Clinical Trial Results Summary

A clinical trial to learn about the safety and effectiveness of erenumab compared to topiramate in the treatment of episodic and chronic migraine headaches

Protocol number: CAMG334ADE01

Thank You!

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. Thank you for taking part in this trial for the drug AMG334, also known as erenumab. You helped researchers learn more about how erenumab works in people with episodic and chronic migraine headaches.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

How long was this trial?

This trial started in February 2019 and ended in July 2020. The trial was designed so that an individual participant could take part for close to 7 months. The trial was completed, as planned, in 1 year and 5 months.

When the trial ended, the researchers collected information on the trial treatments, erenumab (pronounced e-REN-umab) and topiramate (pronounced to-PIR-amate), and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Researchers were looking for a better way to treat migraine headaches. Migraine headaches occur usually, but not always, on one side of the head. A migraine headache generally lasts from 4 to 72 hours, and is often accompanied by other symptoms such as nausea, vomiting and increased sensitivity to light and sound. Migraine headaches are categorized as:

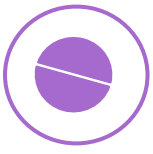
- Episodic when the person has 4 to 14 migraine headache days per month.
- Chronic when the person has 15 or more migraine headache days per month.

In this trial, researchers wanted to compare the effects of erenumab to topiramate in treating participants with episodic and chronic migraines.

Trial drugs

The drugs given in this trial were:

Erenumab: An approved drug to treat migraine headaches in several countries. Erenumab was given by the site staff once a month, as an injection, just under the skin. Erenumab blocks the receptor for a protein called Calcitonin Gene-Related Peptide, or CGRP. It is thought that too much production of CGRP causes a migraine headache, making the pain worse and last longer. By blocking the receptor for CGRP, erenumab may help to prevent migraine headaches and reduce their frequency.



Topiramate: A marketed oral drug and the current standard of treatment for prevention of migraine headaches. Topiramate was taken by the participants once or twice daily, as a tablet, by mouth. Topiramate was an active comparator in this trial, which means it was used as a reference to compare the results of erenumab.

Throughout the trial, the participants could take treatments such as triptans, non-steroidal anti-inflammatory drugs, and psychotherapy when needed to manage the episodes of migraine headaches. This treatment is known as “rescue” treatment.

Trial purpose

After 6 months of treatment, researchers compared the results of all participants with erenumab or topiramate.

The main question the researchers wanted to answer in this trial was:

> How many participants stopped treatment with erenumab due to adverse events compared with topiramate?

Medical problems that happen in clinical trials are called “adverse events”. Adverse events are defined on Page 8 in this summary.

The other question researchers wanted to answer in this trial was:

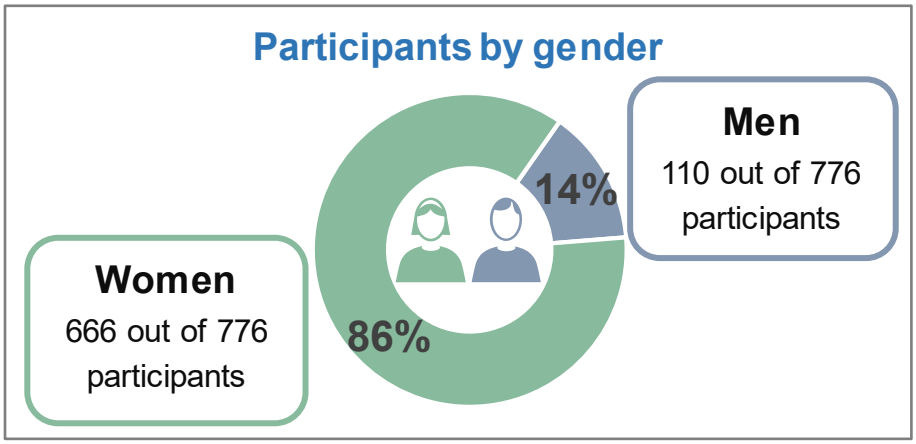
- How many participants who took erenumab had at least a 50% reduction in the number of monthly migraine days in the last 3 months of treatment compared with topiramate?

