# Clinical Trial Results – Layperson Summary

## A study called POLYP 2 to compare 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 (December-2019). More information may now be known.

The study started in November 2017 and ended in March 2019. This summary presents the full results of the study up until it ended in March 2019.

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.

### Contents of the summary



### 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.

## Key information about this study

- This study was done to assess a medicine (the 'study medicine') in people with nasal polyps who have ongoing inflammation of the sinuses and inside of the nose.
- In this study, people received the study medicine (called 'Xolair®') or an identical dummy (called a 'placebo). It was decided by chance which medicine each person would be given.
- This study included 127 people in 10 countries.
- The study showed that people receiving Xolair® had less nasal congestion compared with people who received placebo.
- Nasal polyp size was also reduced in people receiving Xolair® compared with people receiving placebo.
- People receiving Xolair® also had improvements in their well-being and their symptoms affected them less than people receiving placebo.
- Overall, Xolair® was well-tolerated in this study, and safety was consistent with our understanding of the safety of Xolair® for other diseases (such as asthma and chronic idiopathic/spontaneous urticaria).

# 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 (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 inflammation does not improve, some people develop nasal polyps.

People with nasal polyps can have symptoms such as:

- Nasal congestion (also called a blocked-up or stuffy nose);
- Runny nose;
- A thick yellow or green mucus discharge from the nose;
- Reduced ability to smell;
- Cough;
- 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 inflammation in nasal polyps is similar to that seen in asthma, a condition where the airways are sensitive and become inflamed. Because the inflammation is similar, scientists are testing existing asthma medicines, such as Xolair®, to see if they can also help people with nasal polyps.

## What is the study medicine?

A medicine called Xolair® (also known as 'omalizumab') is the focus of this study. Xolair® has been approved to treat asthma since 2003 and long-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 that works by sticking to and blocking a second antibody, called IgE. IgE normally causes allergic symptoms and allergic inflammation. When Xolair® blocks IgE, this can reduce allergic symptoms and allergic inflammation.
- Xolair® is given as an injection just below the skin every 2 or 4 weeks.

Xolair® was compared with a 'placebo.'

- You say this as 'plah – see – bo.'
- The placebo looks like Xolair® but did not contain any real medicine. This means it had no medicine-related effect on the body.
- The placebo is injected under the skin just like Xolair®.
- Researchers compared Xolair® with a placebo to look at the benefits and/or side effects of Xolair®.

## What did researchers want to find out?

Researchers did this study to compare Xolair® to placebo in people with nasal polyps to see if Xolair® improves nasal polyps and related symptoms (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® or a placebo during this study (see section 5 "What were the side effects?").

**The main questions that researchers wanted to answer were:**

1. Did people with nasal polyps have reduced nasal congestion after 24 weeks of Xolair® treatment compared with before treatment?
2. Did people with nasal polyps have smaller nasal polyps after 24 weeks of Xolair® treatment compared with before treatment?

**Other questions that researchers wanted to answer included:**

3. Did people with nasal polyps have a reduction in the impact of their symptoms on their well-being after taking their medicine?
4. Did people who took the medicine experience any side effects, and if so, what were they?

## What kind of study was this?

This study was a 'Phase 3' study. This means that Xolair® had been tested before this study in a **smaller** number of people with nasal polyps. In this study, a **larger** number of people with nasal polyps were studied and received either Xolair® or a placebo.

