

Clinical Study Results

Study Sponsor: UCB Biopharma SPRL

Treatments Studied: Levetiracetam and carbamazepine

Protocol Number: N01061

Short Study Title: A study to learn if levetiracetam works when taken by itself in people with newly diagnosed epilepsy who have focal seizures or grand mal seizures

Thank you!

UCB thanks all the participants of this study. All the participants helped the researchers learn more about using levetiracetam in people with epilepsy.

This is a summary of the main results of this study. An independent, non-profit organization called CISCRP helped prepare this summary of the study results.

We think it is important to share the results with the participants and the public. We hope this summary helps the participants understand and feel proud of their important role in medical research.

The purpose of this summary is only to share information. If you need medical advice, please contact your doctor. If you participated in this study and have questions about the results, please speak with your study doctor or the study staff.

Why was the research needed?

Before a treatment is available to all patients, researchers do clinical studies to get information about how well the treatment works and about how safe it is.

The researchers in this study wanted to learn if levetiracetam worked in a large number of participants with recently diagnosed epilepsy. They also wanted to learn if the participants had any medical problems during the study.

People with epilepsy have seizures that happen again and again. Seizures are caused by uncontrolled electrical activity in the brain. Levetiracetam helps to reduce uncontrolled electrical activity in the brain that causes seizures.

Some seizures start in just 1 part of the brain. These are called focal seizures, also called partial onset seizures. The term focal seizures is used in this summary.

There are other types of seizures that seem to start in both sides of the brain at once. The most severe type of these seizures is a generalized tonic clonic seizure, also called a grand mal seizure. The term grand mal seizure is used in this summary.

The participants in this study had focal seizures or grand mal seizures. The researchers in this study wanted to find out if levetiracetam worked when taken by itself. They compared levetiracetam to an anti-seizure medicine called carbamazepine. When the study started, doctors often used carbamazepine by itself as the first treatment for patients' seizures. Carbamazepine was also the medicine that many researchers chose to compare with other treatments for seizures.

What were the main questions studied?

The main questions the researchers wanted to answer in this study were:

- How many participants did not have seizures for 6 months in a row?
- What medical problems did the participants have during the study?

Who participated in the study?

Males and females with recently diagnosed epilepsy participated in this study. They were 15 to 82 years old.

In this study, the researchers planned to include participants who:

- Had at least 2 focal seizures or grand mal seizures in the year before the study. The seizures had to be at least 48 hours apart.
- Had at least 1 focal or grand mal seizure in the 3 months before starting the study.
- Had never taken levetiracetam or carbamazepine before.
- Weighed at least 40 kilograms.

The study included 576 participants who took study treatments in 13 countries: Belgium, the Czech Republic, Finland, France, Germany, Hungary, Italy, the Netherlands, Poland, South Africa, Spain, Sweden, and the United Kingdom.

Each participant was in the study for up to a little more than 2 years, but the whole study lasted about 3 years. The study started in June 2002 and ended in July 2005.

What treatments did the participants take?

The participants in this study took levetiracetam or carbamazepine as pills. Doses were measured in milligrams, also called mg.

The researchers used a computer program to randomly choose if the participants took levetiracetam or carbamazepine. This helped make sure the treatments were chosen fairly and that comparing the results of the treatments was as accurate as possible.





None of the participants, study doctors, or study staff knew what treatment each participant was taking. UCB staff also did not know. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study. After the study was completed, UCB learned what treatment each participant took so they could create a report of the results.

The number of pills each participant took each day might have been different based on which study treatment they were taking. To make sure that the participants did not know which study treatment they were taking, the doctors sometimes had the participants take a placebo. The placebo looked just like the study treatment but did not have any study treatment in it. Taking the placebo and the study treatment together meant that the number of pills the participants took was the same each day.

In this study:

- 285 participants took levetiracetam
- 291 participants took carbamazepine

The chart below shows the treatments planned for this study:






 The participants took levetiracetam twice each day for up to 121 weeks.	 The participants took carbamazepine twice each day for up to 121 weeks.
 The dose of levetiracetam was 1,000 mg to 3,000 mg each day.	 The dose of carbamazepine was 400 mg to 1,200 mg each day.

What happened during the study?

This section shows how the study was planned to be done.

