Clinical Study Results

Research Sponsor:	Biogen
Drug Studied:	BIIB074 (Vixotrigine)
ClinicalTrials.gov Identifier:	NCT02935608
EudraCT Number:	2015-004775-78
Protocol Number:	1014802-203
Study Dates:	October 2016 to August 2018
Short Study Title:	A study to learn if vixotrigine is safe and reduces nerve pain in patients with painful lumbosacral radiculopathy (PLSR)

Thank you!

A clinical study participant belongs to a large community of clinical research participants around the world.

By taking part in a study, participants may help researchers answer important health questions, learn more about a condition, or evaluate new potential medical treatments.

This clinical study for the drug vixotrigine helped researchers learn more about the safety of vixotrigine and if it reduces pain from PLSR. Vixotrigine is also known as BIIB074.

Biogen, the sponsor of this study, is grateful to those who took part. We believe it is important to share the overall results of the study. If you have questions, please speak with the doctor or staff at your study research center.

Why was the research needed?

Researchers are looking for other treatments to help patients who have pain from lumbosacral radiculopathy, also known as PLSR. The study looked at different types of pain due to PLSR, but was especially focused on nerve pain from PLSR. People with PLSR can have nerve, muscle, and other types of pain. People with PLSR have a pinched or irritated nerve in their lower back. This can cause pain that spreads from the lower back and into the legs.

The study drug, vixotrigine, was designed to help block some of the signals of nerve pain that the brain receives in patients with PLSR. In this study, the researchers wanted to know if vixotrigine reduced pain from PLSR. The researchers compared 2 different doses of vixotrigine to a placebo. A placebo looks like the study drug but does not have any medicine in it. The researchers used a placebo to help make sure the effects they found in the study were actually caused by vixotrigine.

The main questions the researchers wanted to answer were:

- Did patients with PLSR have less leg pain after taking vixotrigine?
- What adverse events did the patients have? Adverse events are medical problems that may or may not be caused by the study drug.

What happened during the study?

This study took almost 2 years to complete. It initially included 502 patients at 57 research centers in Austria, Belgium, Bulgaria, the Czech Republic, Estonia, France, Georgia, Italy, Latvia, the Netherlands, Romania, Serbia, Slovakia, Spain, and the United Kingdom. At the start of the study, the age range of the patients was 20 years to 75 years. The patients in this study had PLSR according to their doctor and met other criteria.

When the study ended, the sponsor Biogen reviewed the data and created a report of the results. This is a summary of that report.

Before the study began, the doctors examined each patient and checked to make sure they could join the study. This part of the study took about 4 weeks. The doctors checked each patient's heart rhythm using an electrocardiogram, also called an ECG. The doctors also checked each patient's PLSR-related pain, which the patients put into an electronic diary during the study. The researchers also asked about the patients' medical history, took laboratory samples, and performed other assessments and exams.

During treatment, 502 patients took the placebo for the first 2 weeks. During this time, the patients had to stop taking certain pain medicines. If the patients still met pain criteria during most of the 2 weeks, then they could continue in the study.

After the first 2 weeks were done, 424 patients took 1 of the 2 doses of vixotrigine or the placebo as a tablet for about 12 weeks. This part of the study was "double-blind". This means that the patients, study doctors, and study nurses did not know which treatment the patients took. The sponsor also did not know. A computer program randomly chose the treatment each patient took.

The doses of vixotrigine were measured in milligrams, also called mg. The patients took 1 of 3 treatments:

- the placebo twice a day
- 200 mg of vixotrigine twice a day
- 350 mg of vixotrigine twice a day

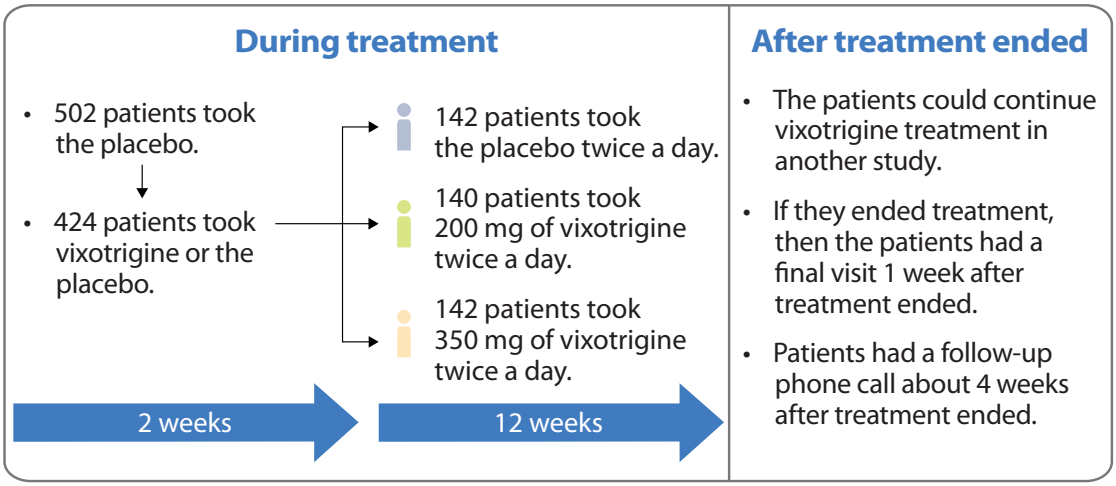
During the main part of the study, the patients visited their research center about 5 times. At these visits, the study doctors:

- checked each patient's health and asked how each patient was feeling and what medicines they were taking
- took blood and urine samples
- measured each patient's blood pressure, heart rate, breathing rate, and temperature
- checked each patient's heart rhythm using an ECG
- reviewed the patients' electronic diaries to check the patients' daily PLSR symptoms

Throughout the study, the patients used an electronic diary to keep track of their leg and lower back pain, how much it caused problems with their sleep, and when they took their study treatment. The patients also answered survey questions about their pain from PLSR, how PLSR was affecting their daily lives, and any medical problems they were having.

After the treatment ended, the patients had the option of continuing vixotrigine treatment in another study. If they decided not to, the patients returned to the research center for a final visit about 1 week after their last study treatment. These patients also had a follow-up phone call about 4 weeks after their last study treatment.

The figure below shows how the study was done.



What were the study results?

Below is an overall summary of the results and the key questions the researchers asked during the study.

The results shown below include information for the 424 patients in the study who took vixotrigine or the placebo after the first 2 weeks of the study.

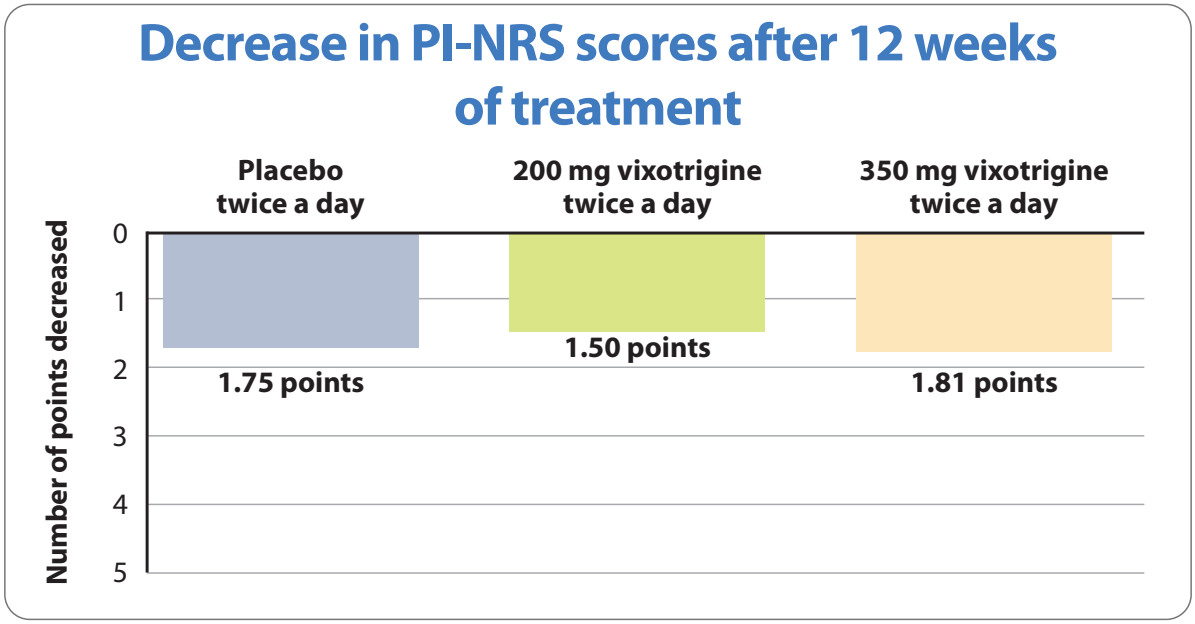
Did patients with PLSR have less leg pain after taking vixotrigine?

To answer this question, the patients reported their PLSR pain using a scale called the pain intensity numerical rating scale, also known as the PI-NRS. The patients used the PI-NRS to rate their leg and lower back pain on a scale from 0 to 10. A 0 on the scale meant the patient had no pain, while a 10 on the scale meant the patient had the worst pain they could imagine. The patients entered their leg and lower back pain scores in their electronic diary throughout the study. The patients did this before the main part of the study, and while they took their study treatment for 12 weeks. The researchers then looked at the change in this score in each treatment group. A larger decrease in the score meant that the patients had more improvement after treatment.

