

An open-label extension of 2 identical studies called POLYP 1 and POLYP 2, which compared Xolair® with placebo in people with nasal polyps who have ongoing inflammation of the nose and sinuses

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a study in this document), written for:

- Members of the public; and
- People who took part in the study.

This summary is based on information known at the time of writing (November 2020). More information may now be known.

The study started in March 2019 and ended in March 2020. This summary presents the full results of the study up until it ended in March 2020.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about soft growths inside the nose (called nasal polyps) and the study medicine, called Xolair®.

Key information about this study

- This study was done to assess a medicine (called the study medicine, or more specifically, Xolair®) in people with nasal polyps who have ongoing swelling of the sinuses and inside of the nose.
- This type of study is known as an open-label extension study. This type of study is sometimes available after a clinical study has ended. People from the original study may choose to take part in the open-label extension and continue receiving the study medicine.
- This study included 249 people. They had previously completed 1 of 2 earlier trials of the study medicine (called Xolair®) vs a placebo, which looks like the study medicine but has no medicine-related effect on the body. In this summary, these earlier trials are called the original studies.
- People in this study received 28 weeks of treatment with Xolair®, regardless of the treatment they received in the original studies.
- After 28 weeks, the researchers followed people for an additional 24 weeks. People did not receive Xolair® during this time.
- Compared with shorter-term treatment in the original studies, people receiving Xolair® for an extended period of time in this study:
 - Had continued improvement in their nasal congestion;
 - Had reduced nasal polyp size;
 - Had continued improvement in their well-being;
 - Were less affected by their symptoms.
- Once people stopped receiving treatment with Xolair®, their nasal polyp scores and nasal congestion scores gradually worsened. However, their scores stayed lower than before they had received Xolair®.
- The nasal congestion and nasal polyp sizes of people who had received Xolair® for the first time during this study quickly improved with Xolair®. These improvements were similar to those of patients who received Xolair® for the first time in 1 of the original studies.
- Overall, Xolair® was well tolerated in this open-label extension study. Safety was consistent with our understanding of the safety of Xolair® for other conditions (such as asthma and hives).

1. General information about this study

Why was this study done?

Nasal polyps are soft, painless growths inside the nose. Nasal polyps can develop in people who have long-term swelling (also called inflammation) of the nose and sinuses, called chronic rhinosinusitis. Sinuses are a connected system of hollow spaces in the bones of the skull and face. They produce mucus to keep the inside of the nose moist. Over time, if the swelling does not improve, some people develop nasal polyps.

People with nasal polyps can have symptoms such as:

- A blocked-up or stuffy nose (also called nasal congestion);
- Runny nose;
- Reduced ability to smell;
- A thick yellow or green mucus discharge from the nose;
- Cough;
- Sinus pressure or facial pain.

Current medicines for people with nasal polyps aim to reduce swelling and symptoms. These treatments usually include steroid nasal sprays, steroid pills, and antibiotics. However, many people continue to have symptoms that interfere with their daily lives, and better medicines are needed. Some people need surgery to remove nasal polyps, but this is not a permanent solution because the polyps often return.

Scientists have found that the swelling in nasal polyps is similar to that seen in asthma, a condition where the airways are sensitive and become inflamed. Because the swelling is similar, scientists are testing existing asthma medicines, such as Xolair[®], to see if they can also help people with nasal polyps. This study in particular examined the longer-term safety and reduction of swelling and symptoms when using Xolair[®] in patients with nasal polyps.

What is the study medicine?

A medicine called Xolair® (also known as omalizumab) was the focus of this study. Xolair® has previously been approved to treat asthma since 2003 and longer-term hives (a condition called chronic idiopathic/spontaneous urticaria) since 2014.

- For Xolair®, you say this as “zoll – air.”
- For omalizumab, you say this as “om – mah – liz – yoo – mab.”
- Xolair® is a type of protein called an antibody. It works by sticking to and blocking a second antibody, called IgE. IgE normally causes allergic symptoms and allergic swelling. When Xolair® blocks IgE, this can reduce allergic symptoms and allergic swelling.
- Xolair® is given as an injection just below the skin every 2 or 4 weeks.

In the identical original studies (called POLYP 1 and POLYP 2), Xolair® was compared with a placebo.

- You say this as “plah – see – bo.”
- The placebo looked like Xolair® but did not contain any real medicine. This means it had no medicine-related effect on the body.
- The placebo was injected under the skin just like Xolair®.
- In the original studies, researchers compared Xolair® with a placebo to look at the benefits and/or side effects of the medicine.

What did researchers want to find out?

Researchers did this study to look at the effects of Xolair® in people with nasal polyps for a period of time after the original studies (called longer-term in this document). They wanted to see if the medicine continued to improve nasal polyp size and related symptoms.

Researchers also looked at how long the beneficial effects of taking Xolair® last after people stop taking the medicine (see section 4 “What were the results of the study?”).

