

# Clinical Study Results

**Study Sponsor:** UCB S.A. Pharma Sector

**Treatment Studied:** Levetiracetam

**Protocol Number:** N138

**Short Study Title:** A study to learn if levetiracetam reduced seizures in participants with epilepsy

## Thank you!

UCB thanks all the participants of this study. All the participants helped the researchers learn more about using levetiracetam in participants with epilepsy. Levetiracetam is also called Keppra®.

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 a doctor or 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 epilepsy. They also wanted to learn if the participants had any medical problems during the study.

Epilepsy is a brain disorder that causes seizures. The symptoms of seizures can be different for each person but often include uncontrollable shaking and loss of consciousness.

In some people with epilepsy, seizures can be controlled by taking only 1 treatment. Other people need to take more than 1 treatment at the same time to control their seizures.

## Clinical Study Results

Epileptic seizures that cannot be controlled by epilepsy medications are also known as refractory seizures or uncontrolled seizures. Researchers think that taking levetiracetam may help reduce uncontrolled seizures.

In this study, the researchers wanted to find out if taking levetiracetam alone or with other epilepsy medications helped reduce uncontrolled seizures in participants with epilepsy.

### What were the main questions studied?

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

- Did levetiracetam affect how many participants completed the study after they stopped taking their regular epilepsy medication?
- Did levetiracetam affect how many seizures the participants had per week when they took study treatment with their regular epilepsy medications?
- What medical problems did the study doctors think might be related to the study treatments?

### Who participated in the study?

There were 286 males and females with epilepsy who participated in this study and took study treatment. The participants were 17 to 70 years old.

The study included participants who took study treatment in 11 countries: the Czech Republic, Denmark, France, Germany, Hungary, the Netherlands, Norway, Poland, Sweden, Switzerland, and the United Kingdom.

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

- Were already taking 1 epilepsy medication but were still having uncontrolled seizures
- Had at least 2 uncontrolled seizures every 4 weeks within the 12 weeks before taking study treatment, and at least 2 more seizures in the first 4 weeks of taking study treatment

Each participant was in the study for up to 14 months, but the whole study lasted for nearly 3 years. The study started in June 1995 and ended in May 1998.

### What treatments did the participants take?

The participants in this study took either levetiracetam or a placebo. They also continued to take their regular epilepsy medication. They took levetiracetam or the placebo as tablets by mouth twice a day for up to 46 weeks. The placebo tablets looked like the levetiracetam tablets but did not have any levetiracetam in them. The researchers used the placebo to help make sure the effects they found in the study were actually caused by levetiracetam.

None of the participants, caregivers, study doctors, or study staff knew what treatments 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 researchers used a computer program to randomly choose if the participants took levetiracetam or the placebo. This helped make sure the treatments were chosen fairly and comparing the results for the treatments was as accurate as possible.

The study happened in 2 Parts.

**In Part 1**, the participants took levetiracetam or the placebo in addition to their regular epilepsy medication for up to 22 weeks. During the first 4 weeks, the participants slowly increased their dose of study treatment. They did this until the participants taking levetiracetam were taking 3,000 milligrams per day, also known as mg. Then, the participants continued taking levetiracetam or the placebo for 12 weeks.

In Part 1:

- 181 participants took levetiracetam
- 105 participants took the placebo

After Part 1 ended, the study doctors looked at the results to see which participants they thought that the study treatment was helping. These participants were known as “responders”. The study doctors decided that participants were responders if the number of seizures they had in the 12 weeks of taking study treatment was less than half the number compared to the 12 weeks before Part 1 of the study.






Only the participants who were responders continued into Part 2 of the study. This was 86 participants. The participants who were not responders had their dose of study treatment slowly decreased over 4 weeks until they were taking none.

## Clinical Study Results

**In Part 2**, the participants took the same study treatment that they took in Part 1 for up to 24 weeks. During the first 12 weeks, the participants slowly decreased the dose of their regular epilepsy medication until they were taking only their study treatment. Then, the participants took levetiracetam or the placebo for 12 weeks.

