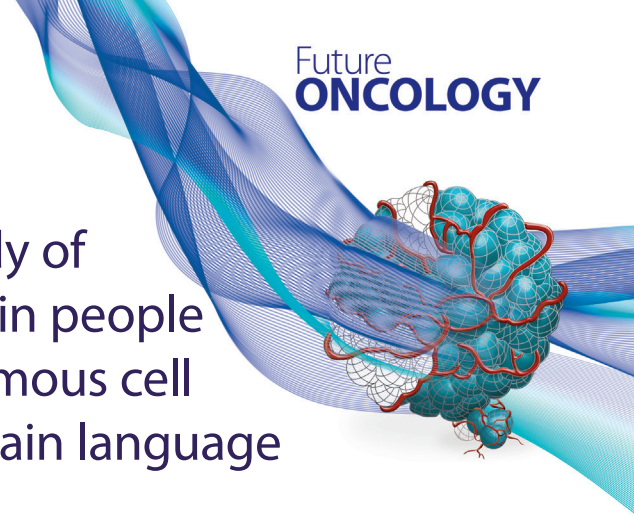
Plain Language Summary of Publication

Future ONCOLOGY



Long-term results from a clinical study of xevinapant plus chemoradiotherapy in people with high-risk locally advanced squamous cell carcinoma of the head and neck: a plain language summary

Yungan TAO[1], Xu-Shan Sun[2], Yoann Pointreau[3], Christophe Le Tourneau[4], Christian Sire[5], Kathrin Gollmer[6], Philippa Crompton[6] & Jean Bourhis[7]

[1]Department of Radiation Oncology, Institut Gustave Roussy, Villejuif, France; [2]Department of Radiation Oncology, Nord Franche-Comté de Montbéliard and CHRU de Besançon, Besançon, France; [3]Oncologie-Radiothérapie, Institut Inter-Régional de Cancérologie, Centre Jean Bernard, Le Mans, France [4]Department of Drug Development and Innovation (D3i), Institut Curie, Paris-Saclay University, Paris, France; [5]South Brittany Hospital Center, Hôpital du Scorff Radiothérapie, Lorient, France; [6]Debiopharm International, Lausanne, Switzerland; [7]CHUV, Radiation Oncology Department, Bâtiment Hospitalier, Lausanne, Switzerland

First draft submitted: 14 April 2023; Accepted for publication: 19 June 2023; Published online: 13 July 2023

Summary

What is this summary about?

Squamous cell carcinoma of the head and neck (SCCHN) is the most common type of head and neck cancer. About half of the people with locally advanced (LA) SCCHN will have surgery to remove their cancer. For people who do not have surgery, chemoradiotherapy is the standard treatment, with the aim of fully removing the cancer. However, in many people, this treatment does not completely kill the cancer. This summary presents the main results of a phase 2 study of a medicine called xevinapant, which is under investigation as a potential future medicine for people with this type of cancer.

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

- **Carcinoma:** KAR-sih-NOH-muh
- **Chemoradiotherapy:** KEE-moh-RAY-dee-oh-THAYR-uh-pee
- **Squamous:** SKWAY-mus
- **TrilynX:** TRY-links
- **Xevinapant:** zeh-VIN-uh-pant

What did the researchers want to find out?

In this study, researchers wanted to find out whether xevinapant plus chemoradiotherapy could stop the cancer from growing back or getting worse in the years after treatment completion in people with LA SCCHN. They also looked at whether people with this type of cancer had side effects from taking this medicine.

Short-term results were collected 18 months after treatment with chemoradiotherapy ended. These results showed that people who received xevinapant plus chemoradiotherapy were less likely to have their cancer grow back, or get worse in the part of the body where it was first found, than people who received liquid placebo—which looked and tasted the same as the active medicine (in this case, xevinapant), but did not contain any medicine—plus chemoradiotherapy.

Researchers then continued to collect information for a longer amount of time (at least 3 years). They wanted to see if treatment with xevinapant plus chemoradiotherapy was stopping the cancer from growing back or getting worse and helping people live longer. After this, people were monitored for a further 2 years to see if they were alive 5 years after treatment.

What were the main findings of the study?

