Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of AMG334 compared to placebo in participants who get episodic migraine headaches

Protocol number: CAMG334A2302

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 being part of this trial for the drug AMG334, also known as erenumab. You helped researchers learn more about how erenumab works in people with episodic 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. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. 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?

The trial started in February 2018 and ended in January 2020. This trial was designed so that an individual participant could take part for close to 7 months. The entire duration, from enrolling the first participant to the last participant completing the trial was nearly 2 years.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments, erenumab (pronounced as e-REN-umab) and placebo, 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 know if erenumab helps to reduce migraine headaches in people with episodic migraines.

Trial drugs

The drugs studied 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 CGRP is produced during 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.

❖ **Placebo**

It looked like the trial drug, but did not have any medicine in it. Placebo was given by the site staff once a month as an injection just under the skin. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes are not happening by chance.

Throughout the trial, the participants were allowed to continue taking their regular migraine headache medicines.

Trial purpose

In this trial, researchers compared the results of all participants after 3 months of treatment with erenumab or placebo.

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

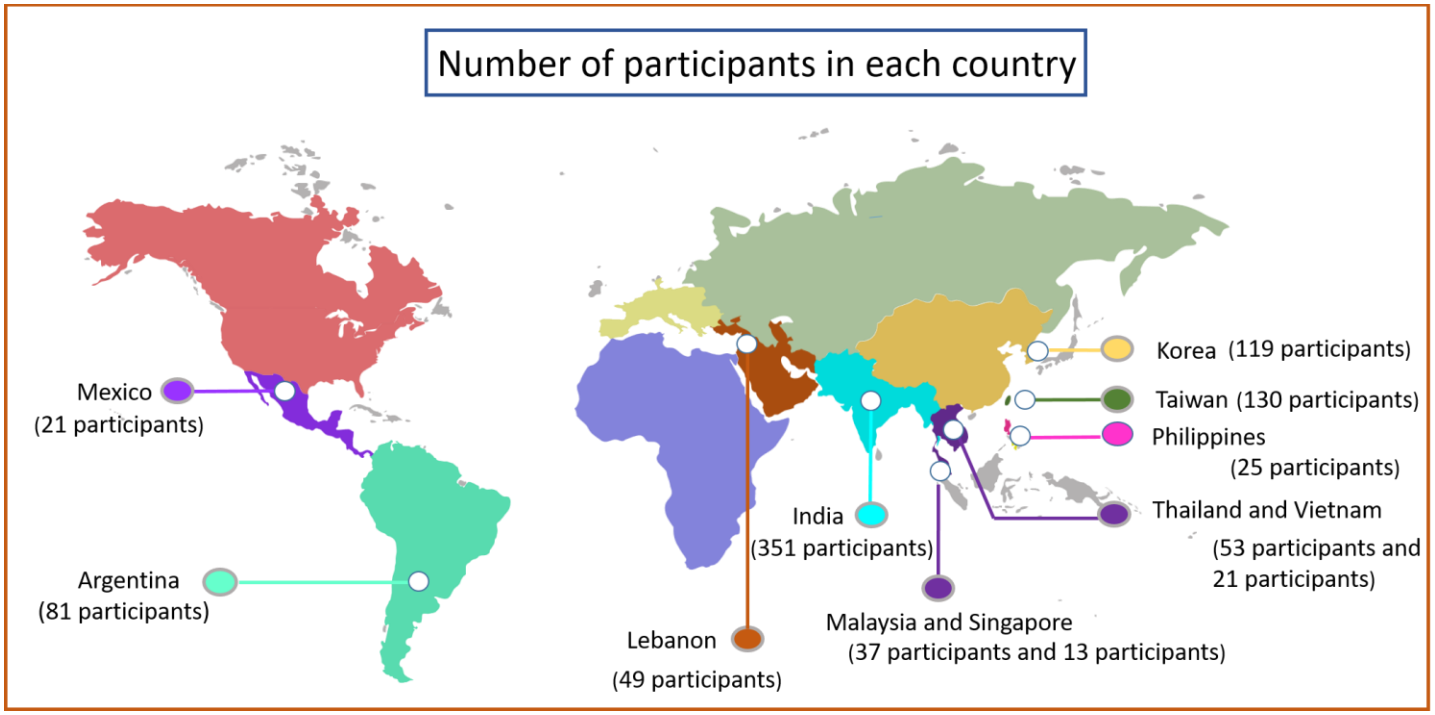
> What was the reduction in migraine headache days in each of the 3 treatment groups after 3 months of treatment?