In Part 2:






- 69 participants took levetiracetam
- 17 participants took the placebo

	<b>In Part 1:</b> <ul style="list-style-type: none"><li>• 181 participants took levetiracetam</li><li>• 105 participants took the placebo</li></ul>
	86 “responders” continued into Part 2
	<b>In Part 2:</b> <ul style="list-style-type: none"><li>• 69 participants took levetiracetam</li><li>• 17 participants took the placebo</li></ul>
	The participants took levetiracetam or the placebo as tablets by mouth
	The participants took 2 doses of levetiracetam or the placebo each day for up to 46 weeks

### What happened during this study?

**Before starting Part 1 of the study**, the participants visited their clinic 4 times. All the participants first learned about the 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 join the study. This part lasted up to 12 weeks.




At some of these visits, the study doctors:

	Kept track of any medical problems reported by the participants or observed by the study doctors or study staff
	Took blood samples
	Checked the participants' heart health using an electrocardiogram, also called an ECG
	Checked the participants' brain health using an electroencephalogram, also called an EEG
	If needed, took pictures of each participants' brain using CT or MRI scans

The study doctors also did some of these tests and measurements at different visits throughout the rest of the study.

**During Part 1 of the study**, the participants visited their clinic 5 times. Part 1 lasted for up to 22 weeks.

The participants:




	Took levetiracetam or the placebo twice each day, once in the morning and once in the evening
	Slowly stopped taking their regular epilepsy medication during the first 12 weeks
	Kept track of their seizures in a diary

## Clinical Study Results

The participants who were responders continued into Part 2. The participants who were not responders had their dose of study treatment slowly decreased over 4 weeks until they were taking none. These participants visited their clinic 3 times. At these visits, the study doctors checked the participants' health and asked about any medical problems they were having.

**During Part 2 of the study**, the participants who were responders visited their clinic 9 times. Part 2 lasted for up to 24 weeks.

The participants:

	Took 2 doses of levetiracetam or the placebo each day
	Slowly stopped taking their regular epilepsy medication
	Kept track of their seizures in a diary

**After Part 2 of the study**, the participants could join a different study for levetiracetam. Or, they had their dose of study treatment slowly decreased over 4 weeks, until they were taking none, and at the same time started taking their regular epilepsy medication again. The participants visited their clinic 3 times during this time. The study doctors checked the participants' health and asked about any medical problems they were having.

## What were the results of the 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.

There were 8 participants who started taking the placebo but switched to taking levetiracetam during Part 2. Their results are still included in the placebo group.

### Did levetiracetam affect how many participants completed the study after they stopped taking their regular epilepsy medication?