The results showed that people with this type of cancer who were treated with xevinapant plus chemoradiotherapy were less likely to die, lived longer on average, and were less likely to have their cancer get worse. A phase 3 study, named TrilynX, in a larger group of people, is currently taking place to confirm the results of this study.

Future Medicine part of fsg

Who should read this article?

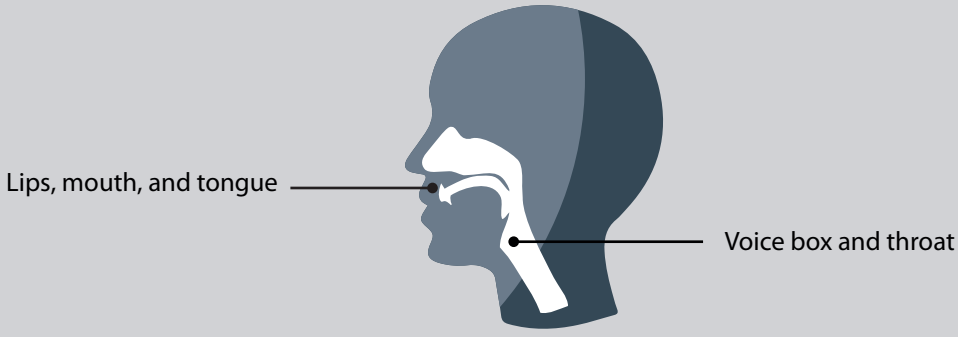
People with LA SCCHN, their families and caregivers, patient advocates, and healthcare professionals, including those who are helping people learn more about new treatments for this type of cancer.

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

This plain language summary summarizes the findings presented in the original article:
Extended follow-up of a phase 2 trial of xevinapant plus chemoradiotherapy in high-risk locally advanced squamous cell carcinoma of the head and neck: a randomised clinical trial.

What is locally advanced squamous cell carcinoma of the head and neck and how is it treated?

Head and neck cancer is the eighth most common type of cancer in the world. The most common type of head and neck cancer is called squamous cell carcinoma of the head and neck (SCCHN). SCCHN includes cancers of the lips, mouth, tongue, throat, and voice box. It is called "locally advanced" (LA) when it has spread to nearby areas but not to other parts of the body.



For many people with this type of cancer, surgery to remove the cancer is not possible or not the best treatment option. The standard treatment for these people is called chemoradiotherapy, and it aims to fully remove the cancer. However, the treatment may not completely remove the cancer or may not work at all. For this reason, new treatment options are needed.

What is xevinapant?

A drug called xevinapant is a new potential cancer treatment. It is a liquid that is taken by mouth or feeding tube. It can be given with chemoradiotherapy with the aim of making the chemoradiotherapy work better against the cancer.

What is chemoradiotherapy?

Chemoradiotherapy is a combination of two treatments (chemotherapy and radiotherapy) used to kill the cancer or stop it from getting worse.

What did the study look at?

The **phase 2** study looked at xevinapant plus chemoradiotherapy to treat people with LA SCCHN. People who took part in the study were treated with either:

- Xevinapant plus chemoradiotherapy, or
- **Placebo** plus chemoradiotherapy

Phase 2: A type of clinical study that provides information about whether a new treatment will be safe and effective in patients with the same type of cancer: in this case, testing xevinapant in patients with LA SCCHN.

Placebo: An inactive substance that looks and tastes the same as a medicine, but does not contain any medicine.

Researchers aimed to answer the following questions:

- How many people's cancer did not grow back or get worse in the part of the body where it was first found?
- How many people were still alive without their cancer getting worse?
- How many people were still alive without their cancer getting worse in the group of people whose cancer had shrunk or disappeared at first with treatment?
- How many people were still alive at the end of the study?
- How many people had late side effects that happened 30 or more days after treatment ended, what were they, and how many of these side effects were severe?

Who took part in the study?

