This document provides a short summary of this study for a general audience. You can find more information in the scientific summaries of the study. Links to those summaries are provided at the end of this document.

Study names

Short Title: A study to assess how well mepolizumab works and how safe it is in patients with severe bilateral nasal polyps.

Full Scientific Title: A randomised, double-blind, parallel group phase III study to assess the clinical efficacy and safety of 100 milligrams subcutaneous mepolizumab as an add on to maintenance treatment in adults with severe bilateral nasal polyps (SYNAPSE study).

Study Number: 205687

Who sponsored this study?

GlaxoSmithKline (GSK)
GSK Clinical Support Help Desk
Website: clinicalsupporthd.gsk.com/contact.html
Email: GSKClinicalSupportHD@gsk.com

General information about the clinical study

When was this study done?

The study started in May 2017 and ended in December 2019.

What was the main objective of this study?

Nasal polyps are growths in the nostrils and/or sinuses. They are caused by long-term inflammation in the inner lining of the nose. In some cases, polyps can grow in both nostrils (bilateral nasal polyps).

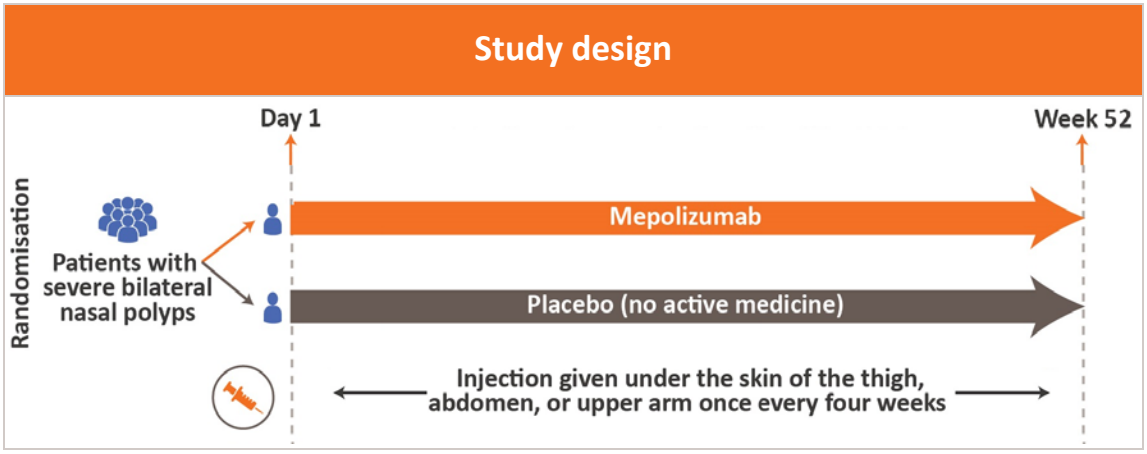
Common symptoms of nasal polyps include blocked nose (nasal obstruction), runny nose, phlegm, loss of smell, and face pain. Patients with severe bilateral nasal polyps

often require surgery to remove polyps (nasal polyp surgery). However, polyps usually return.

Mepolizumab is a medicine that reduces inflammation. Researchers wanted to see how well mepolizumab works when added to regular bilateral nasal polyp treatment compared with regular bilateral nasal polyp treatment alone. The objectives of the study were to see if mepolizumab reduced nasal polyp size, nasal obstruction, and the risk of having nasal polyp surgery. Researchers also studied the safety of mepolizumab.

Which medicines were studied?

During the study, patients were placed in one of two treatment groups by chance (randomisation), as shown in the figure below.



Patients continued taking their regular bilateral nasal polyp treatment throughout the study. Neither the patients nor the study doctors knew who was receiving which treatment. This is called a double-blind study.

Which patients were included in this study?