The researchers found that after 12 weeks of treatment, the patients' leg pain scores decreased by:

- 1.75 points in the patients who took the placebo twice a day
- 1.50 points in the patients who took 200 mg of vixotrigine twice a day
- 1.81 points in the patients who took 350 mg of vixotrigine twice a day

The graph below shows the decrease in leg pain scores after 12 weeks of treatment. The researchers found that all of the treatment groups had less leg pain after treatment. But the researchers could not confirm if patients who took vixotrigine had less pain from PLSR compared to patients who took the placebo.



What adverse events did the patients have?

A lot of research is needed to know whether a drug causes a medical problem, also called an adverse event.

Learning about adverse events was one of the goals of this study. When drugs are being studied, researchers keep track of all adverse events that patients have. This includes during the study and after it ends. Not everyone experiences them, and they may or may not be caused by the study drug.

The results shown below include information for the 424 patients in the study who took vixotrigine or the placebo after the first 2 weeks of the study.

How many patients had adverse events in this study?

The table below shows how many patients in each treatment group had adverse events during the study.

Adverse events during this study

Adverse events during this study	Placebo twice a day Out of 142 patients (%)	200 mg vixotrigine twice a day Out of 140 patients (%)	350 mg vixotrigine twice a day Out of 142 patients (%)
How many patients had adverse events?	36 (25%)	34 (24%)	40 (28%)
How many patients had serious adverse events?	1 (1%)	2 (1%)	1 (1%)
How many patients had to stop treatment because of adverse events?	1 (1%)	5 (4%)	4 (3%)

What serious adverse events did the patients have?

An adverse event is considered "serious" when it results in death, is life-threatening, causes lasting problems, or requires hospital care. An adverse event may also be considered "serious" when the study doctor thinks it is medically important.

The table below shows the serious adverse events that patients had in this study. Some of the patients had more than 1 serious adverse event.

Serious adverse events during this study

Serious adverse events during this study	Placebo twice a day Out of 142 patients (%)	200 mg vixotrigine twice a day Out of 140 patients (%)	350 mg vixotrigine twice a day Out of 142 patients (%)
Alcoholism (condition of being addicted to drinking alcohol)	0 (0%)	1 (1%)	0 (0%)
Alcohol poisoning	0 (0%)	1 (1%)	0 (0%)
Alcohol withdrawal syndrome (condition that happens when someone who drinks a heavy amount of alcohol suddenly quits drinking)	0 (0%)	1 (1%)	0 (0%)
Herniated disc (condition where the soft center of a spinal disc pushes out through its tough, outer layer)	1 (1%)	0 (0%)	0 (0%)
Mini-stroke	0 (0%)	1 (1%)	0 (0%)
Serious dizziness	0 (0%)	0 (0%)	1 (1%)

Study doctors thought the serious adverse event of dizziness was related to study treatment. Study doctors did not think any of the other serious adverse events were related to study treatment.

None of the patients died during this study.

What were the most common adverse events?

The most common adverse events were headache, common cold, diarrhea, and dizziness.

The table below shows all of the adverse events that happened in at least 2% of the patients in any treatment group. All other adverse events happened in fewer than 2% of the patients.

Most common adverse events during this study

Adverse events	Placebo twice a day Out of 142 patients (%)	200 mg vixotrigine twice a day Out of 140 patients (%)	350 mg vixotrigine twice a day Out of 142 patients (%)
Headache	5 (4%)	3 (2%)	3 (2%)
Common cold	6 (4%)	2 (1%)	2 (1%)
Diarrhea	4 (3%)	0 (0%)	3 (2%)
Dizziness	1 (1%)	3 (2%)	3 (2%)
Constipation	3 (2%)	1 (1%)	1 (1%)
Increased levels of alanine aminotransferase (sign of liver damage)	0 (0%)	1 (1%)	4 (3%)
Pain in the muscles, bones, ligaments, or tendons	2 (1%)	0 (0%)	3 (2%)
Fall	3 (2%)	0 (0%)	1 (1%)
Pain in the limbs	3 (2%)	0 (0%)	1 (1%)
Increased levels of aspartate aminotransferase (sign of liver damage)	0 (0%)	0 (0%)	3 (2%)
Joint pain	3 (2%)	0 (0%)	0 (0%)

Where can I learn more about the study?

You can find more information about the study online at www.clinicaltrials.gov. Once on the site, type **"NCT02935608"** into the search box and click **"Search".**

You can also find more information online at www.clinicaltrialsregister.eu. Once on the site, click **"Home and Search"** then type **"2015-004775-78"** in the search box and click **"Search"**.

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

Official study title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of BIIB074 in Subjects With Neuropathic Pain From Lumbosacral Radiculopathy

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

The results presented here are from a single study. Do not make changes to your therapy based on these results without first consulting your doctor. Further studies with vixotrigine in PLSR are not going on.

Thank you!

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The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP helped prepare this summary of the study results. CISCRP is not involved in recruiting participants for clinical trials, nor is it involved in conducting clinical trials.

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