People who took part in the study:

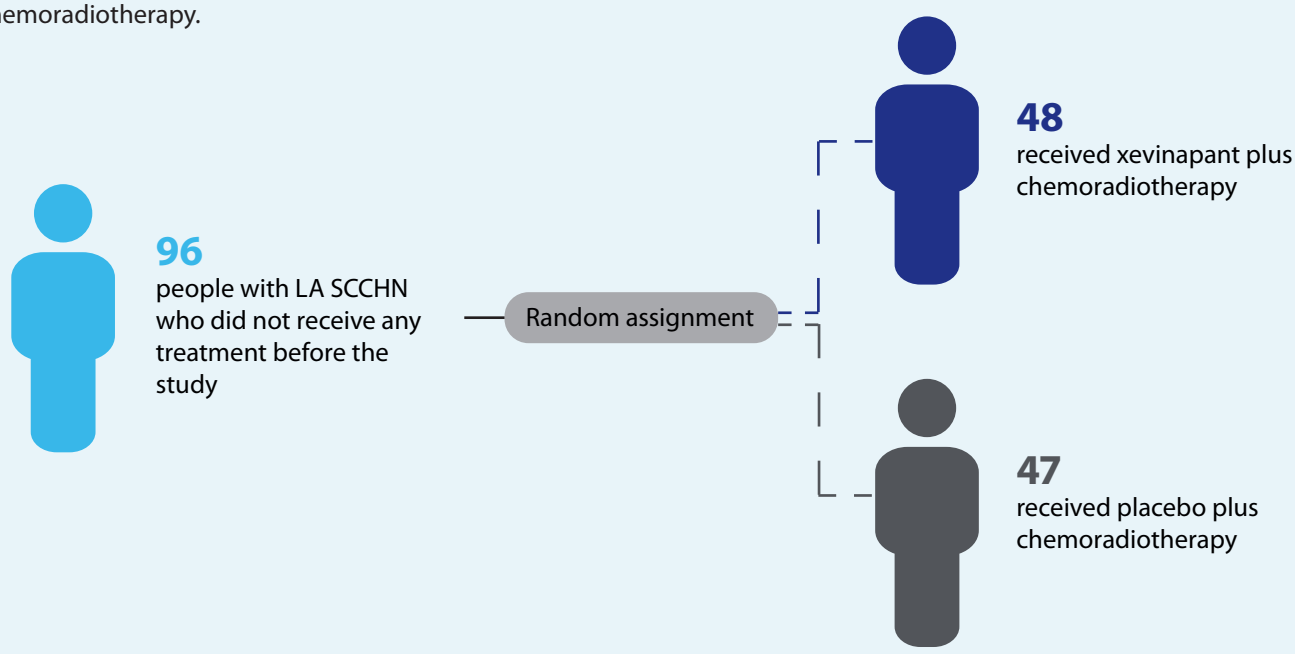
- Were aged 18–75 years
- Had LA SCCHN
- Were either fully active or were unable to do hard physical activity but could do light work
- Had not had surgery or treatment for this cancer
- Were not receiving any other treatments for their cancer during the study

Where did the study take place?

The study took place in France and Switzerland at 19 hospitals.

How was the medicine given?

In this study, people were randomly assigned to receive either xevinapant plus chemoradiotherapy or placebo plus chemoradiotherapy.



- People with LA SCCHN took xevinapant (or placebo) every day for 14 days and then stopped for the next 7 days. This was repeated 3 times
- Chemotherapy was given as an injection into a vein once every 3 weeks. This was done 3 times
- Radiotherapy (low doses of radiation) was given 5 days per week for 7 weeks

To reduce bias, neither the doctors nor the people in the study knew who had received xevinapant or placebo until the end of the study. One person who was scheduled to receive placebo plus chemotherapy did not receive any treatment.

What were the results of the study?

The first results were collected 18 months after treatment with chemoradiotherapy ended. Many people included in this study were heavy smokers with high alcohol use and had cancer that was negative for a certain type of virus (human papillomavirus), which usually makes their treatment outcomes poorer than those of patients who do not smoke or have a cancer that is positive for human papillomavirus. These results showed that fewer people who received xevinapant plus chemoradiotherapy had their cancer grow back or get worse in the part of the body where it was first found than people who received placebo plus chemoradiotherapy.

In both groups, the **side effects** that people had were manageable. A similar number of people in both groups had side effects that happened 30 or more days after treatment ended.