Who was in this trial?

The participants could take part in this trial if they:

- were 18 to 65 years of age,
- suffered from migraine headaches for at least 12 months before the trial,
- were either new to or not suitable for or had failed up to 3 treatments for the prevention of migraines,
- had at least 4 migraine headache days per month on average during the 3 months immediately before participating in the trial.

A total of 776 participants from Germany participated in this trial. The average age of participants was 41 years. Participants’ age ranged from 18 to 66 years. The majority of participants were women, 666 out of 776 (86%). The majority of participants were white, 770 out of 776 (99%).



What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

Treatment Period (6 months)

At the start of the trial, the researchers randomly assigned the participants to either the erenumab or topiramate treatment group. All participants received two sets of treatment.

Erenumab treatment group: Participants received 70 milligrams (mg) or 140 mg of erenumab by injection and topiramate placebo as a tablet by mouth.

Topiramate treatment group: Participants received 25 mg to 100 mg topiramate as a tablet by mouth and erenumab placebo injections.

This is a technique used in trials to compare 2 treatments that cannot be made identical.

Placebo looked like the trial drug, but did not have any medicine in it. It was only used to 'mask' the other drug so that the participants, trial doctors, or trial staff did not know which treatment the participants were taking.

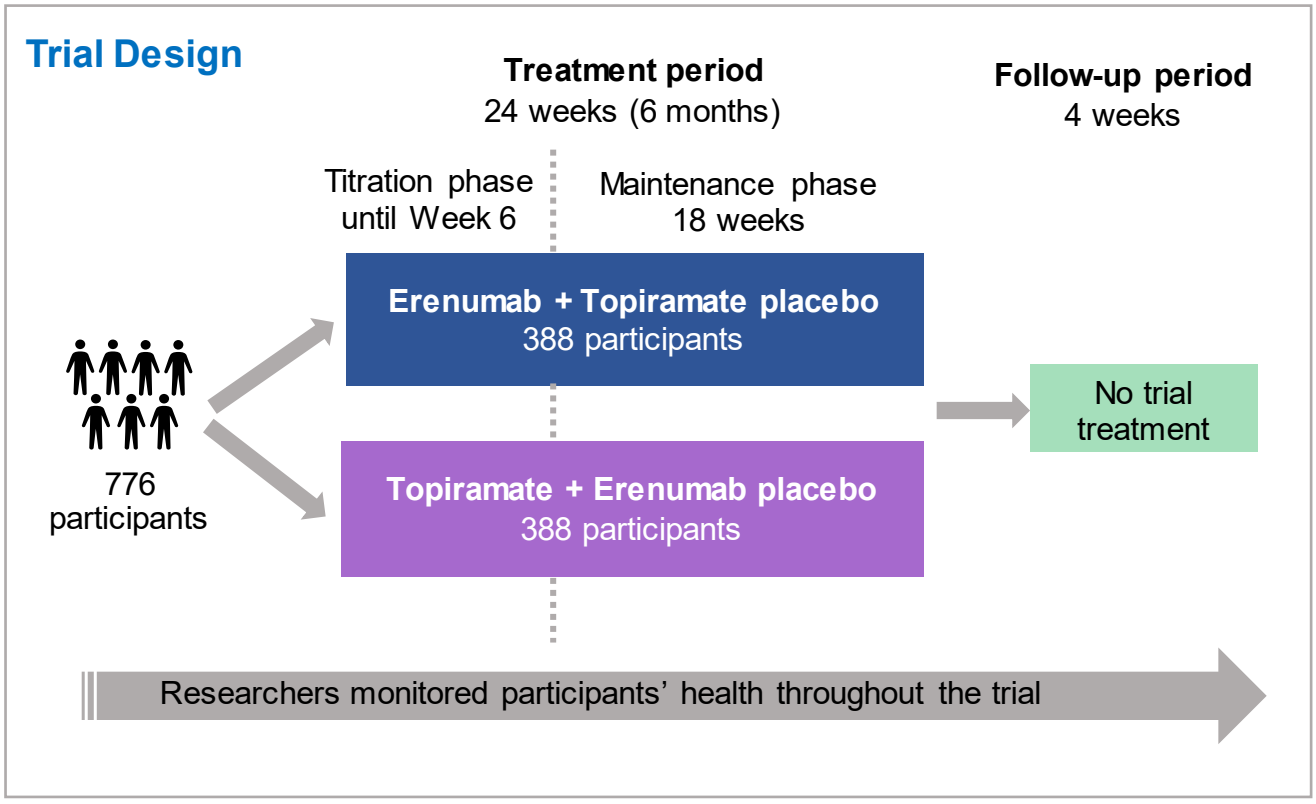
Topiramate was given to participants in 2 phases: titration phase followed by a maintenance phase.