Who was in this trial?

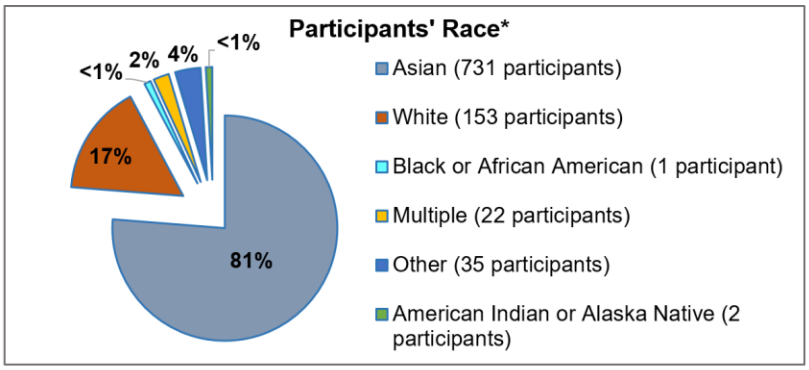
The participants could take part in this trial if they:

- were 18 to 65 years of age,
- had 4 to 14 migraine headache days per month on average across 3 months, before participating in the trial.

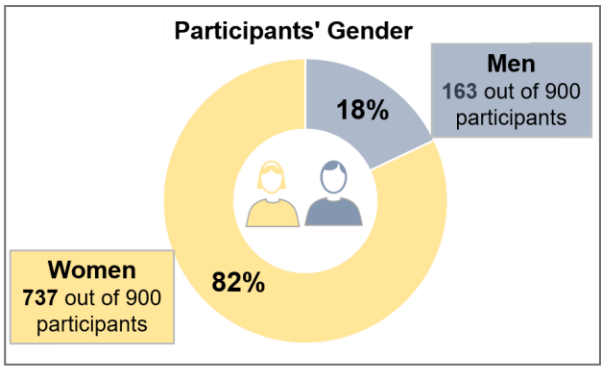
A total of 900 participants from 11 countries in Asia, Middle East and Latin America participated in this trial.



The average age of participants was 38 years. Participants' age ranged from 18 to 64 years. The majority of participants were women, 737 out of 900 (82%).



** If multiple races were reported for a participant, they were categorized as 'multiple' as well as in each selected race category.*



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 participant is getting can affect the results of the trial. Doing a double blind trial helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

During Screening

Participants went through a screening period to confirm that they could take part in the trial. If the participants met the requirements, they entered into a baseline period.

During Baseline

During the baseline period, participants were given a hand held electronic diary (eDiary), about the size of an iPhone, to record questionnaire responses and migraine and non-migraine headache information. At the end of the baseline period, the researchers reviewed the information provided in the eDiaries and confirmed if participants could continue to take part in the trial.

