Clinical Study RESULTS

Biogen

Research Sponsor:	Convergence Pharmaceuticals Ltd., a Biogen Company
Drug Studied:	BIIB074 (vixotrigine)
ClinicalTrials.gov Identifier:	NCT02917187
Protocol Number:	1014802-205
Study Dates:	September 09, 2016 to January 05, 2017
Short Study Title:	A Study of BIIB074 in the Treatment of Erythromelalgia

Thank you!

Convergence Pharmaceuticals Ltd. (now owned by Biogen), the sponsor of this study, is grateful for your participation in this clinical study. We believe it is important to share the overall results of this study with the participants.

As a study participant, you belong to a large community of clinical research participants around the world who help researchers answer important health questions and evaluate potential new medical treatments.

The clinical study for investigational drug, BIIB074 (also known as vixotrigine), helped researchers learn more about its safety and learn more about whether BIIB074 might help people with primary inherited erythromelalgia (EM).

If you have questions, please speak with the doctor or staff at the study research center.

Why was the research needed?

Researchers are looking for additional treatments to help people with primary inherited erythromelalgia (EM). EM is a rare and painful disease that causes burning pain, skin redness, and increased skin temperature, usually in the feet and in the hands. The pain can happen long term or in short episodes. To date, most pain treatments have not been effective for EM.

In this study, researchers studied an investigational drug called BIIB074 (also known as vixotrigine). BIIB074 has been tested in healthy volunteers for safety and in participants with other types of nervous system pain for pain reduction. This was the first BIIB074 study in participants with EM. Researchers wanted to see if BIIB074 would work better than a placebo at lowering the pain of sudden EM pain attacks. A placebo looks like the study drug but contains no real medicine. Comparing the effects with those of a placebo helps researchers learn whether the study drug works.

Researchers wanted to learn:

- Could repeated doses of BIIB074 effectively treat sudden attacks of EM pain?

What happened during the study?

This study took about 4 months to complete. It began in September 2016 and ended in January 2017. The study included 8 participants, 7 of which completed the study, at 5 research centers in the United States. Men and women between the ages of 23 years and 87 years participated. When the study ended, Convergence Pharmaceuticals, now owned by Biogen, reviewed the data and created a report of the results. This is a summary of that report.

The study drug, BIIB074, was tested in participants with EM and a family history of EM. Participants included in this study already tried at least one different treatment for EM that did not work for them or that they could not tolerate.

Before the study began, the researchers asked about the participants' medical history and current medications. The researchers:

- Took blood and other lab samples.
- Checked each participant's heart condition with a test called an electrocardiogram (ECG).

- Took vital signs and performed physical examinations for each participant.

This study was 'double-blinded' which means that no participants and no people involved in the study, not even the study doctor or staff, knew in which order participants were receiving BIIB074 or placebo during the study.

Once selected to participate in the study, every participant received placebo for 2 weeks. Then they entered **Dosing Period 1** and were evenly split into 2 groups:

- 50% of participants were given **BIIB074**
- 50% of participants were given **placebo**

The participants took tablets of BIIB074 or placebo 3 times a day for 4 weeks.

All participants then took placebo for 2 weeks, which allowed the treatments from Dosing Period 1 to wash out of their bodies.