Before the study started, all the participants first learned about this study and then decided to join. This is called “informed consent.” Then the study doctors and study staff asked the participants about their medical history and checked their health to make sure they could stay in the study.


During the study:

	The participants kept track of their seizures every day using diaries.
	The participants had clinic visits about every 1 to 3 months.
	The study doctors kept track of any medical problems reported by the participants or observed by the doctors or study staff.
	The participants gave blood and urine samples at some clinic visits.
	The participants had electrocardiograms, also called ECGs. These are tests that record the electrical activity in the heart.

The study had 3 main parts:

Part 1 lasted for 3 weeks. During Part 1, the doses of study treatments were slowly increased during the first 2 weeks to reach either:

 1,000 mg of levetiracetam each day


 400 mg of carbamazepine each day

After this, the participants stayed on this dose for 1 week.

Part 2 lasted from about 6 months to 1.5 years.

At first, the participants in Part 2 took either:

 1,000 mg of levetiracetam each day

 400 mg of carbamazepine each day

Clinical Study Results

The participants stayed on these study treatments for 26 weeks unless they had a seizure.

If they had a seizure, the study doctors could slowly adjust their treatment doses. They could increase the doses as high as:

 3,000 mg of levetiracetam each day

 1,200 mg of carbamazepine each day

The participants who did not have a seizure for 26 weeks on their final adjusted dose could join Part 3.

Part 3 lasted about 6 months. During Part 3, the participants continued to take levetiracetam or carbamazepine each day.

After Part 3, some participants entered other levetiracetam studies. These participants either:

- Joined another study right away.
- Stayed in this study and took levetiracetam for 2 to 6 more weeks before joining another study.

The participants who did not join another study took a lower and lower dose of study treatment for 1 to 5 weeks until they stopped taking it. The participants had a clinic visit 2 weeks after they stopped taking their study treatment. Then they left this study.

What were the results of this study?

This is a summary of the main results from this study. These are the results from all the participants combined. The individual results of each participant might be different and are not in this summary.

Deciding which treatments work best usually takes results from several studies. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

The researchers included 472 of the 576 participants in the results shown below. They did not include participants who had important changes from the study plan that might have affected the conclusions about the study results. The researchers decided what type of changes might affect their conclusions before they looked at the study results.

How many participants did not have seizures for 6 months in a row?

The researchers wanted to learn if the percentage of participants who had no seizures for 6 months in a row was similar or higher in participants who took levetiracetam compared with participants who took carbamazepine.

To find this percentage, the researchers asked the participants to record the number of seizures they had during Part 2 in their diaries. The researchers counted the number of participants who had no seizures for 6 months in a row on either their original dose, or their final adjusted dose of study treatment.