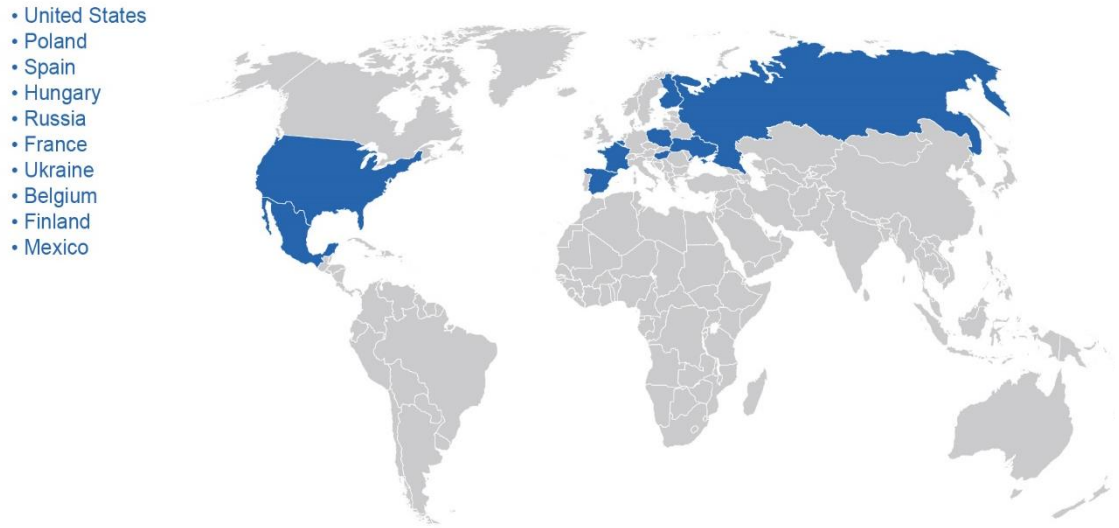
The study was ‘randomized’. This means that it was decided by chance (like tossing a coin), using a computer, which people in the study would receive Xolair®. In this study, 1 person was assigned to receive Xolair® for every 1 person assigned to receive placebo.

This was a ‘double-blind’ study. This means that neither the people taking part in the study nor the study doctors knew which medicine people were taking. ‘Blinding’ of a study is done so that a fair evaluation of the treatment can be made, without people assuming that certain effects are due to the medicine being used.

### When and where did the study take place?

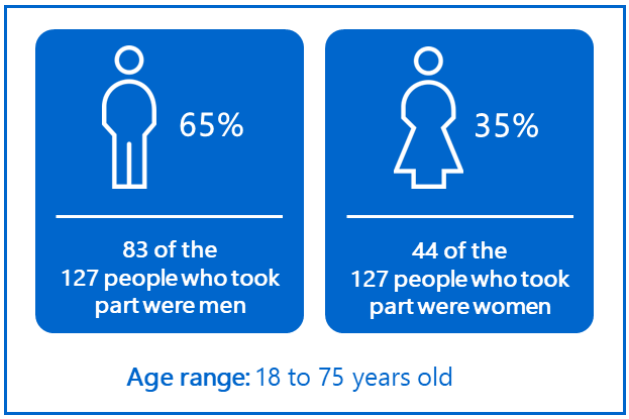
The study started in November 2017 and ended in March 2019. This summary presents the full results of the study up until it ended in March 2019.

The study took place at 45 study centers across 10 countries in North America and Europe. The following map shows the countries where this study took place.




## 2. Who took part in this study?

In this study, 127 people with nasal polyps took part. More information on the people who took part is given below.



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

- Multiple large polyps in both nostrils.
- Symptoms of nasal polyps that interfered with their well-being.
- Congestion in their nose before the study.
- At least 1 symptom of nasal discharge (such as need to blow nose, or drip in back of throat) and/or loss or reduced sense of smell.
- Previous treatment with a nasal steroid spray for at least 4 weeks before the study, which had not worked. People needed to continue this treatment during the study.

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

- A previous reaction to Xolair®.
- Treatment with certain anti-inflammatory medicines for asthma or certain medicines that turn down the immune system.
- Surgery on their nose or sinuses in the last 6 months, including surgery to remove nasal polyps.
- Uncontrolled nose bleeds needing surgery or other treatment in the past 2 months.
- Certain conditions of the lungs or the immune system or another serious medical condition.
- Treatment with another medicine that could affect nasal polyps.
- A recent or long-term infection that required hospital treatment, recent antibiotic treatment, or that their doctor determined was not allowed.
- Alcohol or drug abuse within the last 6 months.

## 3. What happened during the study?

During the study, people were selected by chance to get one of 2 treatments.

The treatment groups were:

- **Xolair®** (the study medicine) – injected under the skin once every 2 or 4 weeks. The dose was 150–600mg, depending on a person's body weight and amount of IgE in the blood.
- **Placebo** (dummy medicine) – injected under the skin once every 2 or 4 weeks.

