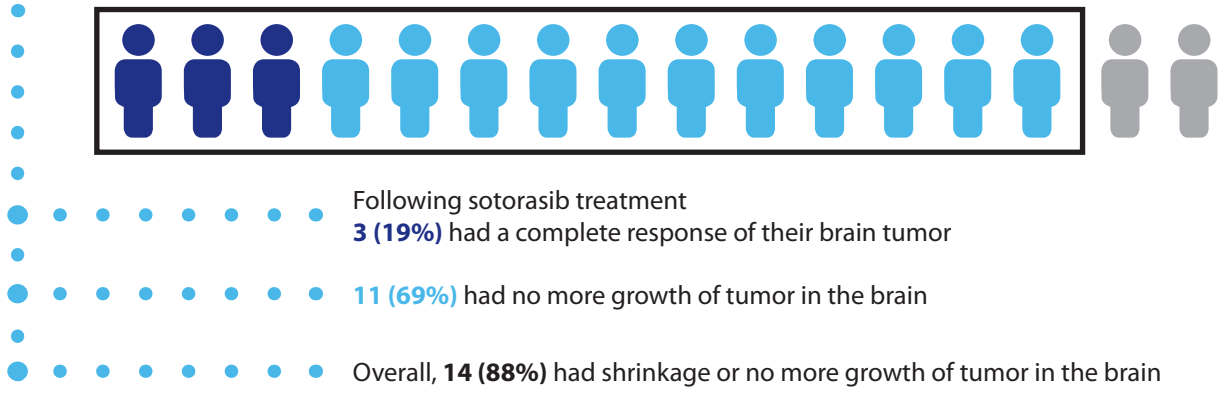
A total of 23% of patients had more than 12 months on sotorasib without worsening of disease or death (long-term benefit).

After 2 years of receiving sotorasib, a total of 33% of patients were still alive.



Patients with tumors that had spread to the brain before treatment with sotorasib.

There were 16 patients in this study who had a measurable tumor that spread to the brain before treatment with sotorasib.



What do the results of the study mean?

These results of the CodeBreaK 100 study show that side effects were manageable, and sotorasib was effective in patients with advanced non-small-cell lung cancer with a *KRAS* G12C mutation.

- Limited treatment options are available for slowing non-small-cell lung cancer growth. Therefore, these results are important
- Another study called CodeBreaK 200 is a global study that compares survival, responses, and outcomes reported by patients receiving sotorasib and for those receiving standard care. Early results from the global CodeBreaK 200 study support the benefits of sotorasib as reported in this CodeBreaK 100 study. The CodeBreaK 200 study is ongoing

Where can I find more information?

Study number: NCT03600883

Study name: CodeBreaK 100

ClinicalTrials.gov webpage for the CodeBreaK 100 study: https://www.clinicaltrials.gov/study/NCT03600883

Original article: The original article discussed in this summary entitled 'Long-term outcomes and molecular correlates of sotorasib efficacy in patients with pretreated *KRAS* G12C-mutated non-small-cell lung cancer: 2-year analysis of CodeBreaK 100' was published in the *Journal of Clinical Oncology* in April, 2023. You can read the original article here: https://ascopubs.org/doi/full/10.1200/JCO.22.02524

ClinicalTrials.gov webpage for the CodeBreaK 200 study: https://www.clinicaltrials.gov/study/NCT04303780

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Financial & competing interests disclosure

All disclosures can be found in the original article.

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