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 hypereosinophilic syndrome.

Full Scientific Title: A randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of mepolizumab in the treatment of adolescent and adult subjects with severe hypereosinophilic syndrome.

Study Number: 200622

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 March 2017 and ended in August 2019.

What was the main objective of this study?

High levels of a type of white blood cell (eosinophils) for a long period of time can lead to a condition called hypereosinophilic syndrome (HES). Eosinophils help the body fight infections, but too many eosinophils may cause inflammation that can damage the body's internal organs. Patients with HES can have flares of disease worsening.

Mepolizumab is a medicine that lowers the number of eosinophils in the blood. Researchers wanted to see how well mepolizumab works in reducing HES flares, when added to their regular HES treatment, in patients with severe HES. For this study, a HES

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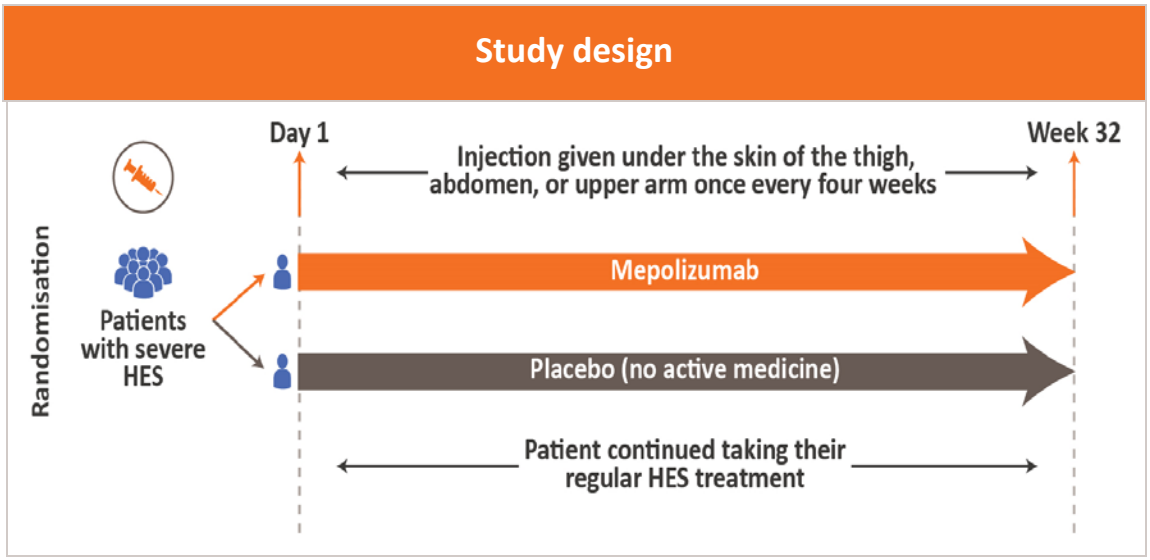
flare was defined as the worsening of HES symptoms or an increase in eosinophil levels that required additional treatment. Researchers also assessed the safety of mepolizumab.

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. 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.

Males and females were included in the study if they:

- Were at least 12 years old.
- Had been diagnosed with HES for at least six months before starting the study treatment.
- Had a blood eosinophil level of at least 1000 cells/microlitre before starting the study.
- Were on stable HES treatment for four weeks before starting the study treatment.
- Had at least two HES flares in the year before starting the study.

Males and females were excluded from the study if they had:

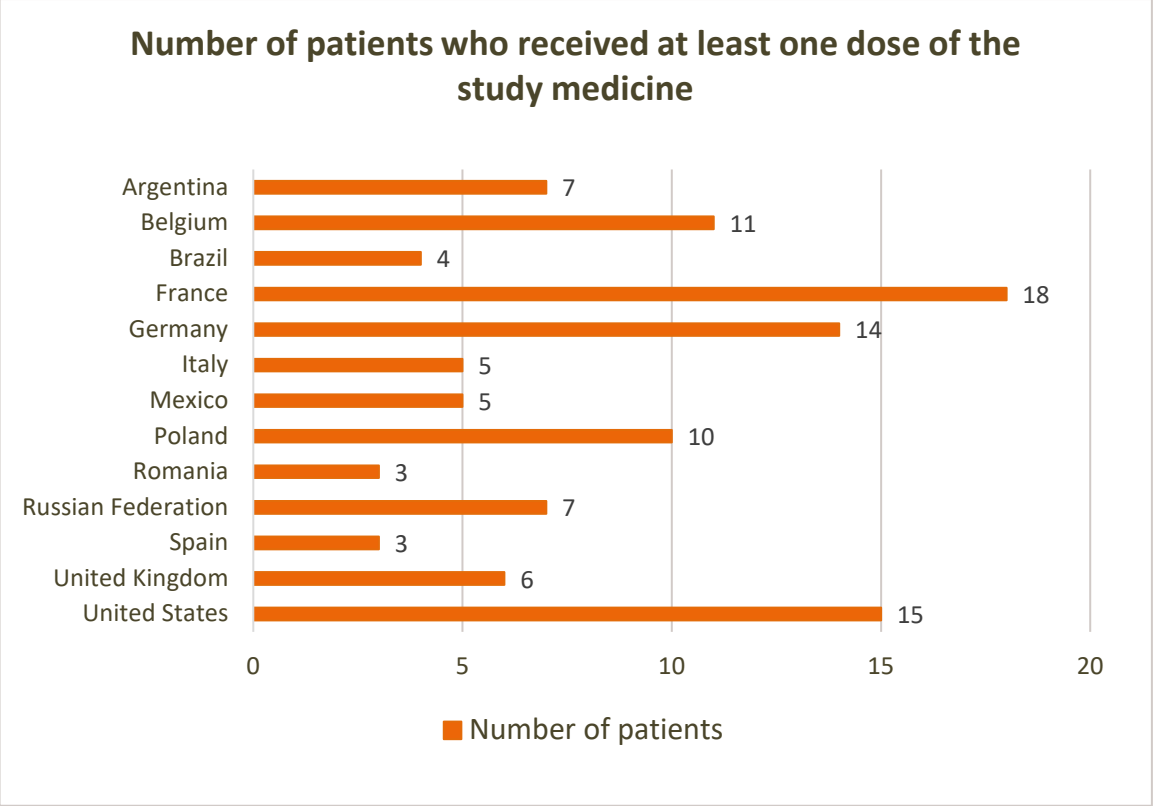
- Life-threatening HES.
- A specific genetic change that could lead to increased eosinophil levels.
- Abnormalities in other laboratory values.
- Received mepolizumab in the four months before starting the study treatment.
- Any other disease(s) or had taken any medicine(s) before starting the study, that the study doctor thought would affect the results of the study.