They also wanted to find out how safe the medicine was by checking how many people had side effects when taking Xolair® longer term during this study (see section 5 “What were the side effects?”).

The main questions that researchers wanted to answer were:

1. Did people continue to show improvement in nasal congestion and nasal polyp size after longer-term treatment with Xolair®?
2. Once people stopped receiving Xolair® during the follow-up period (see section 3 for more information about the follow-up period) of the study, how long did the benefits of treatment last for?
3. How did the nasal congestion and nasal polyp size of people who received placebo in the original studies respond when they received Xolair® for the first time during this study?

Other questions that researchers wanted to answer included:

4. Did people with nasal polyps have a continued improvement in their well-being after longer-term Xolair® treatment?
5. Did people who took longer-term Xolair® have any side effects, and if so, what were they? And did people taking Xolair® for the first time during this study have any side effects?

What kind of study was this?

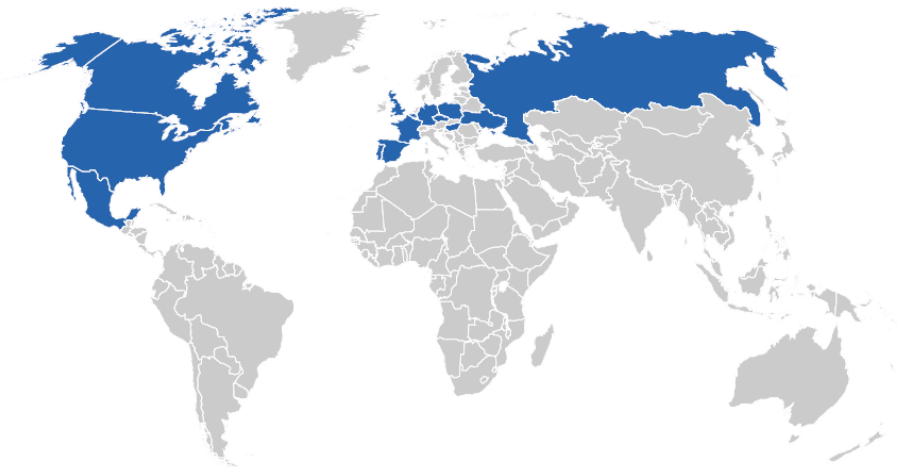
This was an open-label extension study. This means that people who had taken part in a previous study (called the original studies) continued taking the study medicine. Researchers wanted to look at how safe Xolair[®] was longer term. They also wanted to see how peoples' bodies coped with Xolair[®] in the longer term. Because this was an open-label study, both the people taking part and the study doctors knew that the participants were receiving Xolair[®], compared with the original studies in which people could have received Xolair[®] or placebo.

When and where did the study take place?

This study started in March 2019 and ended in March 2020. This summary presents the full results of the study up until it ended in March 2020.

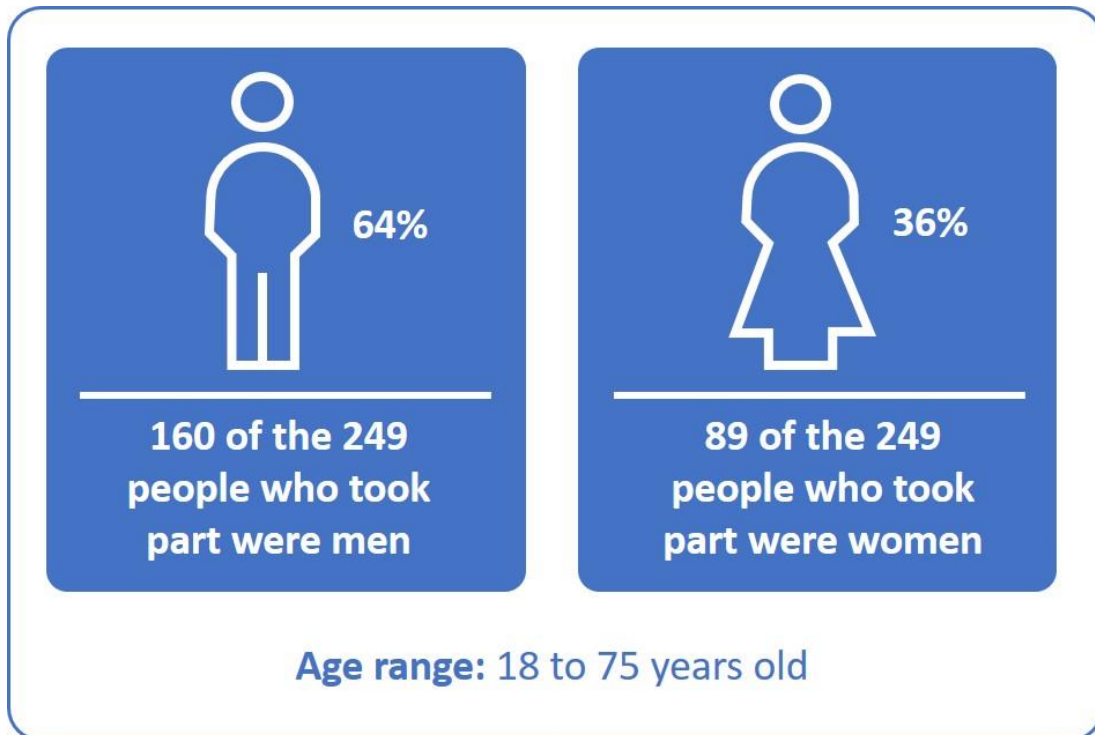
The study took place at 79 study centers across 14 countries in North America and Europe. The following map shows the countries where this study took place.