Titration phase

Researchers started by giving participants 25 mg of topiramate. After 1 week, the dose was increased by 25 mg each week for a maximum of 6 weeks. This was done to find out the highest dose of topiramate participants could tolerate.

Maintenance phase

To enter into the maintenance phase, participants had to reach a dose of at least 50 mg in the titration phase. The maximum dose the participants could take was 100 mg. The maintenance phase continued for 18 weeks. Participants could change dose during the maintenance phase depending on what dose they could tolerate and on the judgment of the trial doctors.



Follow-up Period (4 weeks)

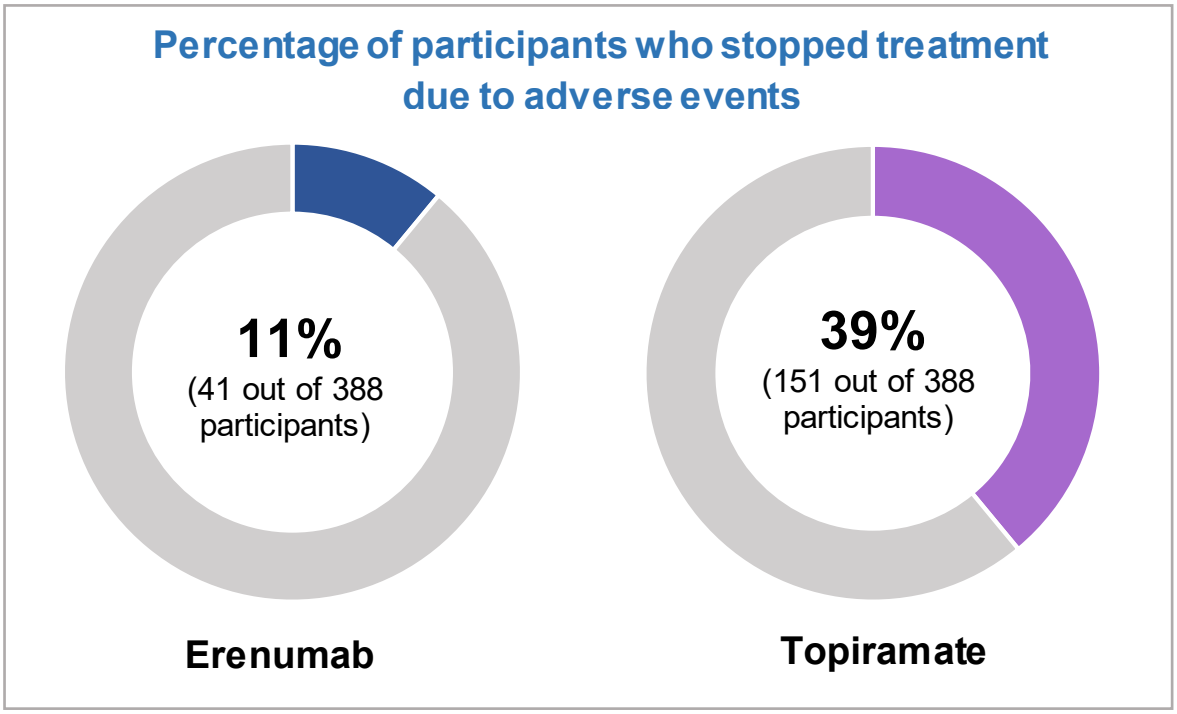
After the treatment period, participants entered into a follow-up period for 4 weeks during which no trial treatment was taken.

