Clinical Study Results

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Study Sponsor: UCB Biopharma SRL

Treatment Studied: Levetiracetam

Protocol Number: N01221

Short Study Title: A study to learn if levetiracetam works in Japanese participants with epilepsy who are taking their usual anti-seizure medicines

Thank you!

The study sponsor, 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 Japanese participants with epilepsy. The participants were already taking 1 to 3 anti-seizure medicines and kept taking them during the study. The researchers 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. 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 throughout this summary. When the participants joined this study, they were taking anti-seizure medicines but were still having focal seizures.

Levetiracetam helps to reduce uncontrolled electrical activity in the brain that causes seizures. At the start of this study, levetiracetam was not available in Japan as a treatment for people with epilepsy.

What were the main questions studied?

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

- Did the participants who took levetiracetam have fewer seizures?
- What medical problems did the participants have during the study?

Who participated in the study?

There were 401 male and female participants in Japan who joined the study. The researchers planned to include Japanese participants with epilepsy who:

- Had focal seizures for more than 2 years before joining the study
- Took steady doses of their usual 1 to 3 anti seizure medicines for at least 1 month before joining the study
- Had never taken levetiracetam by mouth before joining the study
- Weighed at least 40 kilograms

There were 352 participants who continued in the study after the first 12 weeks. These participants were 16 to 64 years of age.

Each participant was in the study for up to 34 weeks, but the whole study lasted for about 2 years. The study started in November 2005 and ended in November 2007.

What treatments did the participants take?

The participants in this study took levetiracetam and placebo as pills. The placebo pills looked like the levetiracetam pills but did not have any levetiracetam in them. The researchers used the placebo to help make sure the effects of levetiracetam they found in the study were actually caused by levetiracetam. The doses of levetiracetam were measured in grams, also called g.

All the participants also took their usual 1 to 3 anti-seizure medicines during the entire study. During the first 12 weeks of the study, all the participants also took the placebo each day. None of the participants knew they were taking the placebo during the first 12 weeks of the study. But the study doctors, other study staff, and UCB knew.

After the first 12 weeks of the study, 352 participants stayed in the study. The researchers used a computer program to randomly choose which study treatment each of these participants took. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible. After the first 12 weeks of the study:

- 70 participants took the placebo each day
- 282 participants took levetiracetam each day

After the first 12 weeks of the study, none of the participants, study doctors, or other study staff knew what treatment each participant was taking. UCB also did not know. This was done 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 chart below shows the treatments planned for this study.

For the first 12 weeks	After the first 12 weeks
All participants took the placebo	The participants took either: • The placebo each day • 0.5 g to 3 g of levetiracetam each day
The participants took the placebo twice each day	The participants took their study treatment twice each day for up to 20 weeks

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 the study and then decided to join. This is called “informed consent”. The study doctors and study staff then asked about their medical history and checked their health to make sure they could join the study.

During the study:

The participants kept track of their seizures every day using diaries.

The participants visited the clinic up to 10 times.

The study doctors kept track of any medical problems reported by the participants or observed by the study 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 participants kept taking their usual 1 to 3 anti-seizure medicines during the entire study.

The study had 3 main parts.

Part 1 lasted 12 weeks. During Part 1, all the participants took the placebo each day.

The participants could join Part 2 of the study if during Part 1 they:

- Had at least 12 focal seizures
- Had focal seizures at least twice every 4 weeks
- Did not change their usual 1 to 3 anti-seizure medicines

Part 2 lasted 4 weeks. During Part 2, the participants took study treatments based on the group the computer had randomly chosen for them:


Group A: The placebo each day


Group B: 0.5 g of levetiracetam each day


Group C: 1 g of levetiracetam each day


Group D: 1 g of levetiracetam each day for 2 weeks, then 2 g of levetiracetam each day for 2 weeks


Group E: 1 g of levetiracetam each day for 2 weeks, then 2 g of levetiracetam each day for 2 weeks

Part 3 lasted 12 weeks. During Part 3, the participants stayed in the same treatment groups they were in during Part 2. They took the following treatments:


Group A: The placebo each day


Group B: 0.5 g of levetiracetam each day


Group C: 1 g of levetiracetam each day


Group D: 2 g of levetiracetam each day


Group E: 3 g of levetiracetam each day

After Part 3, some of the participants joined another study where they took levetiracetam, and the rest did not. The participants could choose to join the other study if they had completed Part 3 of this study.

The participants who joined the other study stayed in this study for 4 more weeks before joining the other study. The study doctors slowly adjusted their levetiracetam doses during this time.

The participants who did not join the other study continued to take study treatments for 4 weeks until they were not taking any. If they were in Groups C, D, or E, the dose of levetiracetam was slowly decreased over the 4 weeks. The participants had a clinic visit 2 weeks after they stopped taking study treatments. Then they left the study.

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.