During Treatment

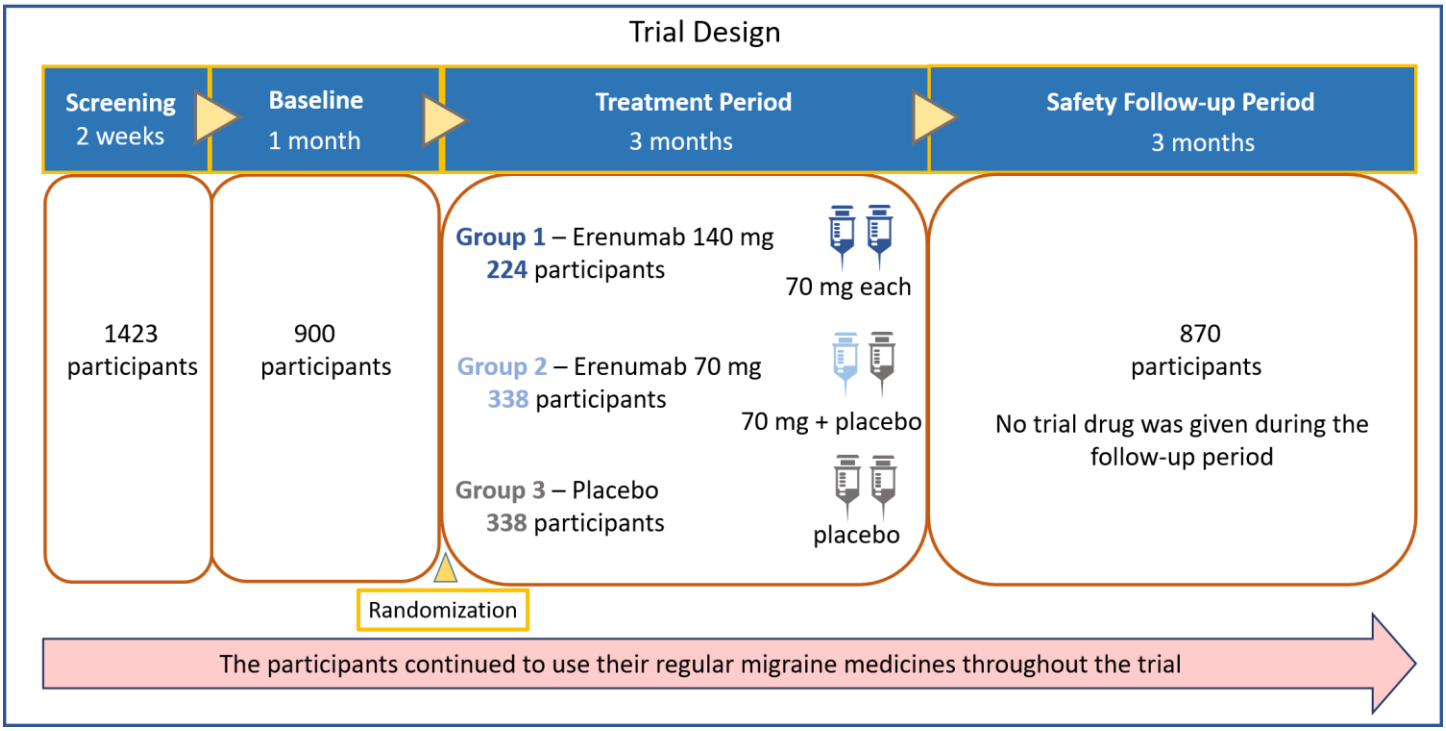
Researchers then placed the participants randomly into 1 of the 3 groups:

- **Group 1** had 224 participants who received a monthly injection of **erenumab 140 mg**.
- **Group 2** had 338 participants who received a monthly injection of **erenumab 70 mg**.
- **Group 3** had 338 participants who a monthly injection of received **placebo**.

6 of the participants did not receive any trial drug. The rest of the participants received 2 injections under the skin as a single dose on Day 1, and at Week 4 and Week 8 during the 3-month treatment period.

During Follow-up

After the treatment period, participants entered into a 3-month follow-up period. During the follow-up period, no trial drug was given to the participants.