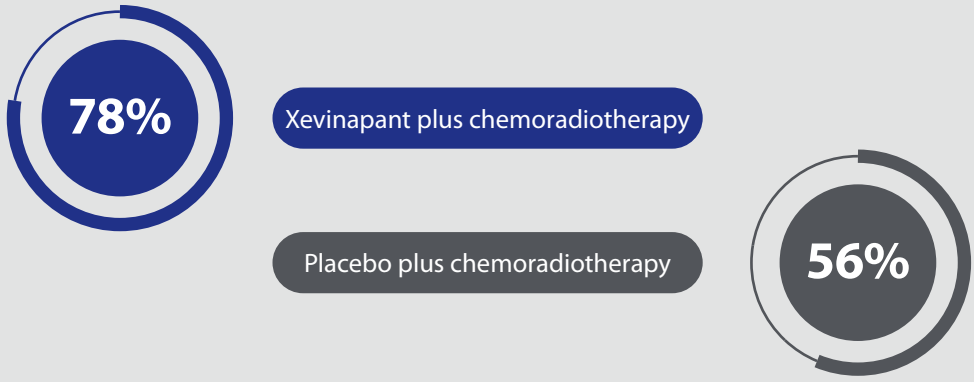
Side effects: Undesired effects of a drug that can range from mild to severe.

Researchers continued to collect information for a longer amount of time (at least 3 years). They wanted to see if xevinapant plus chemoradiotherapy was stopping the cancer from getting worse and helping people live longer.

Researchers monitored people for 2 more years to see if they were still alive.

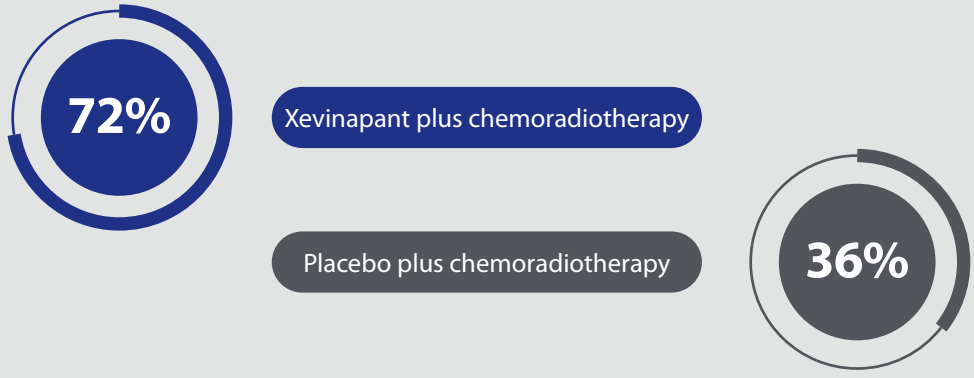
See the answers to the researchers' questions below:

1. **Over at least 3 years, how many people's cancer did not grow back or get worse in the part of the body where it was first found?**



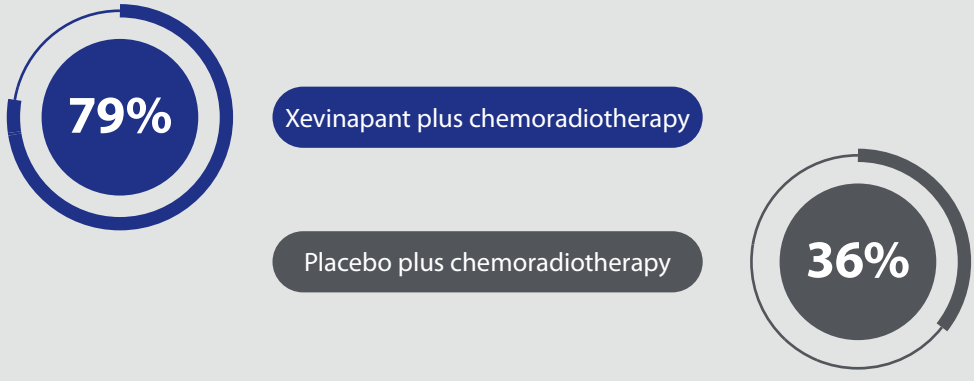
People who received **xevinapant plus chemoradiotherapy** were **54% less likely** to have their cancer grow back or get worse in the part of the body where it was first found than people treated with **placebo plus chemoradiotherapy**.