At the start of the study, 62 people were selected to get Xolair® and 66 people were selected to get placebo. Some people decided not to take part after they had been selected, so the numbers of people who actually completed the study were:

- 55 people in the Xolair® group.
- 63 people in the placebo group.

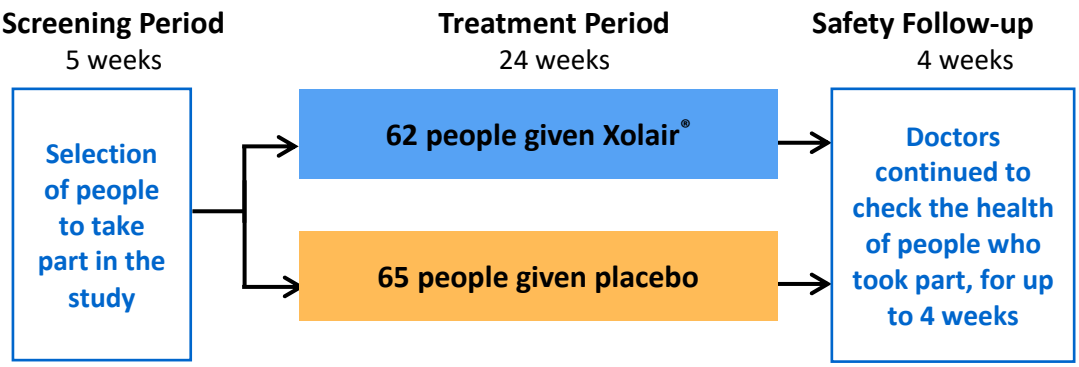
The study included a 5-week screening period (called the 'screening period'), 24-week treatment period (called the 'treatment period') and then a 4-week period where people were monitored for any side effects (called the 'safety follow-up period').

The screening period happened before people received the selected treatment; during this period, they had to have a number of tests to see whether they could be included in the study. Before the screening period and every 4 to 8 weeks during the treatment period, people were also required to have a procedure where an instrument with a camera was inserted into their nose to assess the severity of their nasal polyps (called 'video nasal endoscopy'). They were also provided with a handheld device during this time so they could record their nasal symptoms each day during the study.

People who passed this screening then entered the treatment period, where they received either Xolair® every 2 or 4 weeks or a placebo for 24 weeks.

After the end of the treatment period, people were then followed for 4 more weeks to monitor for any side effects.

The study is now completed so no more people are being treated with the study medicine. Look below to see more information about what happened in the study.




People who completed the current study and did not have a serious reaction to the study medicine were allowed to continue in an open-label extension study, where all people received Xolair® for 28 weeks and were then watched for another 24 weeks. 'Open label' means that both the doctors and the people know which treatment the patient is getting. The purpose of this study is to look at the effect of Xolair® over a longer time and will include people who have completed either of the current studies (i.e. POLYP 1 and POLYP 2).