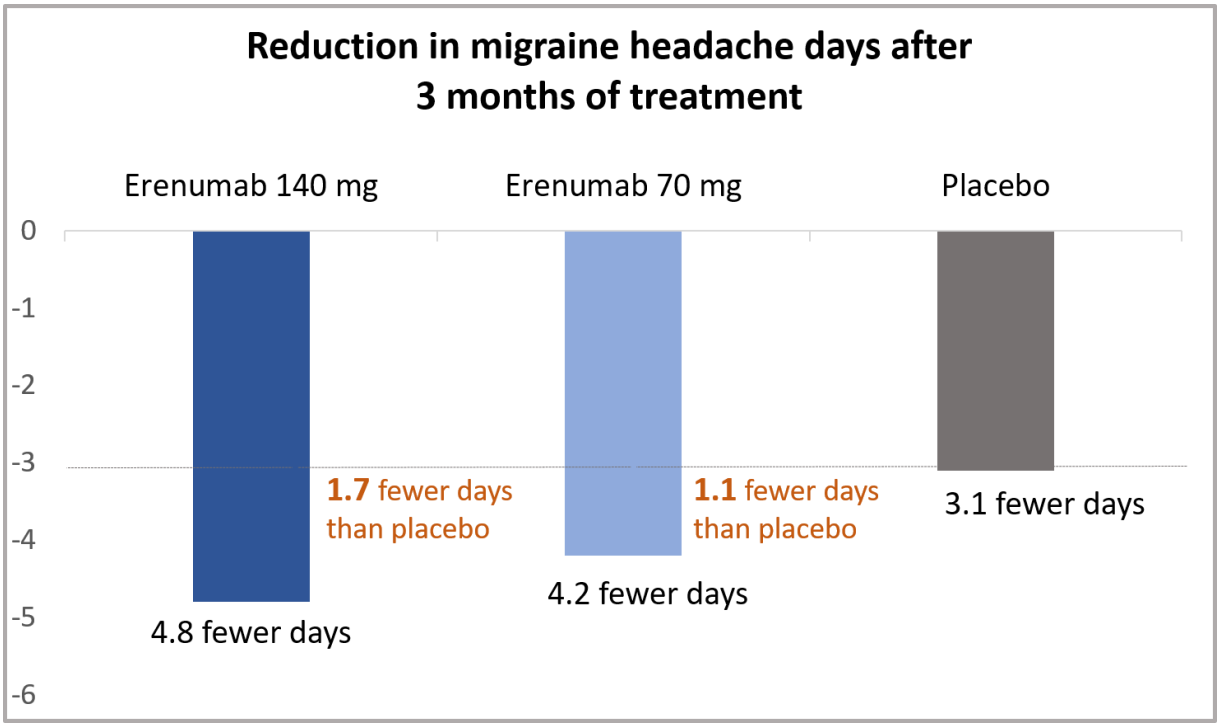
What were the key results of this trial?

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.

What was the reduction in migraine headache days in each of the 3 treatment groups after 3 months of treatment?

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

During the third month of treatment, participants who took erenumab 140 mg had, on average, a reduction of 4.8 migraine days and 1.7 fewer days of migraine headaches compared to placebo. Participants who took erenumab 70 mg had, on average, a reduction of 4.2 migraine days and 1.1 fewer migraine days compared to placebo.



Overall, erenumab treatment showed a greater reduction in the number of migraine headache days compared to placebo.

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?

Adverse events were reported up to 3 months after participants took their last injection of trial drug.

347 out of 894 participants (39%) had 1 or more adverse events. During the trial, 2 out of 335 participants (less than 1%) in the placebo group stopped the drug early because of adverse events. Serious adverse events happened in 10 out of 335 participants (3%) in the erenumab 70 mg group and 5 out of 335 participants (2%) in the placebo group. No participant died during this trial.

Number of Participants (%) With Adverse Events

	Erenumab 140 mg (Out of 224 participants)	**Erenumab 70 mg** (Out of 335 participants)	**Placebo** (Out of 335 participants)
At least 1 adverse event	86 (38%)	129 (39%)	132 (39%)
At least 1 serious adverse event	0 (0%)	10 (3%)	5 (1%)
Stopped drug due to adverse event	0 (0%)	0 (0%)	2 (Less than 1%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 2% (2 out of 100) of participants in any group are presented below.