- Belgium
- Canada
- Czech Republic
- France
- Germany
- Hungary
- Mexico
- Poland
- Portugal
- Russia
- Spain
- Ukraine
- United Kingdom
- United States



2. Who took part in this study?

In this study, 249 people with nasal polyps who completed either of the original studies took part. More information on the people who took part is given below.



People **could** take part in the study if they had:

- Completed 1 of the original studies. This included having examinations at the end of the study, such as a procedure where an instrument with a camera was inserted into the nose to assess the severity of their nasal polyps (called video nasal endoscopy). They had these examinations without stopping their medicine. For additional information regarding the original studies, see section 8 “Where can I find more information?”
- Reported their symptoms in an electronic diary (or eDiary for short), which was a tablet computer provided to each participant at the start of the original studies, for at least 4 out of 7 days in the week before the end of the original study.

People **could not** take part in the study if they had any of the following:

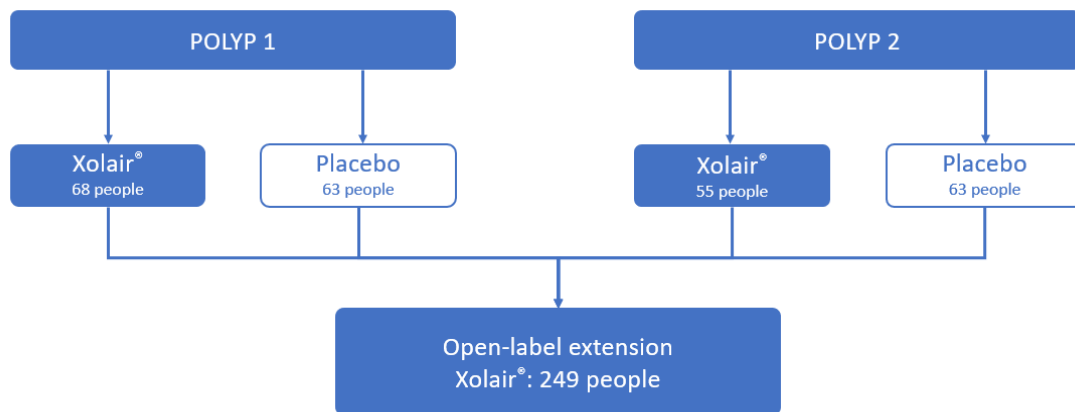
- A previous allergic reaction to Xolair® in either of the original studies;
- Severe nose bleeds during either of the original studies;
- A serious medical condition or abnormality in test results that doctors thought could make it unsafe for the person to take part in the study.

3. What happened during the study?

During this study, people received Xolair® regardless of the treatment they received when they took part in 1 of the original studies.

At the end of the original studies, a total of 249 people chose to take part in this open-label extension study:

- 131 people from the POLYP 1 study:
 - 68 people who had previously received Xolair®;
 - 63 people who had previously received placebo.
- 118 people from the POLYP 2 study:
 - 55 people who had previously received Xolair®;
 - 63 people who had previously received placebo.



Treatment in this study involved:

- **Xolair®** (the study medicine) – injected under the skin once every 2 or 4 weeks for a total of 28 weeks during the study’s treatment period. The dose was 150 – 600 mg, depending on a person’s body weight and amount of IgE in the blood.
- **Nasal steroid spray** – a standard medicine for nasal polyps that patients started receiving in the original studies and continued daily during this study.

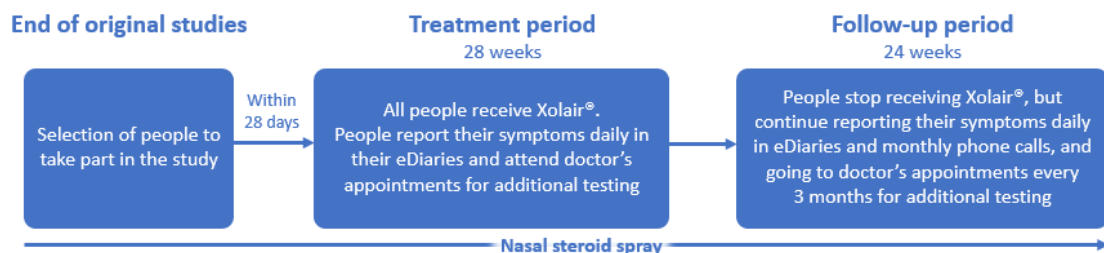
People were given an eDiary to rate their nasal congestion each morning. They recorded their response to the question “is your nose blocked?” as either not at all (score of 0), mild (score of 1), moderate (score of 2), or severe (score of 3).