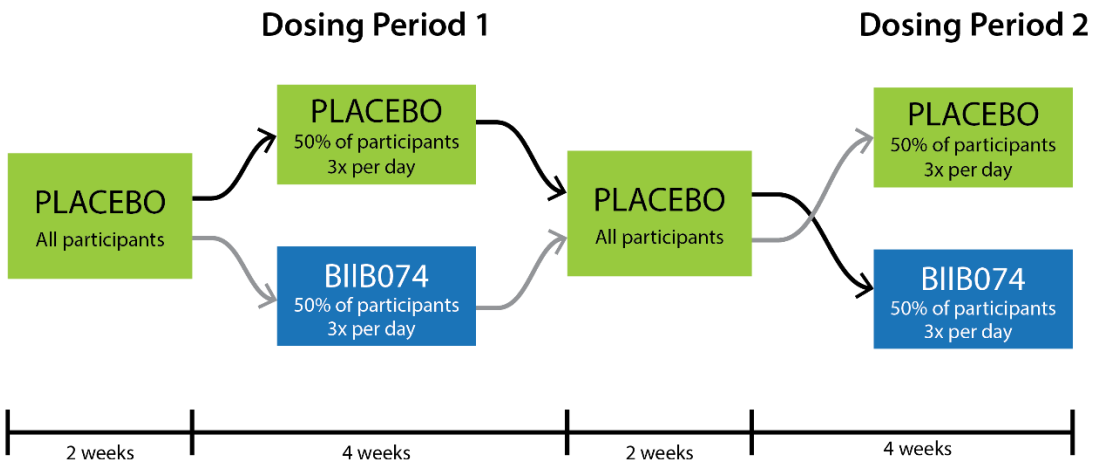
Participants then entered **Dosing Period 2,** but the assigned treatment was switched between the groups:

- Those given **BIIB074 in Dosing Period 1** received **placebo in Dosing Period 2**
- Those given **placebo in Dosing Period 1** received **BIIB074 in Dosing Period 2**

During Dosing Period 2, participants took tablets of BIIB074 or placebo 3 times a day for 4 weeks. After treatment was completed in each part of the study, follow-up appointments with researchers occurred during 7-10 day period.

The figure below shows how the study was done:

Study Design



What were the study results?

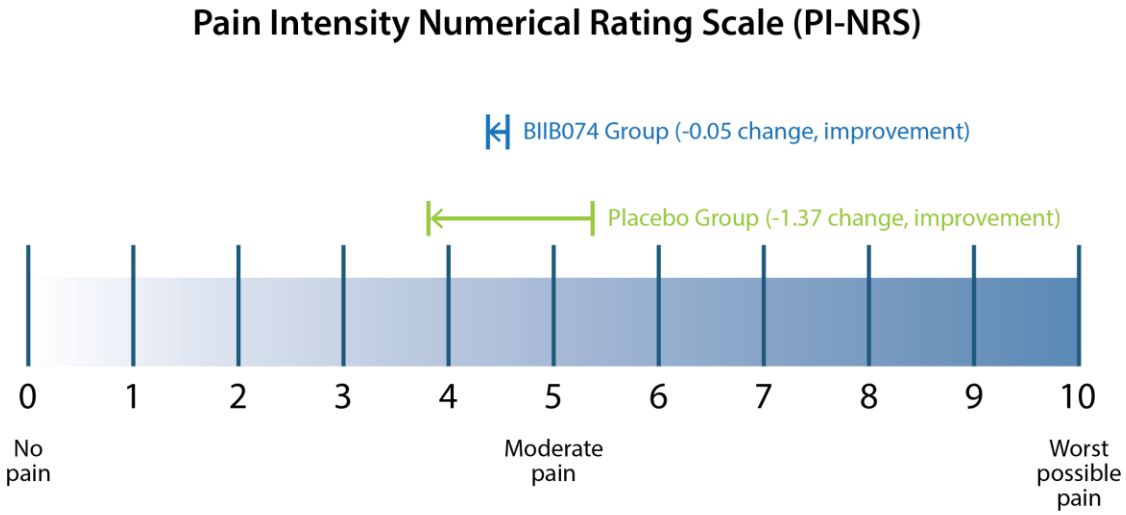
The key question researchers wanted to answer was:

- Could repeated doses of BIIB074 effectively treat sudden attacks of EM pain?

Based on the 7 participants who completed the study, researchers were not able to say that BIIB074, at the dose studied, had any noticeable effect on sudden attacks of EM pain.

Pain was rated by having participants score their daily pain, using a 0-to-10 scale called the Pain Intensity Numerical Rating Scale (PI-NRS). A pain diary recorded the pain rating participants felt for every attack. A PI-NRS rating of 0 = no pain, 10 = the worst possible pain. Each attack was recorded, based on the strength of the pain.