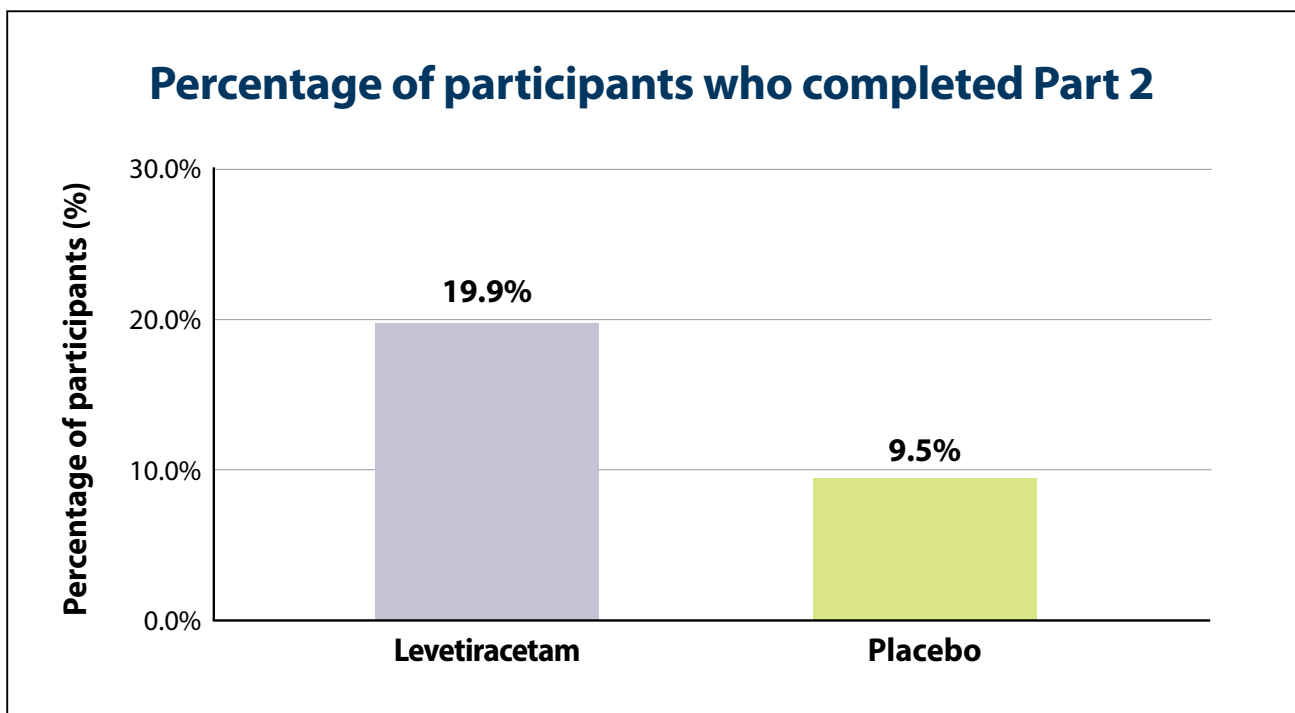
Yes. Overall, more participants who took levetiracetam completed Part 2 of the study when they stopped taking their regular epilepsy medication compared to the participants who took the placebo.

To answer this question, the study doctors looked at how many participants completed Part 2 of the study. They measured this as a percentage of how many participants started Part 1 of the study. They compared the number of participants who took levetiracetam and completed Part 2 with the number of participants who took the placebo and completed Part 2.

Overall, the study doctors found that:

- 19.9% of participants who took levetiracetam completed Part 2. This was 36 out of 181 participants who started Part 1 of the study.
- 9.5% of participants who took the placebo completed Part 2. This was 10 out of 105 participants who started Part 1 of the study.
  - 4 of these 10 participants had switched to taking levetiracetam. Their results are still included in the placebo group.

The chart below shows these results.



## Clinical Study Results

### Did levetiracetam affect how many seizures the participants had per week when they took study treatment with their regular epilepsy medications?