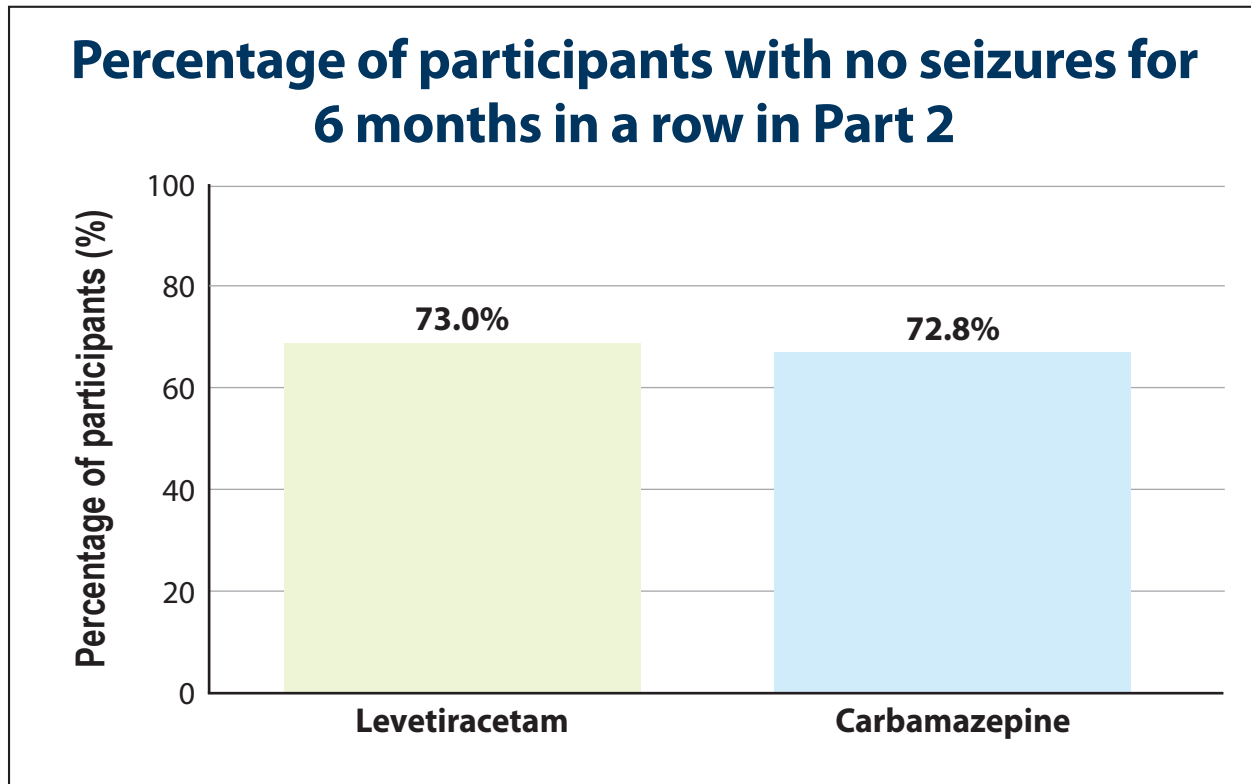
Using mathematical methods, the researchers learned that levetiracetam helped control the participants' seizures about the same as or more than carbamazepine did.

The researchers found that:

- 73.0% of the participants who took levetiracetam did not have seizures for 6 months in a row. This was 173 of 237 participants.
- 72.8% of the participants who took carbamazepine did not have seizures for 6 months in a row. This was 171 of 235 participants.

Clinical Study Results

The graph below shows these results:



What medical problems did the participants have?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the treatments. These medical problems are called “adverse reactions.” Some participants had more than 1 adverse reaction.

An adverse reaction is considered “serious” when it puts the participant’s life at risk, requires hospitalization, causes disability, causes a baby being born with medical problems, or may have turned into one of these problems if not treated.

The adverse reactions shown in this summary may or may not be caused by the treatments in the study. The results from several studies are needed to decide if a treatment causes an adverse reaction.

In this study, adverse reactions include seizures that got worse during the study.

Clinical Study Results

How many participants had serious adverse reactions?

During the study, serious adverse reactions happened in:

- 1.1% of the participants who took levetiracetam. This was 3 out of 285 participants.
- 3.4% of the participants who took carbamazepine. This was 10 out of 291 participants.

None of the participants died due to serious adverse reactions during the study.

What serious adverse reactions did the participants have?

The table below shows the serious adverse reactions that happened during the study. One participant had more than 1 serious adverse reaction. This participant had serious adverse reactions of pregnancy while taking birth control pills and abortion done by choice.

Serious adverse reactions during the study

	Levetiracetam (out of 285 participants)	Carbamazepine (out of 291 participants)
Abortion done by choice	0.0% (0)	0.3% (1)
<u>Blockage of electrical activity in the heart (complete)</u>	0.4% (1)	0.0% (0)
Depression	0.4% (1)	0.0% (0)
Diarrhea	0.4% (1)	0.0% (0)
<u>Feeling of spinning</u>	0.0% (0)	0.3% (1)
<u>Focal seizures</u>	0.0% (0)	0.3% (1)
<u>Increased sensitivity of the body</u>	0.0% (0)	0.3% (1)
Intentional overdose	0.0% (0)	0.3% (1)
Joint swelling	0.0% (0)	0.3% (1)
<u>Lessened blood flow to the limbs</u>	0.0% (0)	0.3% (1)
<u>Liver disease causing cell death</u>	0.0% (0)	0.3% (1)
<u>Pregnancy while taking birth control pills</u>	0.0% (0)	0.3% (1)
<u>Rare, severe problem with the skin and mucous membranes</u>	0.0% (0)	0.3% (1)
<u>Swelling and irritation of the gall bladder</u>	0.0% (0)	0.3% (1)

Clinical Study Results

How many participants had any adverse reactions?