Researchers also looked at whether people had a reduction in their nasal polyp score during the study. To find out the nasal polyp score, researchers measured the size of peoples’ polyps using an instrument with a camera placed in the nose.

After 28 weeks of treatment, everyone stopped receiving Xolair®. They still had doctor’s appointments for 24 more weeks during the study’s follow-up period. People continued using the nasal steroid spray during the follow-up period of this study.

During the follow-up period, people were asked to continue entering their nasal symptoms in their eDiaries daily. People completed a phone interview to report their nasal symptoms every month. They also returned to the doctor’s office every 3 months for additional tests of their blood and nasal symptoms to see how their body was responding to the medicine.

The study is now completed, so no more people are receiving the study medicines. Look below to see more information about what happened in the study.



4. What were the results of the study?

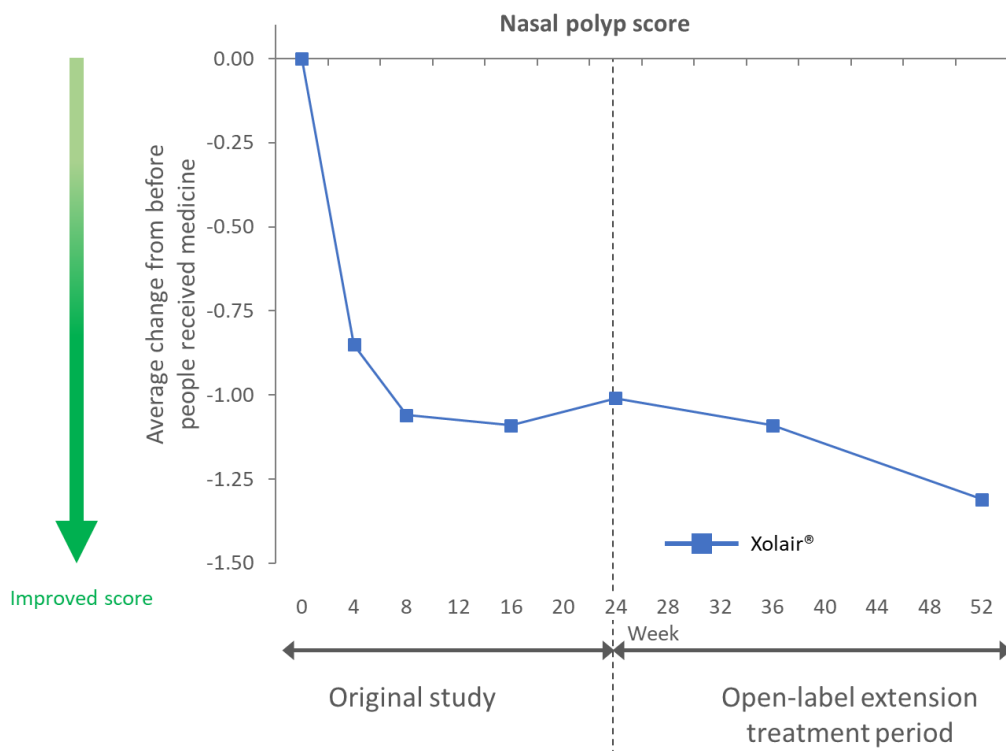
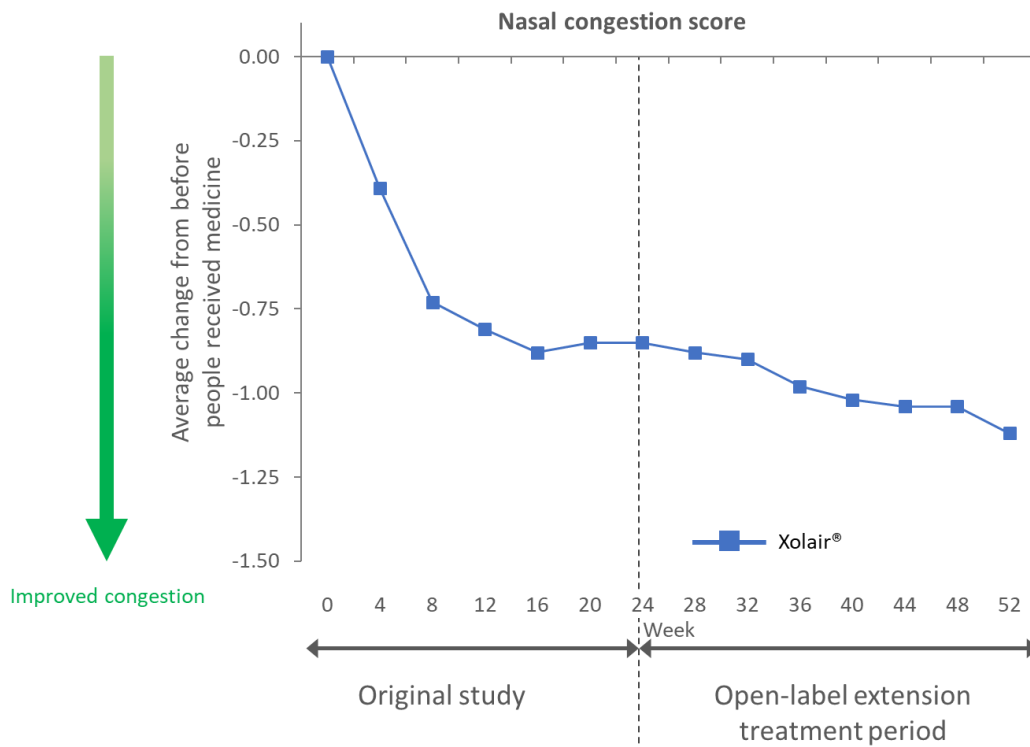
Question 1: Did people continue to show improvement in nasal congestion and nasal polyp size after longer-term treatment with Xolair®?