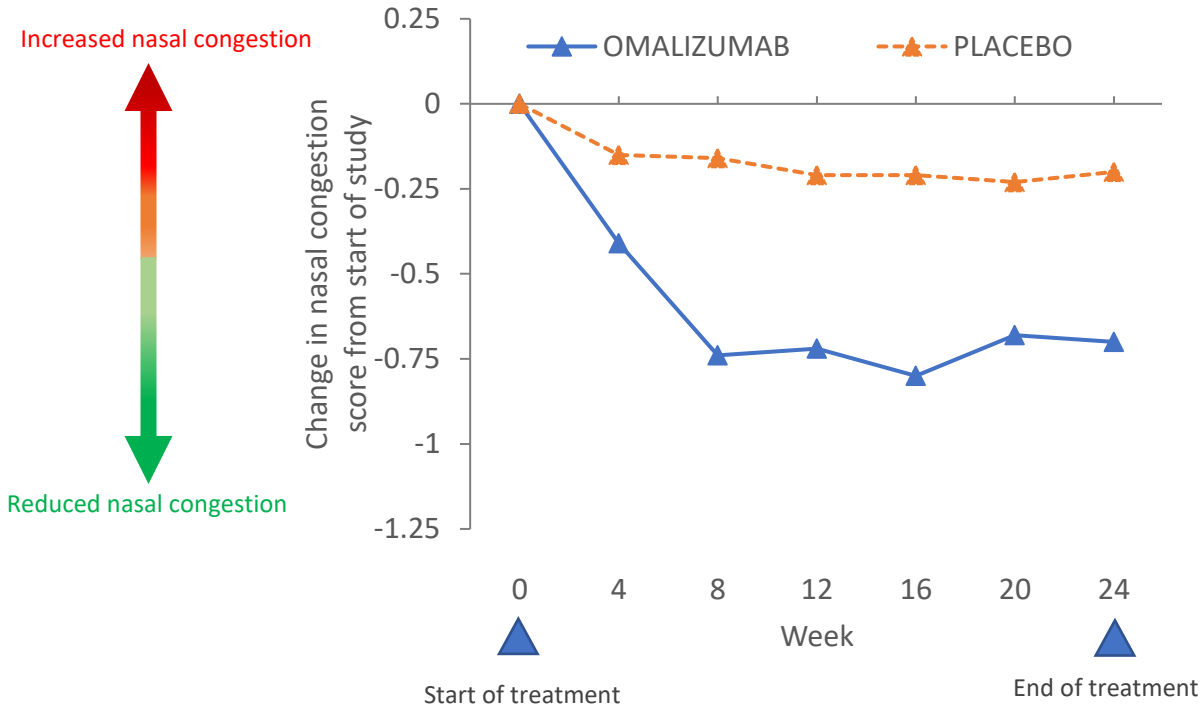
## 4. What were the results of the study at this point?

### **Question 1:** Did people with nasal polyps have reduced nasal congestion after 24 weeks of Xolair® treatment compared with before treatment?

People were given a handheld device to rate their nasal congestion each morning by recording a response to the question "is your nose blocked?" – '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 by comparing the average daily score at the end of the treatment to the score before treatment (*Figure*). This was compared between the Xolair® and placebo groups.

- People who received Xolair® had a larger reduction in their symptoms of nasal congestion compared with people who received placebo.
- People experienced a reduction in their symptoms of nasal congestion as early as week 4, which continued to improve to week 24 (end of the study).

**People who received Xolair® had a larger reduction in their nasal congestion compared with people who received placebo.**