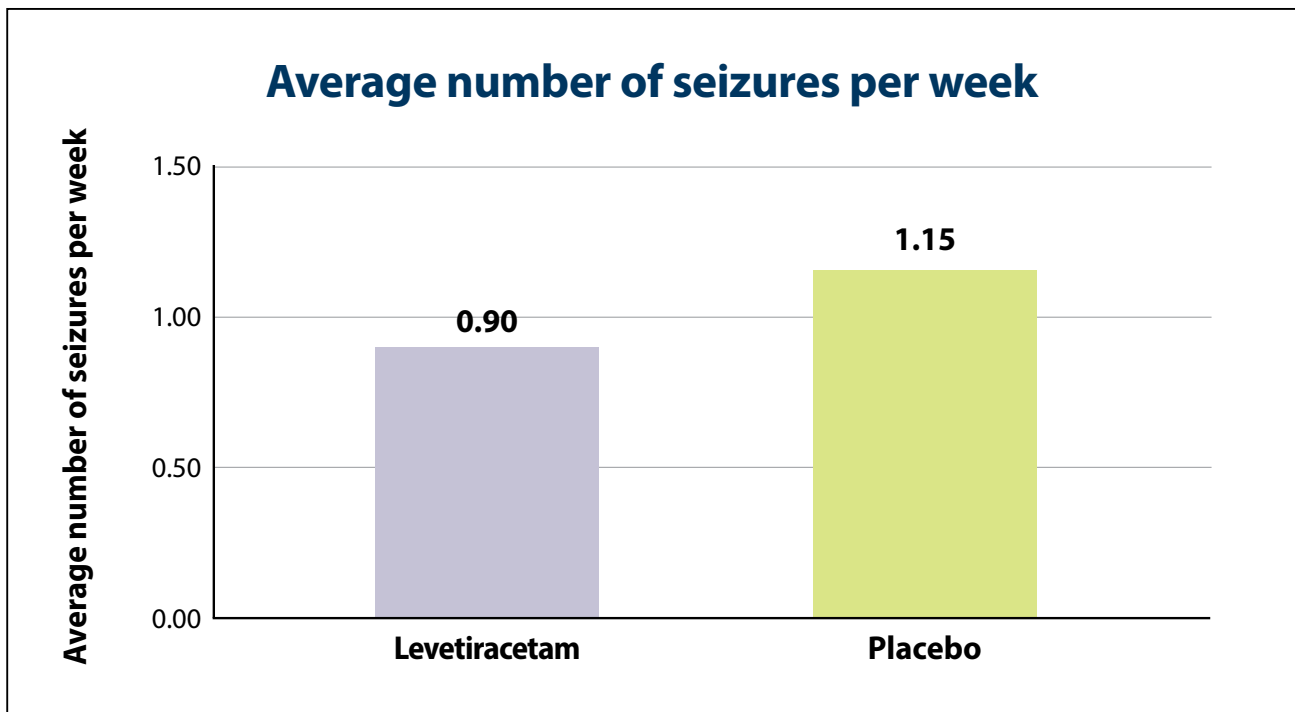
Yes. Overall, the participants who took levetiracetam had fewer seizures per week when they took study treatment with their regular epilepsy medications than the participants who took the placebo.

To answer this question, the study doctors counted the number of seizures the participants had during Part 1 of the study. Then, they estimated the average number of seizures per week.

Overall, the researchers found that the average number of seizures per week during Part 1 was:

- 0.90 seizures per week for the participants who took levetiracetam
- 1.15 seizures per week for the participants who took the placebo

The chart below shows these results.



Then, the researchers compared the average number of seizures per week in the participants who took levetiracetam and in the participants who took the placebo. The difference in the average percentage reduction between the groups was 22.2%. This means that the participants who took levetiracetam had 22.2% fewer seizures per week than the participants who took the placebo.



### What medical problems did the study doctors think might be related to the study treatments?

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. In this summary, these medical problems are called “adverse reactions”. Some participants had more than 1 adverse reaction.

This summary also includes information about serious adverse reactions. An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or requires hospital care.

Other studies may or may not show that these medical problems were related to the study treatments. The results from several studies are often needed to decide what medical problems are actually caused by a treatment. Always talk to a doctor before making any treatment decisions.

### How many participants had serious adverse reactions?

In Part 1, serious adverse reactions happened in:

- 2.8% of participants who took levetiracetam. This was 5 out of 181 participants.
- 1.9% of participants who took the placebo. This was 2 out of 105 participants.

In Part 2, serious adverse reactions happened in:

- None of the 69 participants who took levetiracetam.
- 5.9% of participants who took the placebo. This was 1 out of 17 participants.

None of the participants died due to serious adverse reactions.

### What serious adverse reactions did the participants have?

The table below shows the serious adverse reactions that happened during Part 1 and Part 2 of the study. Some of the participants may have had more than 1 serious adverse reaction. The most common serious adverse reaction was a seizure.