People rated their nasal congestion each morning in their eDiary. They recorded their response to the question “is your nose blocked?” as either not at all (score of 0), mild (score of 1), moderate (score of 2), or severe (score of 3). The researchers looked at the change in nasal congestion over the study. They compared the average daily score at the end of each month with the score at the start of the original studies before people received any treatment.

Researchers measured the size of peoples’ polyps using an instrument with a camera placed in the nose to find out their nasal polyp score during the study. They recorded peoples’ nasal polyp scores every 12 weeks and compared these with their scores before treatment.

Researchers looked at these results for people who received Xolair® during the shorter original studies and the extra 28-week treatment period of this study. This helped them to determine the longer-term benefits of the medicine.

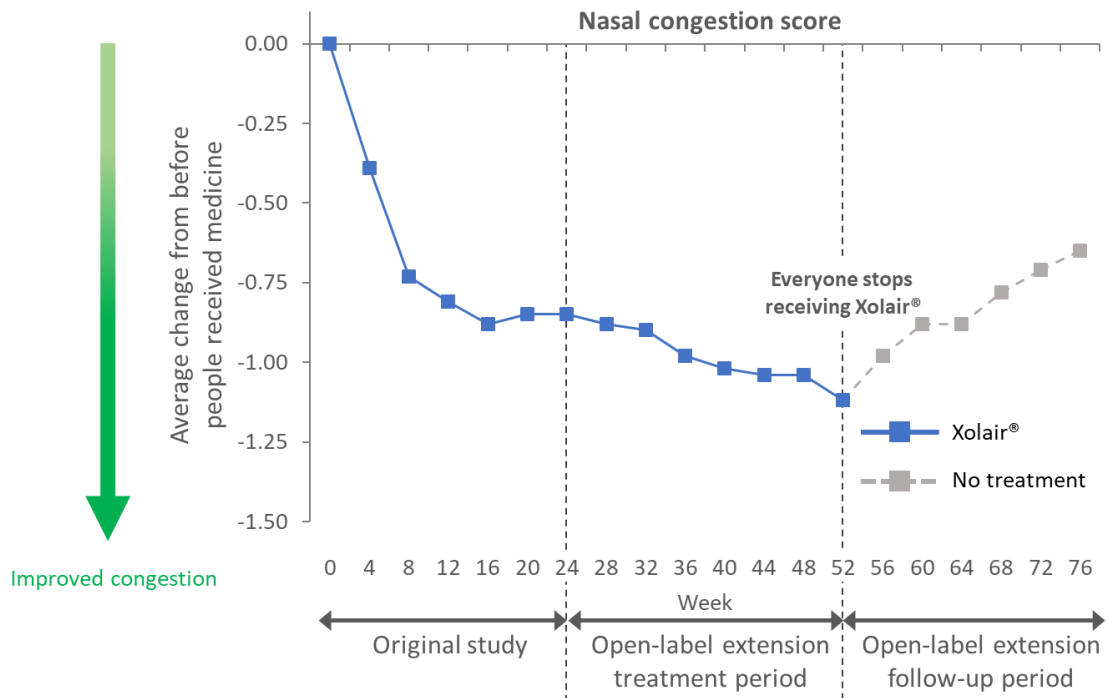
On average, people showed continued improvement in their nasal congestion and nasal polyp size with longer-term Xolair® treatment during the open-label extension treatment period.