2. **Over at least 3 years, how many people were still alive without their cancer getting worse?**



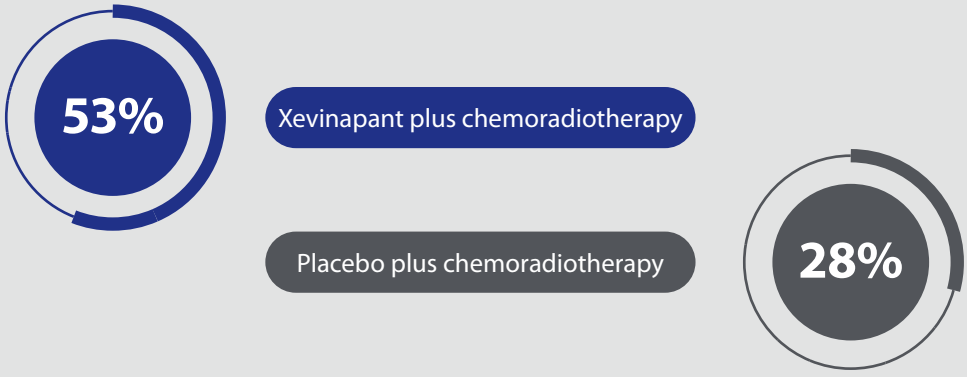
People who received **xevinapant plus chemoradiotherapy** were **67% less likely** to die or have their cancer get worse than people who received **placebo plus chemoradiotherapy**.

3. **In the group of people whose cancer had shrunk or disappeared at first with treatment, how many people were still alive without their cancer getting worse over at least 3 years? This was measured from when the cancer first shrunk or disappeared.**



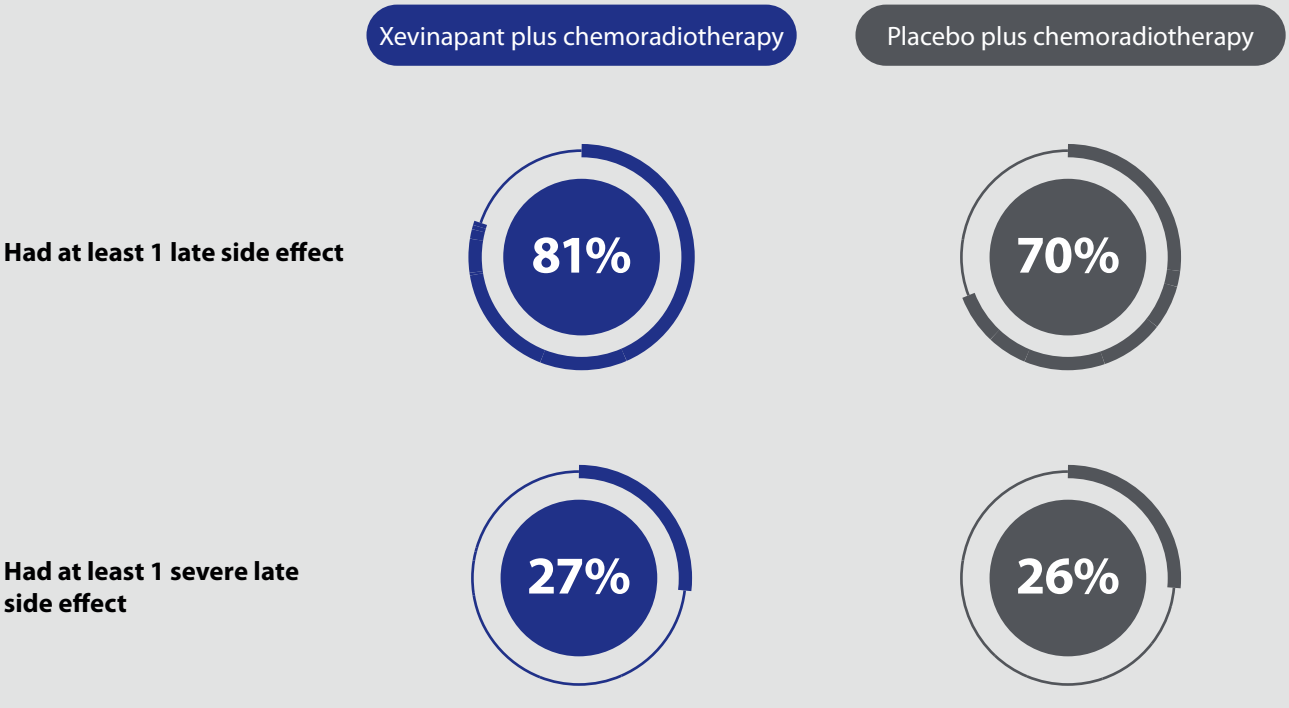
When people whose cancer shrunk or disappeared at first with treatment had received **xevinapant plus chemoradiotherapy**, they had a **79% lower risk** of their cancer getting worse or dying than people treated with **placebo plus chemoradiotherapy**.