The results below include Parts 1, 2, and 3 of the study.

During Parts 1, 2, and 3, adverse reactions that were serious or not serious happened in:

- 49.8% of the participants who took levetiracetam. This was 142 out of 285 participants.
- 56.4% of the participants who took carbamazepine. This was 164 out of 291 participants.

What adverse reactions did the participants have?

During Parts 1, 2, and 3 of the study:

- Tiredness and sleepiness were the most common adverse reactions for the participants who took levetiracetam.
- Tiredness and headache were the most common adverse reactions for the participants who took carbamazepine.

The table below shows the adverse reactions that happened in 5% or more of participants in either group during Parts 1, 2, and 3 of the study. This means they happened in at least 1 out of every 20 participants. There were other adverse reactions, but they happened in fewer participants.

Adverse reactions in 5% or more of participants in either group during Parts 1, 2, and 3

	Levetiracetam (out of 285 participants)	Carbamazepine (out of 291 participants)
<u>Tiredness</u>	14.4% (41)	13.1% (38)
Headache	7.0% (20)	13.1% (38)
<u>Sleepiness</u>	11.2% (32)	8.6% (25)
Dizziness	8.1% (23)	11.0% (32)
Nausea	5.6% (16)	8.9% (26)
Weight increased	2.5% (7)	5.8% (17)
Rash	2.8% (8)	5.2% (15)

How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using levetiracetam by itself in people who have newly diagnosed epilepsy with focal seizures or grand mal seizures. The results might be used in other studies to compare levetiracetam with other treatments for people who have a similar condition.

Deciding which treatments work best for patients almost always takes results from several studies. This summary shows only the main results from this one study. Other studies may provide new information or different results.

The purpose of this summary is only to share information. If you need medical advice about your own health or situation, please contact your physician.

When this study ended, further clinical studies with levetiracetam were planned.

Where can I learn more about this study?

You can find more information about this study at the website listed below:

- <https://clinicaltrials.gov/ct2/show/NCT00150735>

If you have questions about this study, you can contact UCB by e-mail at datasharing@ucb.com.

Study Information

Protocol Number: N01061

Study Sponsor: UCB Biopharma SPRL sponsored this study. It was previously called UCB S.A. and is referred to as UCB in this summary.

Full Study Title: A multicenter, double-blind, randomized, parallel-group, positive-controlled trial comparing the efficacy and safety of levetiracetam (1000 to 3000 mg/day oral b.i.d.) to carbamazepine (400 to 1200 mg/day oral b.i.d.), used as monotherapy for up to a maximum of 121 weeks in subjects (≥ 16 years) newly or recently diagnosed as suffering from epilepsy, and experiencing partial or generalized tonic-clonic seizures.

National Clinical Study Number: NCT00150735

Thank you!

The participants in clinical studies belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

Glossary

Abortion done by choice:	An abortion is the ending of a pregnancy by removing a baby that's not fully formed from the mother's body. An abortion done by choice is called an induced abortion. Also called "abortion induced."
Blockage of electrical activity in the heart (complete):	A complete blockage of electrical activity between parts of the heart. Also called "atrioventricular block complete."
Feeling of spinning:	Also called "vertigo."
Focal seizures:	Seizures that start in just one part of the brain. Also called "partial seizures."
Increased sensitivity of the body:	An unwanted reaction of the body's defense system, also called the immune system. Also called "hypersensitivity."
Lessened blood flow to the limbs:	When blood flow to the limbs is less than usual. The limbs are the legs and arms. This lessened blood flow is also called "peripheral ischemia."
Liver disease causing cell death:	Also called "cytolytic hepatitis."
Pregnancy while taking birth control pills:	Also called "pregnancy on oral contraceptive."
Rare, severe problem with the skin and mucous membranes:	A rare, severe problem with the skin and mucous membranes that is called "Stevens-Johnson syndrome." Mucous membranes are parts of the body other than skin that the air touches. An example is the mucous membranes that line the lungs and mouth.
Sleepiness:	Also called "somnolence."
Swelling and irritation of the gall bladder:	Also called "cholecystitis."
Tiredness:	Also called "fatigue."



This summary was last updated on 04 September 2019.
The final clinical study report is dated 07 December 2005.