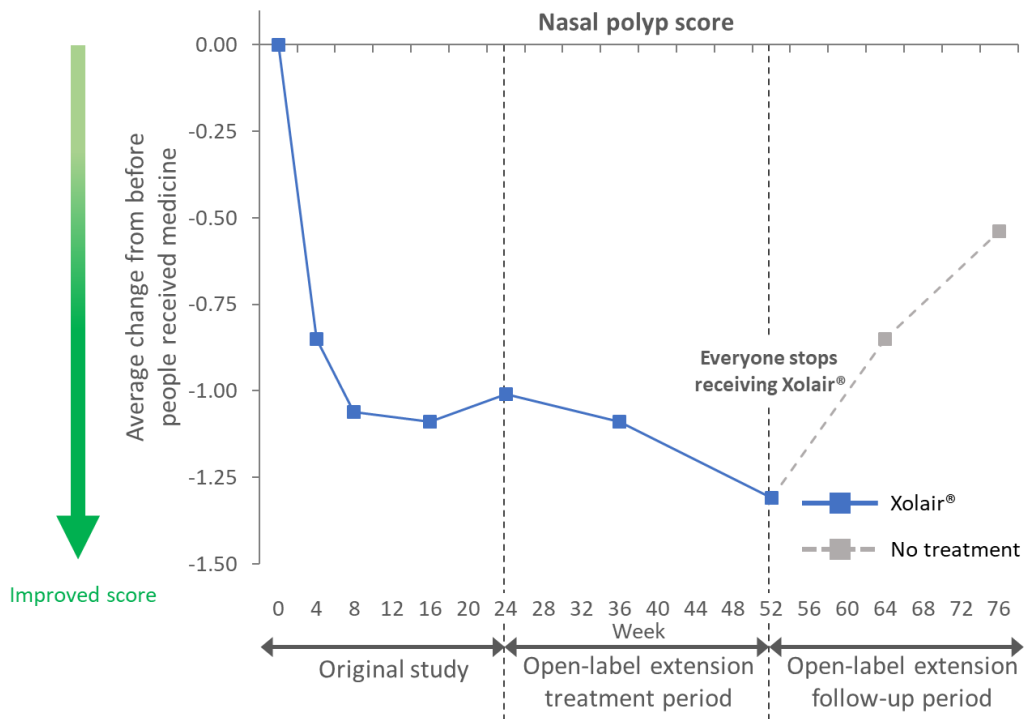


Question 2: Once people stopped receiving Xolair® during the follow-up period of the study, how long did the benefits of treatment last for?

The researchers compared peoples’ nasal polyp scores and nasal congestion scores during the follow-up period with their scores at the end of the treatment period. They wanted to see how the scores changed once treatment stopped.

On average, people gradually worsened in nasal congestion and nasal polyp size once they stopped treatment (gray squares). However, their scores are still improved compared to before they started Xolair®.