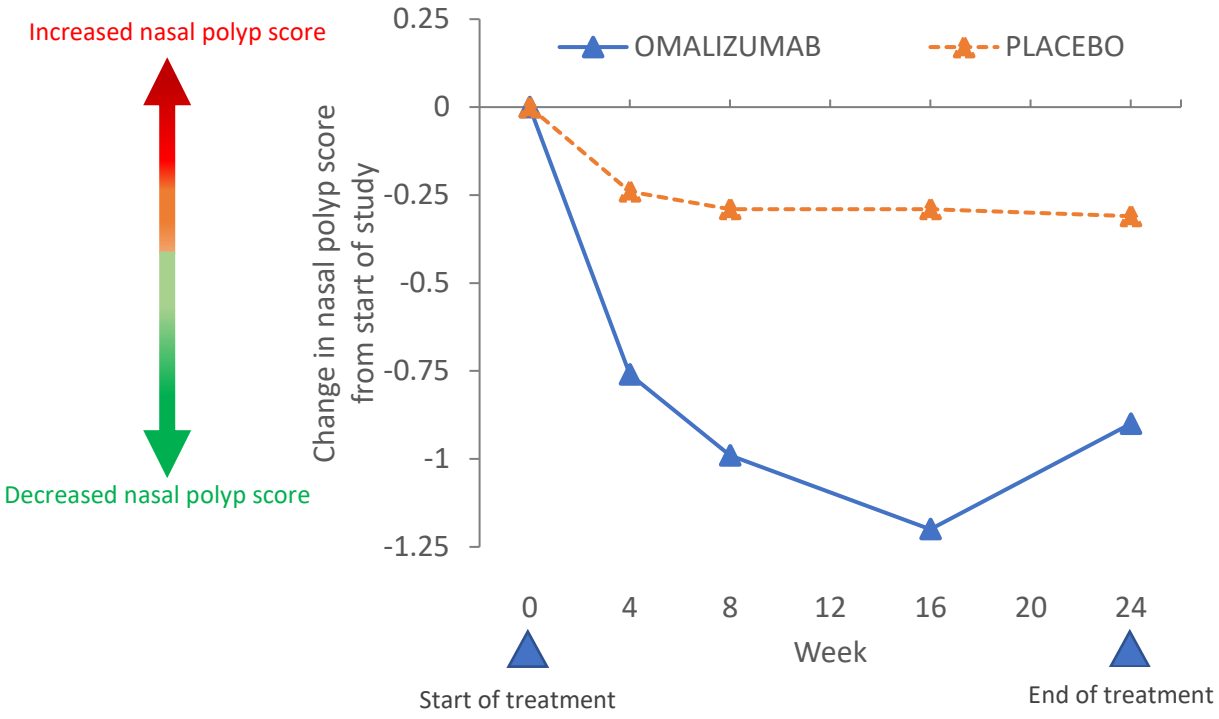


## **Question 2:** Did people with nasal polyps have smaller nasal polyps after 24 weeks of Xolair® treatment compared with before treatment?

Researchers also looked at whether people had a reduction in their nasal polyp score after treatment compared with before treatment. They compared this between the Xolair® and placebo groups. To find out the nasal polyp score, they used an instrument with a camera placed in the nose to measure the size of their polyps.

- People who received Xolair® had a meaningful reduction in their nasal polyp score whereas people who received placebo had a small improvement in their nasal polyp score.
- In people who received Xolair®, the reduction in nasal polyp score happened as early as week 4, and continued to week 24 (end of the study).

**People who received Xolair® had a meaningful reduction in the size of their nasal polyps compared with people who received placebo.**



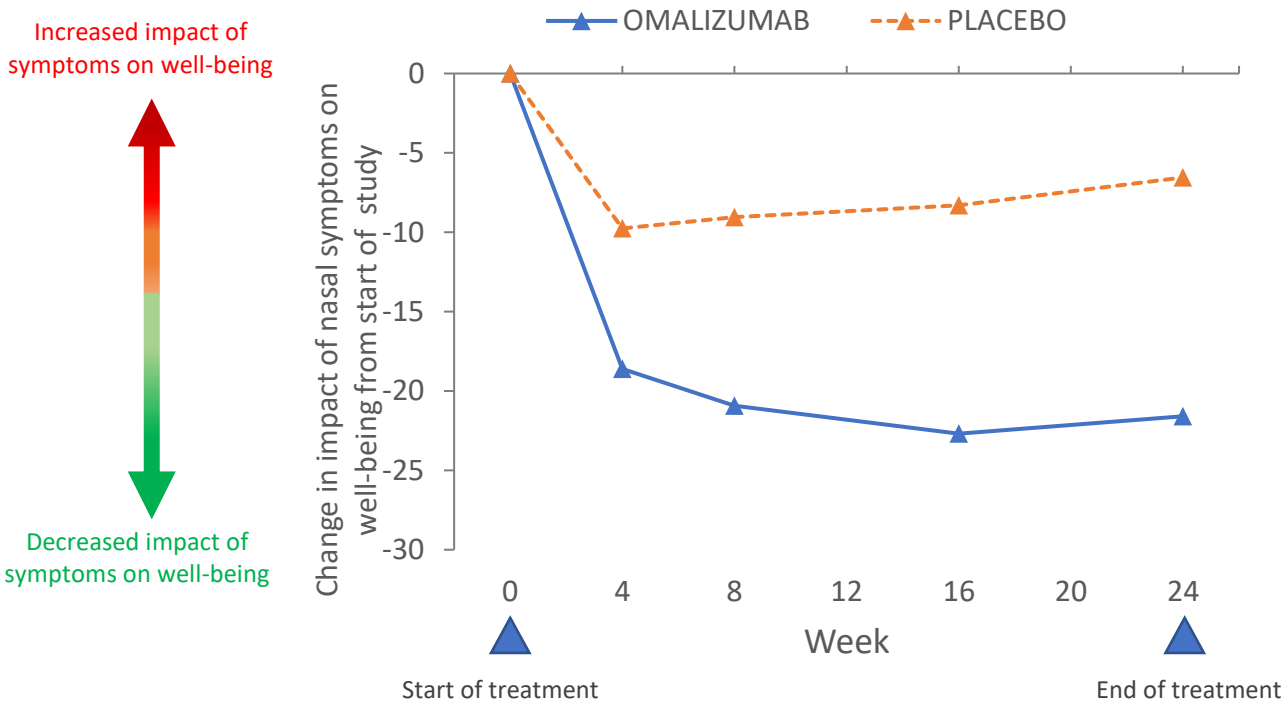
## **Question 3:** Did people with nasal polyps have an improvement in the impact of their symptoms on their well-being after 24 weeks of Xolair® treatment compared with before treatment?