What were the key results of this trial?

This is a summary of the average results for all participants in different treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How many participants stopped treatment with erenumab due to adverse events compared with topiramate?

The figure below shows the percentage of participants who stopped treatment due to adverse events. Fewer participants stopped treatment with erenumab due to adverse events than participants who took topiramate. The detailed summary of adverse events is provided on Page 8.

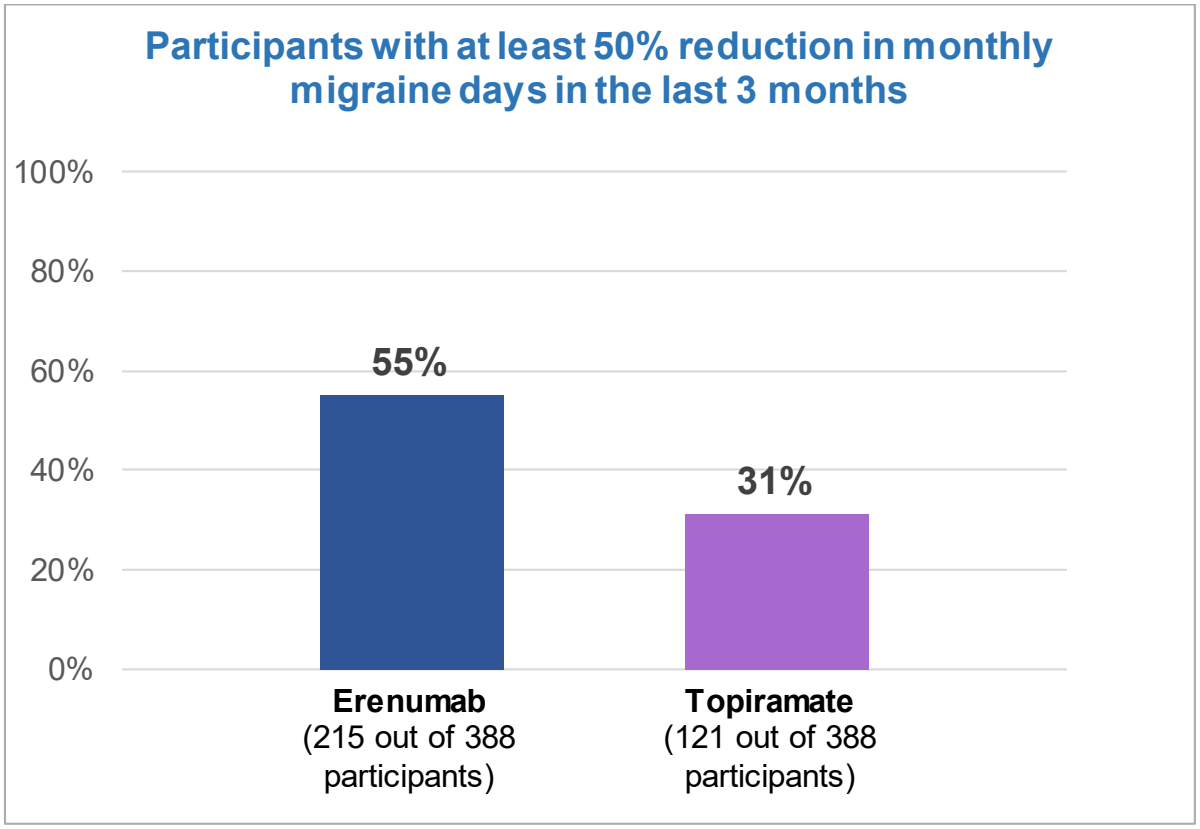


What were the other results of this trial?