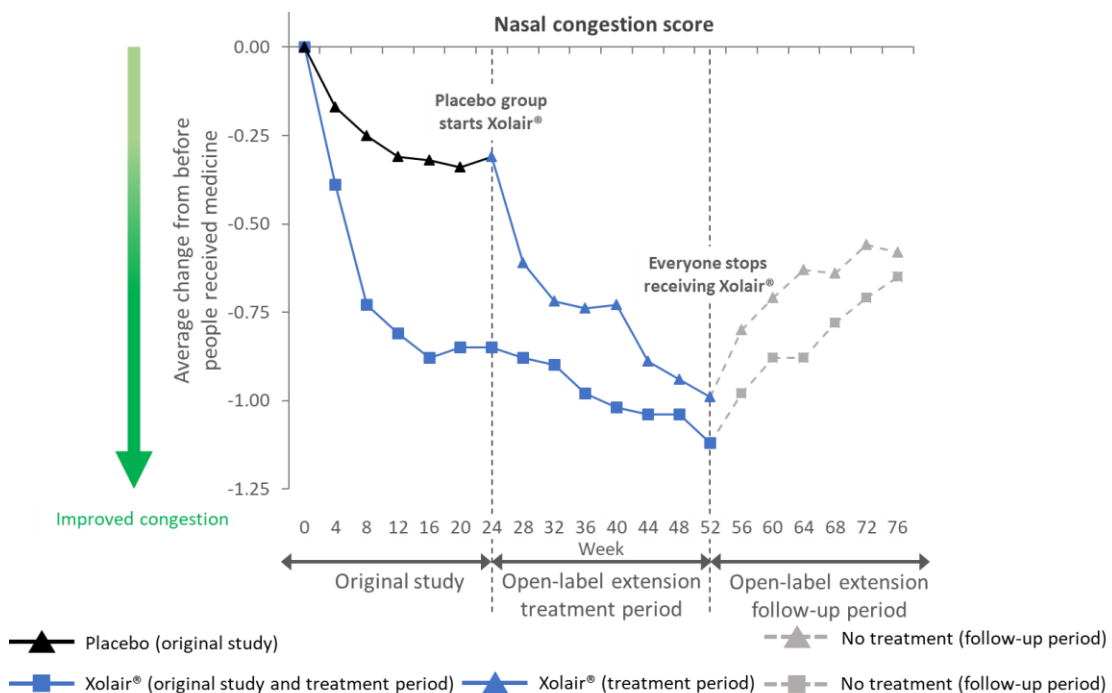


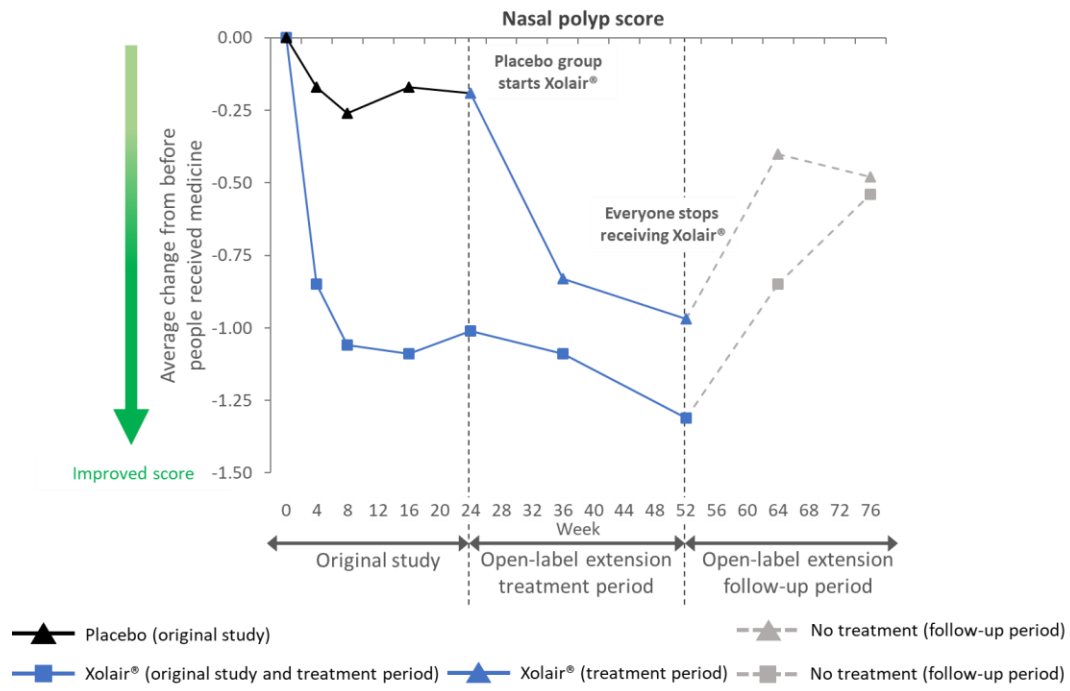
Question 3: How did the nasal congestion and nasal polyp size of people who received placebo in the original studies respond when they received Xolair® for the first time during this study?

Half of the people receiving Xolair® during the treatment period of this study had previously received placebo in their original study. The other half of the people received Xolair® during their original study and during this study. Researchers looked at the nasal congestion scores and nasal polyp scores of these 2 groups to compare the benefits of longer-term Xolair® treatment with the benefits for first-time users.

- On average, people who received Xolair® for the first time during the treatment period of this study (blue triangles) had quick improvements in nasal congestion and nasal polyp size.
- This quick improvement was similar to the people who received Xolair® for the first time during the original studies (blue squares).
- At 52 weeks, people who received longer-term Xolair® (blue squares) generally had improved congestion and nasal polyp scores when compared to people who received Xolair® for the first time during this study (blue triangles).

People saw improvements in nasal congestion and nasal polyp size regardless of when they began treatment.