Researchers asked people at their in-clinic visits during the study about their well-being. This included the impact of their nasal polyp symptoms, such as runny nose, need to blow their nose, cough, and loss of their sense of smell on their well-being.

People used their handheld devices to rate the effect of their nasal symptoms on their well-being over the past 2 weeks – 'no problem (score of 0), 'very mild problem' (score of 1), 'mild or slight problem' (score of 2), or 'moderate problem' (score of 3), 'severe problem' (score of 4), or 'problem as bad as it can be (score of 5). The researchers compared the total score at each treatment visit against the total score before treatment to assess the change in impact of symptoms on their well-being from the start of the study (*Figure*). This was compared between the Xolair® and placebo medicine groups.

- People in both Xolair® and placebo groups reported that symptoms during the study had less of an impact on their well-being than before the study.
- These improvements were larger in people receiving Xolair® than in people receiving placebo.
- People experienced an improvement in the impact of their symptoms on their well-being as early as week 4, which continued to week 24 (end of the study) in people taking Xolair®.

**People who received Xolair® reported that their symptoms had less of an impact on their well-being than people who received placebo.**



## 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, and no patient stopped taking Xolair® due to side effects. The most common unwanted events (>5% of people) that occurred during the study were:

- Asthma: 2 (3.2%) people taking Xolair® versus 5 (7.8%) people taking placebo
- Nose bleed: 4 (6.3%) people taking Xolair® versus 1 (1.6%) people taking placebo
- Nasal polyps: 1 (1.6%) person taking Xolair® versus 4 (6.3%) people taking placebo
- Nasopharyngitis (e.g. swelling of the nose and throat): 5 (7.9%) people taking Xolair® versus 9 (14.1%) people taking placebo
- Headache: 7 (11.1%) people taking Xolair® versus 3 (4.7%) people taking placebo
- Injection site reaction: 5 (7.9%) people taking Xolair® versus 2 (3.1%) people taking placebo

Overall, Xolair® was well-tolerated in the study and safety was similar to our understanding of the safety of Xolair® for other diseases (such as asthma and chronic idiopathic/spontaneous urticaria).

### 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 a study of 127 people with nasal polyps. 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?

Another study looking at the effects and safety of Xolair® is currently taking place.

- An open-label extension study is ongoing at the time of this publication. The purpose of the open-label study is to look at the effect of Xolair® over a longer time and includes people who have completed phase 3 studies (i.e. POLYP 1 and POLYP 2).

The current study started in November 2017 and ended in March 2019. This summary includes the full results up until the study ended in March 2019. At the time of writing this summary, the study has been completed and no more information is being collected.

## 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/NCT03280537
- https://ichgcp.net/clinical-trials-registry/NCT03280537

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Efficacy and Safety of Omalizumab in Patients with Nasal Polyposis: Results from Two, Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase III Trials (POLYP 1 and POLYP 2)". The authors of the scientific paper are: P. Gevaert, T. A Omachi, J. Corren, J. Mullol, J. Han, and others.

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

If you have any further questions after reading this summary:

- Contact F. Hoffman-La Roche of Basel, Switzerland or a representative at your local Genentech (if in the US)/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 organised and paid for this study?

This study was organised 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: "A Phase III, Randomized, Multicenter, Double-Blind, Placebo-Controlled Clinical Trial of Xolair® in Patients with Chronic Rhinosinusitis With Nasal Polyps".

The study is known as 'POLYP 2'.

- The protocol number for this study is: GA39855.
    - The ClinicalTrials.gov identifier for this study is: NCT03280537.
    - The EudraCT number for this study is: 2017-001718-28.