How many participants who took erenumab had at least a 50% reduction in the number of monthly migraine days in the last 3 months of treatment compared with topiramate?

To answer this question, researchers noted the number of days participants had migraine headaches, from the start of the trial until the sixth month of treatment.

During the last 3 months (Months 4, 5, and 6) of treatment, more participants who took erenumab had at least a 50% reduction in the number of monthly migraine days than those who took topiramate.



What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called “adverse events”.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is an unwanted sign, symptom, or disease that participants have during a trial.

An adverse event is considered “serious” when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

How many participants had adverse events?

A total of 699 out of 776 participants (90%) had 1 or more adverse events. During the trial, 192 out of 776 participants (25%) stopped the drug early because of adverse events. Serious adverse events happened in 29 out of 776 participants (4%) in the trial. No participant died during this trial.

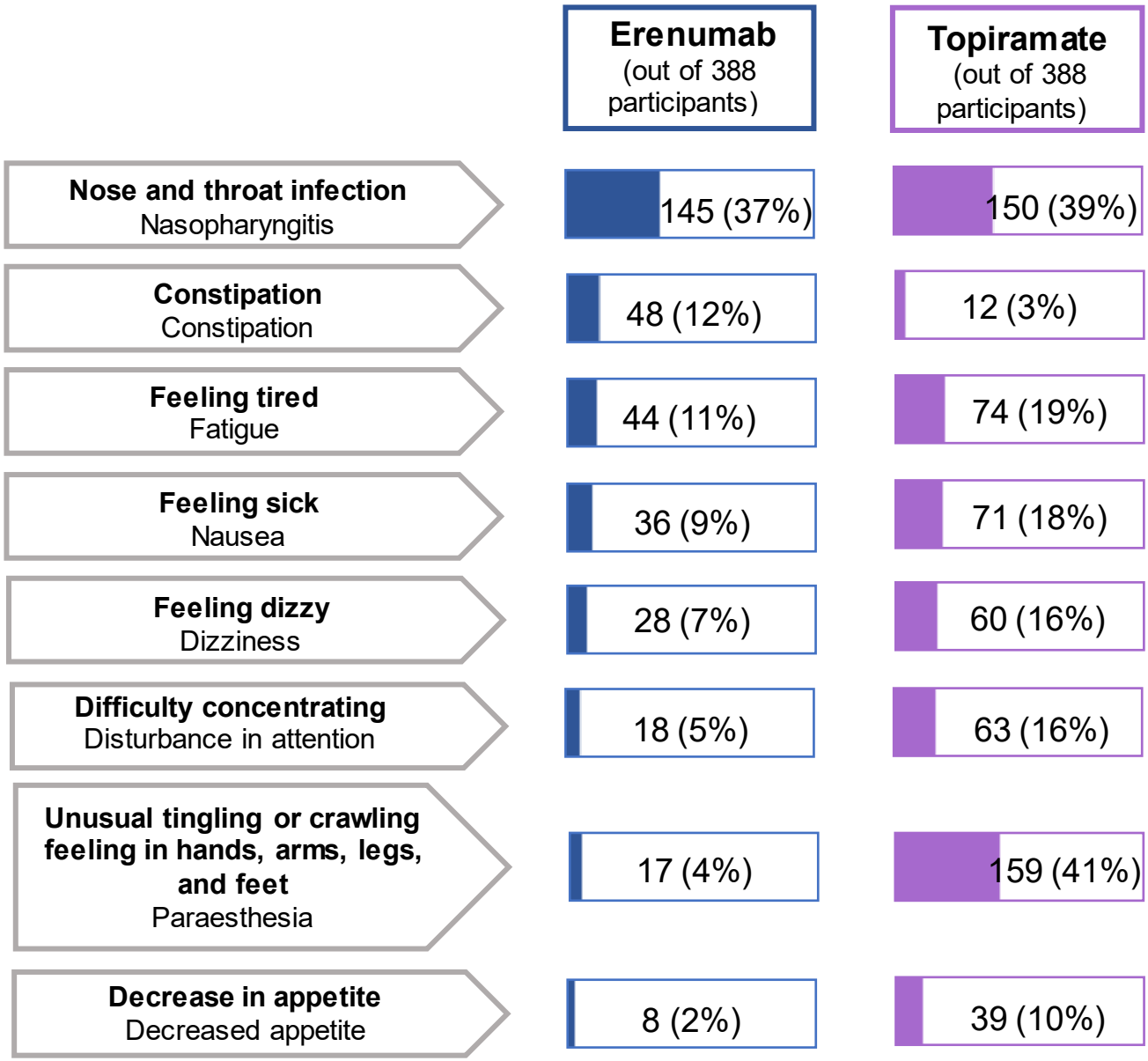
Number of participants (%) with adverse events