Serious adverse reactions during the study				
Serious adverse reaction	Part 1		Part 2	
	Levetiracetam (out of 181 participants)	Placebo (out of 105 participants)	Levetiracetam (out of 69 participants)	Placebo (out of 17 participants)
Seizure	1.7% (3)	0.0% (0)	0.0% (0)	0.0% (0)
Increased liver enzymes	0.5% (1)	0.0% (0)	0.0% (0)	0.0% (0)
<u>Miscarriage</u>	0.5% (1)	0.0% (0)	0.0% (0)	0.0% (0)
<u>Rash with both raised and flat areas</u>	0.5% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Confusion	0.0% (0)	1.0% (1)	0.0% (0)	0.0% (0)
Accidental injury because of a seizure	0.0% (0)	0.0% (0)	0.0% (0)	5.9% (1)

The participant who had a serious adverse reaction in the placebo group in Part 2 had switched to taking levetiracetam at the time of the serious adverse reaction.

### How many participants had any adverse reactions?

In Part 1, adverse reactions happened in:

- 37.0% of participants who took levetiracetam. This was 67 out of 181 participants.
- 48.6% of participants who took the placebo. This was 51 out of 105 participants.

In Part 2, adverse reactions happened in:

- 14.5% of the participants who took levetiracetam. This was 10 out of 69 participants.
- 29.4% of participants who took the placebo. This was 5 out of 17 participants.

## Clinical Study Results

### What adverse reactions did the participants have?

The table below shows the adverse reactions that happened in 5.0% or more participants in either of the treatment groups. This means they happened in at least 5 out of every 100 participants in either of the treatment groups. There were other adverse reactions, but these happened in fewer participants.

Adverse reactions in 5.0% or more of participants in either treatment group				
Adverse reaction	Part 1		Part 2	
	Levetiracetam (out of 181 participants)	Placebo (out of 105 participants)	Levetiracetam (out of 69 participants)	Placebo (out of 17 participants)
<u>Weakness or lack of energy</u>	12.7% (23)	5.7% (6)	1.4% (1)	5.9% (1)
<u>Sleepiness</u>	5.5% (10)	3.8% (4)	0.0% (0)	11.8% (2)
Dizziness	2.8% (5)	1.0% (1)	0.0% (0)	5.9% (1)
Nervousness	2.2% (4)	0.0% (0)	0.0% (0)	5.9% (1)
Headache	2.2% (4)	5.7% (6)	1.4% (1)	0.0% (0)
Seizure	2.2% (4)	3.8% (4)	2.9% (2)	5.9% (1)
Accidental injury	0.0% (0)	1.9% (2)	0.0% (0)	5.9% (1)
Abnormal thinking	0.0% (0)	0.0% (0)	0.0% (0)	5.9% (1)
<u>Lack of interest or enthusiasm</u>	0.0% (0)	0.0% (0)	0.0% (0)	5.9% (1)

### How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using levetiracetam alone and with other epilepsy medications in people with epilepsy.

Deciding which treatments work best for patients almost always takes results from several studies. This summary shows only the main results from this 1 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 doctor.

The results of this study may be used in other studies to compare levetiracetam with other treatments for people who have epilepsy.

## Clinical Study Results

At the time this study ended, further clinical studies in epilepsy with levetiracetam were planned.

### Where can I learn more about this study?

If you have questions about this study, contact information for UCB is available at [www.ucb.com/UCBCares](http://www.ucb.com/UCBCares).

### Study Information

**Protocol Number:** N138

**Study Sponsor:** UCB S.A Pharma Sector sponsored this study. It is referred to as UCB in this summary. UCB S.A. Pharma Sector is now called UCB Biopharma SRL.

**Full Study Title:** Evaluation of the efficacy and tolerability of ucb L059 (1500 mg b.i.d., 500 mg tablets) monotherapy in epileptic patients with complex partial onset seizures, having experienced improved seizure control under add-on treatment

### Thank you!

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

Description	Also called
Lack of interest or enthusiasm	Apathy
Miscarriage	Spontaneous abortion
Rash with both raised and flat areas	Maculopapular rash
Seizure	Convulsion
Sleepiness	Somnolence
Weakness or lack of energy	Asthenia



This summary was last updated on 21 May 2021.  
The final clinical study report is dated 30 November 1998.