Clinical Study Results

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Study Sponsor: UCB Japan Co. Ltd., an affiliate of UCB Biopharma SRL

Treatment Studied: Levetiracetam

Protocol Number: N01159

Short Study Title: A study to learn if levetiracetam reduced generalized tonic-clonic seizures in Japanese and Chinese participants with epilepsy

Thank you!

UCB thanks all the participants of this study and their caregivers. All the participants and caregivers helped the researchers learn about using levetiracetam in Japanese and Chinese 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, their caregivers, and the public. We hope this summary helps the participants and their caregivers 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. Epileptic seizures that cannot be controlled by epilepsy medications are also known as refractory seizures or uncontrolled seizures.

The type of seizure that can cause someone to lose consciousness and shake violently is called a generalized tonic-clonic seizure. This is also known as a GTC seizure. Researchers think that taking levetiracetam may help reduce GTC seizures.

In this study, the researchers wanted to find out if levetiracetam helped reduce uncontrolled GTC seizures in Japanese and Chinese participants with epilepsy.

What were the main questions studied?

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

- Did levetiracetam reduce how many uncontrolled GTC seizures the participants had per week?
- What medical problems did the participants have during the study?

Who participated in the study?

There were 251 males and females with epilepsy in Japan and China who participated in this study and took study treatment. The participants were 16 to 70 years old.

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

- Were already taking 1 or 2 epilepsy medications but were still having uncontrolled GTC seizures
- Had at least 3 uncontrolled GTC seizures within the 8 weeks before starting the study

Each participant was in the study for up to 42 weeks, but the whole study lasted for 3 and a half years. The study started in October 2010 and ended in May 2014.

What treatments did the participants take?

The participants in this study took either levetiracetam or a placebo in addition to their regular epilepsy medication. They took levetiracetam or the placebo as tablets by mouth once in the morning and once in the evening for up to 32 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.

The study happened in 2 parts.

In **Part 1** of the study, all of the participants took the placebo for 4 to 8 weeks.

The participants in this part did not know what treatment they were taking. But the study doctors, study staff, and UCB staff did know. Some studies are done this way because if the participants know what treatment they are taking, this can affect the results of the study.

Then, in **Part 2** of the study, all of the participants took their study treatment for 28 weeks:

- 126 participants took levetiracetam
- 125 participants took the placebo

In Part 2, none of the participants, caregivers, study doctors, or study staff knew what treatment each participant was taking. UCB staff also did not know. 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 chart below shows the treatments the researchers studied:

	126 participants took levetiracetam
	125 participants took the placebo
	The participants took levetiracetam and the placebo as tablets by mouth
	The participants took 2 doses of levetiracetam or the placebo each day for about 28 weeks

What were the doses of levetiracetam?

The doses of levetiracetam were measured in milligrams per day, also known as mg/day.

For the first 12 weeks of taking levetiracetam in Part 2 of the study, the participants started taking a dose of 1,000 mg/day. The study doctors could increase each participant's dose up to 3,000 mg/day depending on their epilepsy symptoms.

During this time, the study doctors found the dose for each participant that seemed to help the most and caused the fewest medical problems. This could be different for each participant.

After the study doctors found a dose for each participant, the participants took this dose for the next 16 weeks of the study.

After this, the participants either:

- Had their dose slowly decreased over 6 weeks until they were not taking any levetiracetam
- Started taking levetiracetam as part of their regular treatment

	The first 12 weeks of Part 2	The next 16 weeks of Part 2	Then until the end of the study
Treatment with levetiracetam during and after Part 2	Started on 1,000 mg/day Increased up to 3,000 mg/day depending on epilepsy symptoms	Stayed on the levetiracetam dose that seemed to help the most and caused the fewest medical problems	Either decreased the dose over 6 weeks until the participants were not taking any levetiracetam Or started taking levetiracetam as part of their regular treatment

What happened during the study?

During Part 1 of the study, the participants visited their clinic at least 2 times. Each participant or their caregiver learned about the study and decided that the participant would join the study. This is called "informed consent." Then, the study doctors and study staff asked about the participants' medical history and checked their health to make sure they could join the study. The participants also kept a diary of their seizures.

At 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 and urine samples
	If needed, checked the participants' heart health using an electrocardiogram, also known as an ECG
	If needed, checked the participants' brain health using an electroencephalogram, also known as an EEG
	If needed, took pictures of each participant's brain using CT or MRI scans

During Part 2 of the study, the participants visited their clinic up to 8 times. They took levetiracetam or the placebo at home for 28 weeks. They also took their regular epilepsy medication and kept a diary of their seizures.