Studies have a list of requirements for patients who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Men and women with severe bilateral nasal polyps were included in the study if they:

- Were at least 18 years old.
- Needed nasal polyp surgery based on polyp size and symptom scores.
- Had at least one previous nasal polyp surgery in the past ten years before starting the study.
- Had nasal obstruction or runny nose for at least 12 weeks before starting the study and at least one of the following three - runny nose, loss of smell, or face pain.
- Were receiving nasal steroid medicines that reduce inflammation for at least eight weeks before starting the study.

Men and women were excluded from the study if they had:

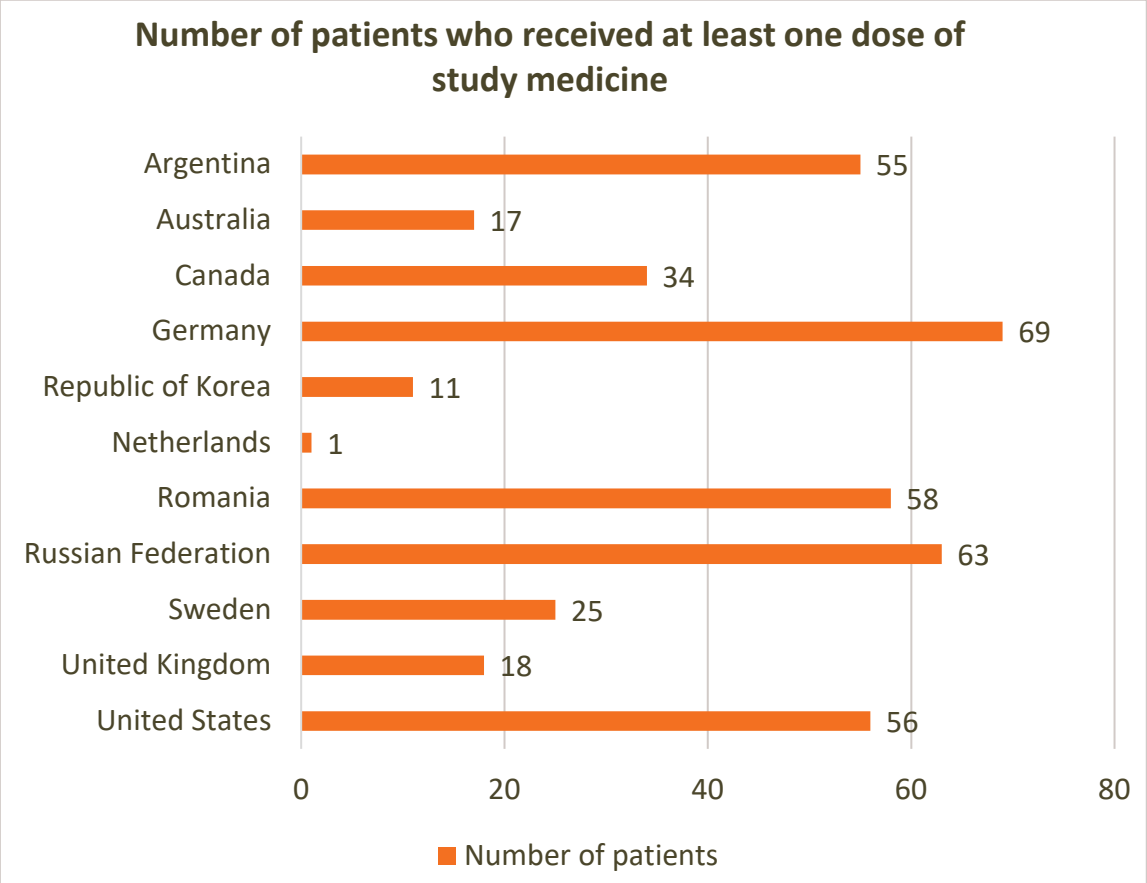
- Cystic fibrosis (disease of the lungs).
- Some specific diseases that cause inflammation of the airways.
- Inflammation in sinuses or upper respiratory tract infection within two weeks before starting the study.
- Hospitalisation due to worsening of asthma within four weeks before starting the study.
- A blocked nostril due to a shift in the wall that separates the nostrils.
- Nasal surgery within six months before starting the study.
- Any other disease(s) or treatment(s) that the study doctor thought would affect the results of the study.