The results shown below include 339 of the 352 participants who continued in the study after Part 1. The researchers did not include 12 of the 352 participants in the results because they left the study during Part 2. Another participant was not included because the study doctor accidentally gave the participant the wrong study treatment at the beginning of Part 2.

The researchers included results for:

- 69 out of 70 participants in Group A
- 68 out of 71 participants in Group B
- 68 out of 70 participants in Group C
- 68 out of 70 participants in Group D
- 66 out of 70 participants in Group E

Group	Part 2	Part 3
Group A	Placebo daily	Placebo daily
Group B	0.5 g of levetiracetam daily	0.5 g of levetiracetam daily
Group C	1 g of levetiracetam daily	1 g of levetiracetam daily
Group D	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	2 g of levetiracetam daily
Group E	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	3 g of levetiracetam daily

Did the participants who took levetiracetam have fewer seizures?

In this study, the researchers could not conclude that participants who took levetiracetam had fewer seizures than participants who took the placebo.

The researchers counted the number of focal seizures the participants recorded in their diaries in Part 1 and Part 3. Before the study started, the researchers decided to:

- First review and compare the results for the participants in Groups A, C, and E
- Then determine if the differences between these groups were unlikely to be due to chance alone
- Not make conclusions about Groups B and D if they found that the differences between the other groups were too likely to be due to chance alone

The researchers compared the percentage change in the number of seizures from Part 1 to Part 3. They found that the differences between Groups C and E who took levetiracetam and Group A who took the placebo were likely due to chance alone. For this reason, the researchers could not know if levetiracetam decreased the number of seizures more than the placebo.

The researchers looked at the results using the median. The median is the middle number in a set of numbers. It is between the highest and lowest numbers.

The researchers found that the median percentage decreases in the number of seizures were:

- 12.50% for Group A
- 18.00% for Group C
- 31.67% for Group E

Group	Part 2	Part 3
Group A	Placebo daily	Placebo daily
Group B	0.5 g of levetiracetam daily	0.5 g of levetiracetam daily
Group C	1 g of levetiracetam daily	1 g of levetiracetam daily
Group D	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	2 g of levetiracetam daily
Group E	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	3 g of levetiracetam daily

Because the researchers found that the differences between Groups A, C, and E were too likely to be due to chance alone, they could not make any conclusions about the other 2 groups. So, the results for the Groups B and D are not shown above.

What medical problems did the participants have?

A medical problem that happens during a study is called an “adverse event.” An adverse event 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.

This section is a summary of the adverse events the participants had during the study that the study doctors thought might be related to the study treatments or were not likely related to the study treatments. The adverse events that the study doctors thought were not related to the study treatments are **not** included below. Some participants had more than 1 adverse event.

These adverse events 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 event.

Of the 352 participants who joined Part 2, 351 participants are included in the results shown below. There was 1 participant who was not included because the study doctor accidentally gave the participant the wrong study treatment at the beginning of Part 2. This participant did not have any serious adverse events.

The results below do not include Part 1, because all of the participants took the placebo in Part 1.

How many participants had serious adverse events during or after Part 2?

This section includes information about serious adverse events that happened during or after Part 2. This means they happened in Part 2, Part 3, or after Part 3. This section does not include the serious adverse events that the study doctors thought were not related to treatment.

During or after Part 2, serious adverse events happened in:

- 2.9% of the participants in Group A. This was 2 out of 70 participants.
- 1.4% of the participants in Group B. This was 1 out of 71 participants.
- 1.4% of the participants in Group C. This was 1 out of 70 participants.
- 1.4% of the participants in Group D. This was 1 out of 70 participants.
- 5.7% of the participants in Group E. This was 4 out of 70 participants.

Group	Part 2	Part 3
Group A	Placebo daily	Placebo daily
Group B	0.5 g of levetiracetam daily	0.5 g of levetiracetam daily
Group C	1 g of levetiracetam daily	1 g of levetiracetam daily
Group D	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	2 g of levetiracetam daily
Group E	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	3 g of levetiracetam daily

There was 1 participant who died due to a serious adverse event. The serious adverse event was stomach cancer. The participant was in Group E and took 3 g of levetiracetam each day. The study doctor thought the serious adverse event was unlikely due to study treatment.

What serious adverse events did the participants have during or after Part 2?

The list below shows the serious adverse events that happened during or after Part 2. Some of the participants had more than 1 serious adverse event.

Serious adverse events during or after Part 2

	Placebo each day	Levetiracetam each day			
	Group A (out of 70 participants)	Group B 0.5 g (out of 71 participants)	Group C 1 g (out of 70 participants)	Group D 2 g (out of 70 participants)	Group E 3 g (out of 70 participants)
Bruising	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)
Bruising of the brain	1.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Decrease in the number of white blood cells	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)
Feeling nervous	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)
Irritability	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)
Lower part of the heart beating too fast	0.0% (0)	0.0% (0)	1.4% (1)	0.0% (0)	0.0% (0)
Mind not working properly	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)	0.0% (0)
Seizure	0.0% (0)	1.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Seizures that last too long or happen back to back	1.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Stomach cancer	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)
Trouble sleeping	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)

How many participants had any adverse events during Parts 2 and 3?