	Erenumab (Out of 388 participants)	**Topiramate** (Out of 388 participants)
At least 1 adverse event	338 (87%)	361 (93%)
At least 1 serious adverse event	10 (3%)	19 (5%)
Stopped drug due to adverse event	41 (11%)	151 (39%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 10% of participants in any group are presented below. They are presented in order of the most common to the least common in the erenumab treatment group.

Number of participants (%) with most common non-serious adverse events



What were the serious adverse events?

The most common serious adverse events according to the organs affected were:

- **Infections due to bacteria, viruses, etc in the body** (Infections and infestations): **less than 1%** (1 out of 388) participants in the erenumab group and **2%** (7 out of 388) participants in the topiramate group.
- **Injuries** (Injury, poisoning and procedural complications): **1%** (4 out of 388) participants in the erenumab group and **less than 1%** (2 out of 388) participants in the topiramate group.
- **Stomach problems** (Gastrointestinal disorders): **less than 1%** (2 out of 388) participants in the erenumab group and less than **less than 1%** (2 out of 388) participants in the topiramate group.

How many participants stopped trial drug due to adverse events?

During the trial, 192 out of 776 (25%) participants stopped treatment early due to adverse events: 41 out of 388 (11%) participants in the erenumab group and 151 out of 388 (39%) participants in the topirimate group.

Number of participants (%) who stopped trial drug due to adverse events

	Erenumab (out of 388 participants)	**Topiramate** (out of 388 participants)
Feeling tired Fatigue	9 (2%)	29 (8%)
Feeling sick Nausea	8 (2%)	26 (7%)
Difficulty concentrating Disturbance in attention	7 (2%)	36 (9%)
Unusual tingling or crawling feeling in hands, arms, legs, and feet Paraesthesia	0	38 (10%)

How was this trial useful?

This trial helped researchers learn about the safety and effectiveness of erenumab in episodic and chronic migraine headaches. Fewer participants stopped treatment with erenumab due to adverse events than participants who took topiramate. Doctors treating migraine patients can use the data from this trial to compare with the current available treatment options.

Please remember, this summary only shows the results of a single clinical trial. Other clinical trials may have different results. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).

You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT03828539 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2018-000943-15 in the search field.

Full clinical trial title: Randomized, double-blind, multicenter, Head-to-head study of Erenumab against topiRamate – Migraine study to assess tolerability and efficacy in a patiEnt-centered Setting (HER-MES)

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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