Overall, 407 patients received at least one dose of the study medicine. The study included 264 (65%) men and 143 (35%) women. The average age was 49 years. The youngest patient was 18 years old and the oldest patient was 82 years old.

For more detailed information about the patients included in this study, see the scientific results summaries (links to those summaries are provided at the end of this document).

Where was this study done?

Study sites were in 11 countries.



What were the main results of the study?

The main results of the study included assessments of nasal polyp size, nasal obstruction score, and the risk of having nasal polyp surgery.

Nasal polyp size

During the study, study doctors measured and scored patients' polyp size in each nostril every four weeks. Total nasal polyp scores ranged from zero (no polyps) to eight (large polyps causing blockage in both nostrils). The difference between the total nasal polyp score at Day 1 and after 52 weeks of treatment was calculated.

Patients in the mepolizumab group showed a one-point average improvement from Day 1 in total nasal polyp score. An improvement in the total nasal polyp score means a reduction in nasal polyp size. On average, patients in the placebo group showed no improvement from Day 1 in total nasal polyp score.

Nasal obstruction score

Patients rated the severity of their nasal obstruction once daily. Nasal obstruction scores ranged from 0 (none) to 10 (as bad as you can imagine). The difference between the average nasal obstruction score for the week before Day 1 and four weeks before Week 52 was calculated.

Patients in the mepolizumab group showed a more than four-point average improvement from Day 1 in nasal obstruction score. An improvement in the nasal obstruction score means a reduction in nasal obstruction. Patients in the placebo group showed a less than one-point average improvement from Day 1 in nasal obstruction score.

Risk of having nasal polyp surgery

Study doctors recorded the time (in weeks) from Day 1 to the patient's first nasal polyp surgery in this study. Researchers then calculated the risk of a patient having nasal polyp surgery. The risk value was then converted to a percentage to show the degree to which mepolizumab reduced the risk of having nasal polyp surgery compared with placebo.

When used in addition to regular bilateral nasal polyp treatment, mepolizumab reduced the risk of having nasal polyp surgery by 57%, compared with placebo.

More information about the study results is available in the scientific results summaries (links to those summaries are provided at the end of this document).

What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of these events can be found in the scientific results summaries (links to those summaries are provided at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, they record this as a possible side effect (adverse reaction).

In this summary, side effects refer to those events that the study doctor thinks may have been caused by the study medicine. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

In blinded studies, the doctor does not know which study medicine the patient is taking. In some cases, side effects will be assigned to placebo.

One serious side effect was reported during the study. One patient (less than 1%) from the placebo group had a mini-stroke with no lasting effects. No patients in the mepolizumab group reported serious side effects.

Headache was the only non-serious side effect that was reported by 3% or more of patients in any treatment group. This was reported by eight patients (4%) in the mepolizumab group and two patients (less than 1%) in the placebo group.

How has this study helped patients and researchers?

The study showed that adding mepolizumab to regular bilateral nasal polyp treatment was better than regular bilateral nasal polyp treatment alone. Patients who received mepolizumab had a reduction in nasal polyp size, nasal obstruction, and the risk of having nasal polyp surgery. One patient in the placebo group had a serious side effect. The non-serious side effects reported in the study were low in number and as expected.

Are there plans for further studies?

Other studies on mepolizumab in patients with bilateral nasal polyps have been conducted and more are underway.

Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study numbers associated with this study are shown below with internet links to scientific summaries.

The scientific summaries include more details about the requirements for study enrolment, the study visit schedule, results from other endpoints, and more detailed information about adverse events.

Organisation and Website	Study Number
European Medicines Agency (www.clinicaltrialsregister.eu)	2016-004255-70[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT03085797[2]

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with severe bilateral nasal polyps.

The content for this document was finalised by GSK on the 11th of September 2020. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-004255-70
[2] https://clinicaltrials.gov/ct2/show/study/NCT3085797