4. At 5 years, how many people were still alive?



Over 5 years of follow-up, people who were treated with **xevinapant plus chemoradiotherapy** were more than **twice as likely** to be alive than people who were treated with **placebo plus chemoradiotherapy**.

5. How many people had late side effects that happened 30 or more days after treatment ended, what were they, and how many of these side effects were severe?



Severe side effects: Side effects that limit someone's ability to take care of themselves, need hospital treatment, or have a risk of death.

Most common late side effects that happened 30 or more days after treatment ended:

	Xevinapant plus chemoradiotherapy	Placebo plus chemoradiotherapy
Dry mouth:	35% Severe in 6%	26% Severe in 4%
Change in taste:	17% Severe in 2%	13% Severe in 4%
Difficulty swallowing:	13% Severe in 6%	13% Severe in 6%
Thickening and scarring of body tissue:	13% Severe in 0%	13% Severe in 2%

What do the results of the study mean?

- Over at least 3 years, people treated with xevinapant plus chemoradiotherapy were less likely to die or have their cancer get worse
- Over 5 years of follow-up, xevinapant plus chemoradiotherapy more than halved the risk of dying compared with placebo plus chemoradiotherapy
- A similar number of people in both treatment groups had any side effects and severe side effects that happened 30 or more days after people stopped receiving treatment

This study in 96 people found that more people who received xevinapant plus chemoradiotherapy lived longer without their cancer getting worse or dying than people who received placebo plus chemoradiotherapy. This is the first study in more than 20 years to show improved treatment outcomes in people with LA SCCHN by adding a new treatment to the standard treatment, chemoradiotherapy.

What are the next steps?

- The results of this study suggest that xevinapant could be used with chemoradiotherapy in the future to improve treatment outcomes
- Researchers are now studying xevinapant plus chemoradiotherapy in a larger **phase 3** study of around 700 people. Researchers hope that this new study, called TrilynX, will confirm the results of this smaller study

Phase 3: A type of clinical study that compares new treatments with the best currently available treatment and often involves more patients than earlier phase studies.

Where to find out more information

For more information on this study, please visit:
ClinicalTrials.gov trial number NCT02022098

For more information on the new phase 3 TrilynX study, please visit:
ClinicalTrials.gov trial number NCT04459715

You can read more about head and neck cancers at the following website:
https://www.cancer.net/cancer-types/head-and-neck-cancer

Patient guidelines on head and neck cancers from the National Comprehensive Cancer Network and European Society of Medical Oncology are available at:
https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1437
https://www.esmo.org/guidelines/guidelines-by-topic/head-and-neck-cancers

Acknowledgments

The authors of this article thank the people who participated in this study and their families, as well as the investigators, co-investigators, and staff at each of the clinical sites.

Financial & competing interests disclosure

Full author disclosure information can be found in the original article. Writing support for this summary was provided by Jamie Ratcliffe of Clinical Thinking and funded by Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945).

This study was sponsored by Debiopharm International, Lausanne, Switzerland. In March 2021, Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945) gained exclusive rights to develop and commercialize xevinapant worldwide (https://www.merckgroup.com/en/news/xevinapant-01-03-2021.html).

Disclaimer

Xevinapant is not yet approved to treat any condition. This summary reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.