	Erenumab 140 mg (out of 224 participants)	**Erenumab 70 mg** (out of 335 participants)	**Placebo** (out of 335 participants)
Common cold Upper respiratory tract infection	6 (3%)	13 (4%)	9 (3%)
Constipation Constipation	12 (5%)	20 (6%)	10 (3%)
Cough Cough	5 (2%)	3 (1%)	4 (1%)
Feeling dizzy Dizziness	7 (3%)	4 (1%)	6 (2%)
Fever Pyrexia	5 (2%)	11 (3%)	19 (6%)
Flu Influenza	3 (1%)	8 (2%)	5 (1%)
Nose and throat infection Nasopharyngitis	9 (4%)	2 (1%)	13 (4%)
Pain or swelling at the site of injection Injection site erythema	1 (0.4%)	4 (1%)	8 (2%)

What were the serious adverse events?

The table below shows the serious adverse events that happened in any group.

	Erenumab 140 mg (out of 224 participants)	Erenumab 70 mg (out of 335 participants)	Placebo (out of 335 participants)
A stroke Cerebral infarction	0	1 (0.3%)	0
Blood clot in a vein Deep vein thrombosis	0	1 (0.3%)	0
Depression Depression	0	1 (0.3%)	0
Discomfort below rib region Epigastric discomfort	0	1 (0.3%)	0
Ending of the pregnancy Abortion	0	0	2 (0.6%)
Infection in the stomach and intestines Gastroenteritis	0	1 (0.3%)	1 (0.3%)
Infection of the inner ear Labyrinthitis	0	1 (0.3%)	0
Migraine headache Migraine	0	2 (0.6%)	1 (0.3%)
Miscarriage Abortion spontaneous	0	1 (0.3%)	0
Severe eye infection Cellulitis orbital	0	0	1 (0.3%)
Viral infection Viral infection	0	0	1 (0.3%)
Weakness Asthenia	0	1 (0.3%)	0

How many participants stopped trial drug due to adverse events?

During the trial, 2 out of 335 (less than 1%) participants in the placebo group stopped taking placebo early due to adverse events. One participant stopped due to **double vision** (diplopia) and the other participant stopped due to **pain in the upper or lower parts of the body like the hands or feet** (pain in extremity) and **numbness** (hypoesthesia).

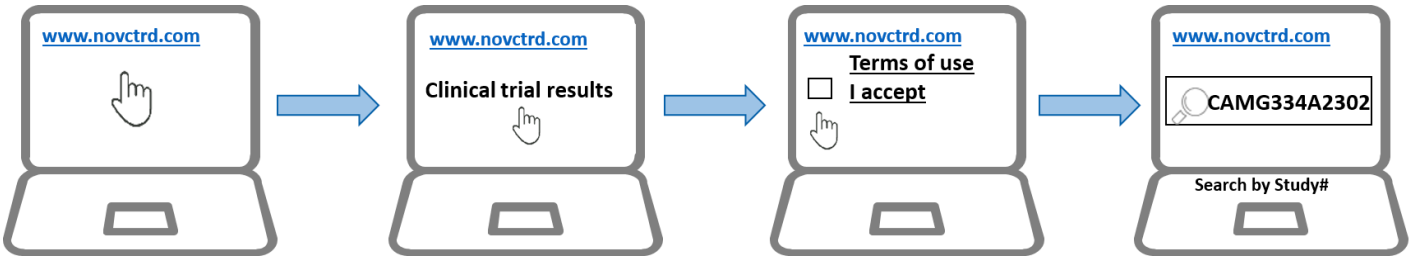
How was this trial useful?

This trial helped researchers learn about the effects of erenumab in preventing migraine headaches. Participants who took monthly doses of 70 mg or 140 mg erenumab injections had fewer episodic migraine headache days per month compared to participants who took placebo. Therefore, erenumab was effective at reducing the number of migraines that participants had. The effect seen with erenumab was comparable to that seen in previous erenumab studies. Data from this trial was used to characterize the effects of erenumab in this population and to support registration in Asia.

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 website:

- www.clinicaltrials.gov Use the NCT identifier NCT03333109 in the search field.

Full clinical trial title: A 12-week double-blind, randomized, multi-center study comparing the efficacy and safety of once-monthly subcutaneous AMG334 against placebo in adult episodic migraine patients (EMPOwER)

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.

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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