Overall, 108 patients received at least one dose of the study medicine. The study included 51 (47%) males and 57 (53%) females. The average age was 46 years. The youngest patient was 12 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 13 countries.

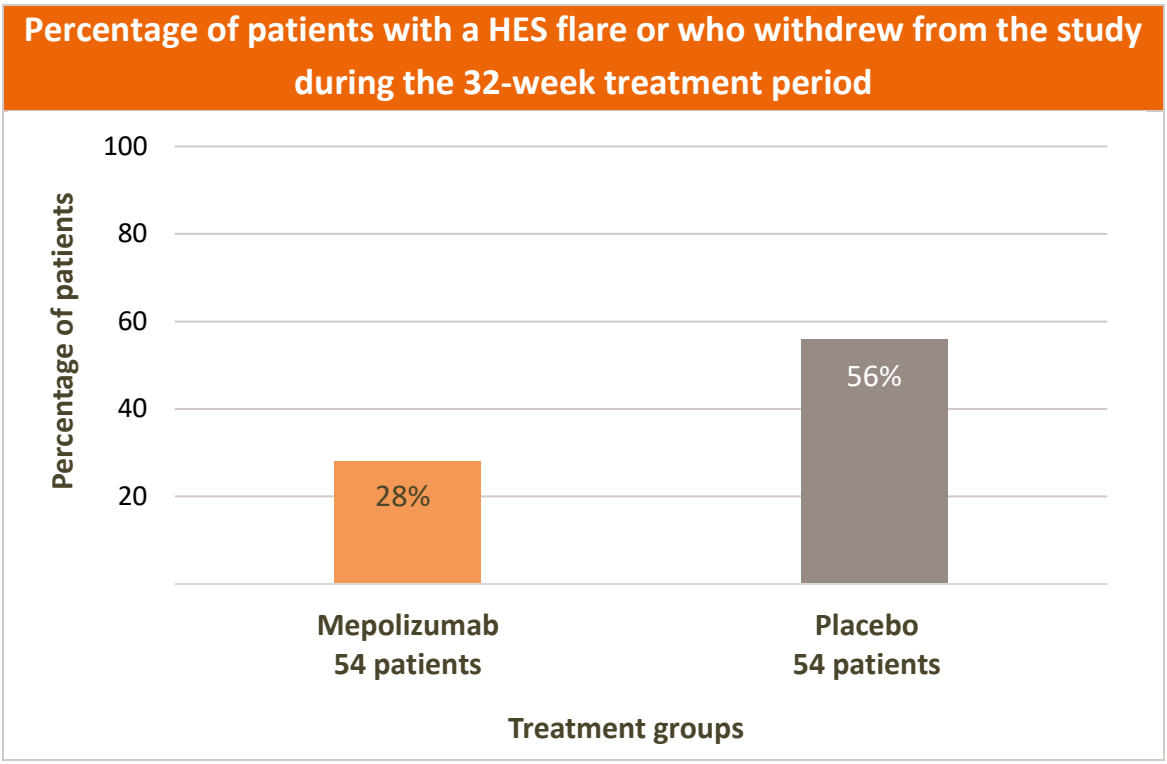


What were the main results of the study?

The study compared the percentage of patients who had a HES flare during the 32-week treatment period.

One patient from the mepolizumab group and two patients from the placebo group did not have a HES flare and withdrew from the study before 32 weeks. Researchers counted these three patients as having had a HES flare in the results.

Results are shown in the figure below.



When taken in addition to regular HES treatment, the study results showed that 50% fewer patients in the mepolizumab group had a HES flare compared with those in the placebo group.

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.

No serious side effects were reported in the study.

Non-serious side effects were reported by 12 patients (22%) in the mepolizumab group and 7 patients (13%) in the placebo group. The only non-serious side effect reported by 2 or more patients in either treatment group was injection site reaction. This happened in 3 patients (6%) in the mepolizumab group and in 2 patients (4%) in the placebo group.

How has this study helped patients and researchers?

This study showed that mepolizumab, when added to regular HES treatment, worked better than only regular HES treatment in reducing the number of HES flares in patients with severe HES. Similar side effects were reported between the treatment groups.

Are there plans for further studies?

Other studies on mepolizumab in patients with HES 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 and other information.

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	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2014-001232-11[1]
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02836496[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 HES.

The content for this document was finalised by GSK on the 4th of June 2020. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-001232-11

[2] https://clinicaltrials.gov/ct2/show/study/NCT02836496?term=NCT02836496&rank=1