This section includes information about adverse events that happened during Part 2 and Part 3, but not after Part 3. This does not include the adverse events that the study doctors thought were not related to treatment.

Group	Part 2	Part 3
Group A	Placebo daily	Placebo daily
Group B	0.5 g of levetiracetam daily	0.5 g of levetiracetam daily
Group C	1 g of levetiracetam daily	1 g of levetiracetam daily
Group D	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	2 g of levetiracetam daily
Group E	• 1 g of levetiracetam daily for 2 weeks • 2 g of levetiracetam daily for 2 weeks	3 g of levetiracetam daily

During Parts 2 and 3 of the study, adverse events that were either serious or not serious happened in:

- 58.6% of the participants in Group A. This was 41 out of 70 participants.
- 60.6% of the participants in Group B. This was 43 out of 71 participants.
- 61.4% of the participants in Group C. This was 43 out of 70 participants.
- 58.6% of the participants in Group D. This was 41 out of 70 participants.
- 64.3% of the participants in Group E. This was 45 out of 70 participants.

What adverse events did the participants have during Parts 2 and 3?

The most common adverse events for each group were:

- Headache in Group A
- Inflammation of the nose and throat area in Groups B, C, and E
- Sleepiness in Group D

The table below shows the adverse events that happened in 5% or more of the participants in any of the groups during Parts 2 and 3 of the study. This means they happened in at least 1 out of every 20 participants in any group. There were other adverse events, but they happened in fewer participants. The table does not include the adverse events that the study doctors thought were not related to treatment.

Adverse events in 5% or more of the participants in any treatment group during Parts 2 and 3

	Placebo each day	Levetiracetam each day			
	Group A (out of 70 participants)	Group B 0.5 g (out of 71 participants)	Group C 1 g (out of 70 participants)	Group D 2 g (out of 70 participants)	Group E 3 g (out of 70 participants)
Inflammation of the nose and throat area	11.4% (8)	14.2% (10)	18.6% (13)	15.7% (11)	21.4% (15)
Sleepiness	7.1% (5)	7.0% (5)	10.0% (7)	17.1% (12)	17.1% (12)
Headache	12.9% (9)	5.6% (4)	1.4% (1)	2.9% (2)	4.3% (3)
Dizziness	4.3% (3)	7.0% (5)	1.4% (1)	5.7% (4)	5.7% (4)
Diarrhea	4.3% (3)	9.9% (7)	2.9% (2)	0.0% (0)	1.4% (1)
Decrease in the number of blood cells called neutrophils	1.4% (1)	4.2% (3)	2.9% (2)	1.4% (1)	7.1% (5)
Bruising	2.9% (2)	1.4% (1)	0.0% (0)	7.1% (5)	4.3% (3)
Pain in the abdomen	2.9% (2)	5.6% (4)	0.0% (0)	1.4% (1)	0.0% (0)
Increase in the number of white blood cells	5.7% (4)	0.0% (0)	0.0% (0)	0.0% (0)	1.4% (1)

How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using levetiracetam in people who have epilepsy with focal seizures. The results of this study may be used in other studies to compare this drug with other treatments for people who have a similar condition.

The results of this study are based only on the participants included in the study.

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 health or situation, please contact your study doctor.

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 websites listed below:

- https://www.clinicaltrials.gov/ct2/show/NCT00280696?term=N01221&rank=2
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-004333-57/3rd

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

Study Information

Protocol Number: N01221

Study Sponsor: UCB Biopharma SRL sponsored this study. It was previously called UCB Japan Co., Ltd and is referred to as UCB in this summary.

Full Study Title: A double-blind, randomized, placebo-controlled 5 parallel groups, confirmatory trial on the efficacy and safety of Levetiracetam used as add-on therapy at doses of 0.5 to 3g/day in patients from 16 to 65 years with epilepsy with partial onset seizures under treatment with 1 to 3 anti-epileptic drug(s)

NCT Number: NCT00280696

EudraCT Number: 2014-004333-57

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
Bruising	contusion
Bruising of the brain	brain contusion
Decrease in the number of blood cells called neutrophils	neutrophil count decreased
Decrease in the number of white blood cells	white blood cell count decreased
Feeling nervous	anxiety
Increase in the number of white blood cells	white blood cell count increased
Inflammation of the nose and throat area	nasopharyngitis
Lower part of the heart beating too fast	ventricular tachycardia
Mind not working properly	mental impairment
Pain in the abdomen	abdominal pain
Seizure	convulsion
Seizures that last too long or happen back to back	status epilepticus
Sleepiness	somnolence
Stomach cancer	gastric cancer
Trouble sleeping	insomnia

This summary was last updated on 13 January 2020.
The final clinical study report is dated 09 September 2008.