Researchers investigated whether BIIB074, at the dose studied, could effectively treat sudden attacks of EM pain by looking at the average weekly pain caused by the pain attacks over the course of the study. The weekly average pain was defined as the total of pain scores during a week divided by the total number of episodes during that week.



The average change in participants' PI-NRS scores during the study was a **0.05 decrease** in pain score while taking BIIB074 and a **1 .37 decrease** in pain score while on placebo. Based on these findings, researchers judged that the results did not show that BIIB074, at the dose studied, was effective at treating EM pain.

The study results may or may not have been affected by several things, such as:

1. The number of participants was smaller than originally planned.
2. Since EM is rare, the participants in this study were from a limited group.
3. Many of the participants had already been involved in other studies, which could have changed the way they rated their pain.
4. In the group that received BIIB074 before placebo, the average age and weight was higher than the group that received placebo before BIIB074.
5. Since some patients with EM experience more, or worse, pain attacks when the weather is warm, it is possible that differences in the weather, during the periods when subjects took BIIB074 and placebo, may have masked a possible beneficial effect of the drug.

What adverse events did participants have?

A lot of research is needed to know whether a drug causes a medical problem, also called an adverse event. Not everyone experiences an adverse event, and adverse events may or may not be related to the study drug. When new drugs are being studied, researchers keep track of all adverse events that participants have both during and after the study is completed.

An adverse event is considered serious when it results in death, is life-threatening, causes lasting problems, or requires hospital care. One of the objectives of this study was to learn more about the adverse events of BIIB074.

In this study, BIIB074 was well tolerated, and the safety profile was similar to other BIIB074 studies that had been completed in the past.

How many participants taking BIIB074 had adverse events?

The table below shows how many participants had adverse events and how many participants had serious adverse events.

Participants with Adverse Events and Serious Adverse Events During This Study

Adverse Events/Serious Adverse Events During This Study	BIIB074 out of 8 participants	Placebo out of 7 participants
How many participants had adverse events?	1 (12.5%)	2 (28.6%)
How many participants had serious adverse events?	0	0
How many participants had to stop treatment due to adverse events?	0	0

Eight participants were enrolled in this study and received BIIB074. Only 7 received placebo, because 1 participant in this group chose to drop out of the study during Dosing Period 1.

There were no serious adverse events and no adverse events that led to participants dropping out of the study. There were no deaths in this study.

This table shows all the adverse events that happened during the study.

Adverse Events During This Study		
Adverse Events During This Study	**BIIB074** out of 8 participants	**Placebo** out of 7 participants
Animal bite	1 (12.5%)	0
Ear pain	0	1 (14.3%)
Headache	0	1 (14.3%)
Nausea	0	1 (14.3%)
Rash	0	1 (14.3%)
Infection of tonsils	0	1 (14.3%)

Adverse events were reported by 1 out of 8 participants while on BIIB074 and by 2 out of 7 participants while on placebo. One participant reported 3 adverse events (ear pain, headache, and rash) that were determined as related to placebo; no other adverse events were considered related to BIIB074 or placebo.

Where can I learn more about the study?

You can find more information about this study online at www.clinicaltrials.gov. Once on the site, type **NCT02917187** into the search box and click "**Search**".

If you have questions about BIIB074 or the results of this study, please speak with the doctor or staff at the study research center.

Official study title: An Exploratory, Randomized, Double-Blind, Crossover Study to Compare the Efficacy and Safety of BIIB074 Versus Placebo in the Treatment of Primary Inherited Erythromelalgia

Biogen, the sponsor of this study, has its headquarters in Cambridge, Massachusetts (USA).

The results presented here are for a single research study. You should not make changes to your therapy based on these results without first consulting your doctor. Further clinical studies with BIIB074 are ongoing.

Thank you.

Biogen
225 Binney Street
Cambridge, MA 02142
USA
ClinicalTrials@Biogen.com