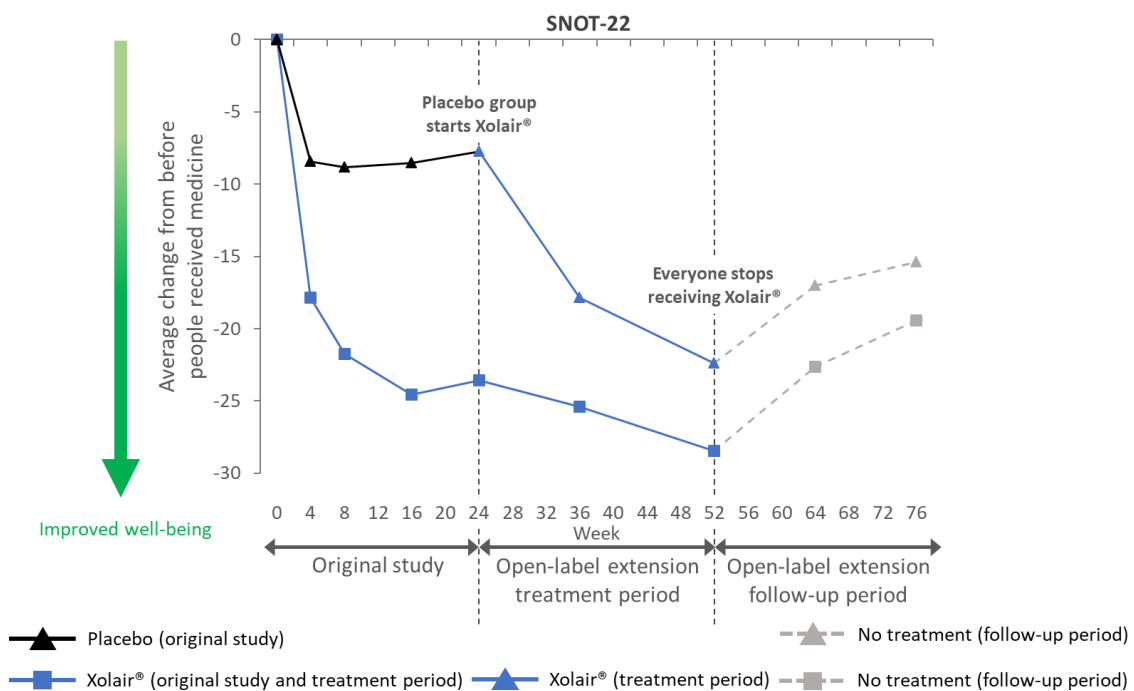


Question 4: Did people with nasal polyps have a continued improvement in their well-being after longer-term Xolair® treatment?

Researchers asked people about their well-being at their clinic visits during this study using a 22-item questionnaire called the Sino-Nasal Outcome Test (SNOT-22 for short). On the questionnaire, people rated the impact their nasal polyps had on their nasal symptoms, ear and face symptoms, sleep symptoms, and emotional symptoms over the previous 2 weeks. Each symptom was rated as either no problem (score of 0), very mild problem (score of 1), mild or slight problem (score of 2), moderate problem (score of 3), severe problem (score of 4), or problem as bad as it can be (score of 5). The researchers calculated people's total scores at each clinic visit and compared that score with their total score before they received treatment to determine the change in well-being from the start of the study. A decrease in score indicates an improvement in symptoms and well-being.

- People who received Xolair® during the original studies (blue squares) had continued reduction in the impact of symptoms on their well-being during the treatment period of this study.
- People who received placebo during the original studies (blue triangles) had considerable reduction in the impact of symptoms on their well-being after receiving Xolair® for the first time during the treatment period of this study.
- When people stopped receiving Xolair® during the follow-up period of this study, their symptoms gradually worsened regardless of how long they had received treatment (gray triangles and squares). However, their symptoms and scores are still improved compared to before they started Xolair®.

People typically reported improved well-being during the treatment period of this study. This was regardless of whether they had received Xolair® in the original studies.



5. What were the side effects?

Side effects (also known as adverse reactions) are unwanted medical problems (such as a headache) that happen during the study.

During this study, no patient taking Xolair[®] experienced a serious side effect related to the medicine. One person stopped taking Xolair[®] due to itchiness (called pruritus) related to the medicine. One person was diagnosed with cancer of the prostate, which was not considered related to Xolair[®] treatment. One person was diagnosed with autoimmune hepatitis, which was not considered related to Xolair[®] treatment.

There were no unwanted events that occurred in more than 5% of people during the treatment period of this study. The most frequent event was nasopharyngitis (swelling of the nose and throat), which occurred in 12 (4.8%) people in this study.

Overall, Xolair[®] was well tolerated in this study. Safety was similar to our understanding of the safety of Xolair[®] for other diseases (such as asthma and hives).

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from an open-label extension study of 249 people with nasal polyps who have previously completed either the POLYP 1 or POLYP 2 trials. The results are helping researchers learn more about nasal polyps and Xolair[®].

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.

7. Are there other studies taking place or planned?

The current study started in March 2019 and ended in March 2020. This summary includes the main results of the study up until it ended in March 2020. At the time of writing this summary (November 2020), the study has been completed and no more information is being collected.

No other studies of Xolair[®] for the treatment of nasal polyps are currently planned.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

- <https://clinicaltrials.gov/ct2/show/NCT03478930>
- <https://ichgcp.net/clinical-trials-registry/NCT03478930>

You can find more information about the original POLYP 1 and POLYP 2 studies on the websites listed below:

- <https://clinicaltrials.gov/ct2/show/NCT03280550>
- <https://clinicaltrials.gov/ct2/show/NCT03280537>

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

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- Contact F. Hoffman-La Roche of Basel, Switzerland, or a representative at your local Genentech (if in the US) or Novartis (if in Europe) office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., a member of the Roche Group, and Novartis Pharma AG.

Full title of the study and other identifying information

The full title of this study is: “Open-Label Extension Study of Omalizumab in Patients With Chronic Rhinosinusitis With Nasal Polyps”

The study is also known as “An Extension Study of Omalizumab in Participants With Chronic Rhinosinusitis With Nasal Polyps.”

- The protocol number for this study is: WA40169.
- The ClinicalTrials.gov identifier for this study is: NCT03478930.
- The EudraCT number for this study is: 2017-003450-16.