At 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 and urine samples
	Checked the participants' heart health using an electrocardiogram, also known as an ECG

At the end of the study, the participants visited their clinic 2 times. The study doctors checked the participants' health and asked about any medical problems they were having. This part of the study lasted for up to 6 weeks.

The participants who were taking levetiracetam could either stop taking it or they could keep taking levetiracetam as part of their regular epilepsy treatment. For the participants who stopped taking levetiracetam, the study doctors slowly decreased the participants' dose of levetiracetam until they were not taking any. The participants who were taking the placebo could also start taking levetiracetam as part of their regular epilepsy treatment.

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 below include 226 out of 251 participants. This is because some participants did not finish all of their treatments or study tests and measurements.

Did levetiracetam reduce how many uncontrolled GTC seizures the participants had per week?

Yes. Overall, the researchers found that the number of seizures per week was reduced more in the participants who took levetiracetam than in those who took the placebo after 28 weeks of treatment.

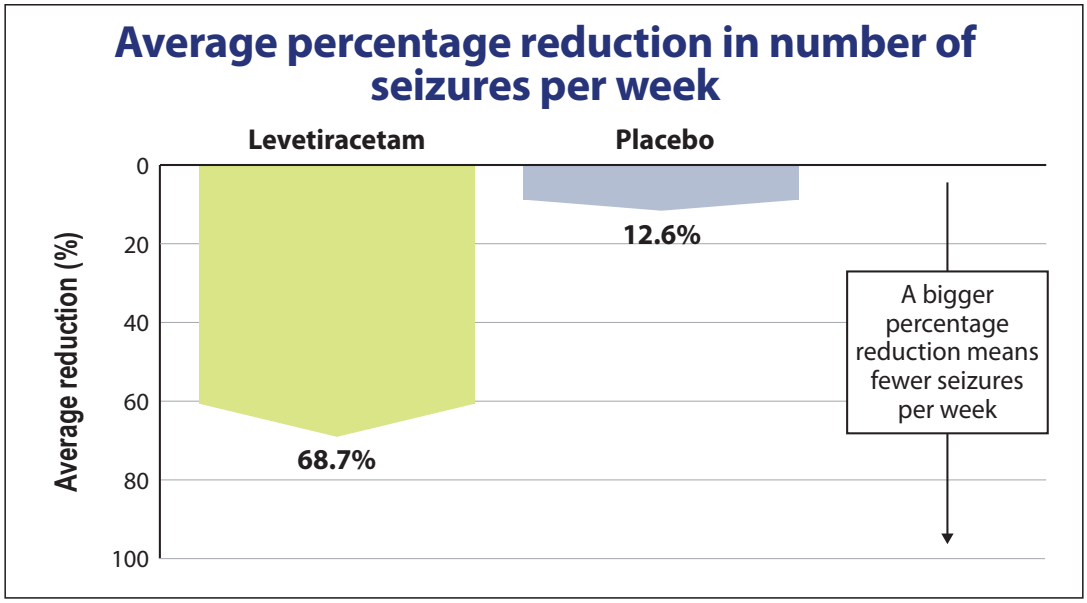
To answer this question, the study doctors counted the number of uncontrolled GTC seizures the participants had during the study. They divided this by the number of weeks in the study to calculate the average number of seizures per week. The researchers compared this to the average number of seizures per week before the participants started taking study treatment. They calculated the percentage difference in the average number of seizures per week before and after treatment, known as the "average percentage reduction". A bigger percentage reduction means fewer seizures per week.

The researchers found that after 28 weeks of treatment, the average percentage reduction in the number of seizures per week was:

- 68.7% for the participants who took levetiracetam
- 12.6% for the participants who took the placebo

The difference in the average percentage reduction between the groups was 56.1%. This means that the participants who took levetiracetam had 56.1% fewer seizures per week than the participants who took the placebo.

The chart 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.”

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 1 of these problems if not treated.

These adverse reactions 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. Always talk to a doctor before making any treatment decisions.

How many participants had serious adverse reactions?

- None of the participants who took levetiracetam had a serious adverse reaction.
- There was 1 participant out of 125 participants who took the placebo who had a serious adverse reaction. This was 0.8% of participants who took the placebo. This participant died due to the serious adverse reaction of sudden unexplained death related to epilepsy.

How many participants had any adverse reactions?

- 23.8% of participants who took levetiracetam had adverse reactions during the study. This was 30 out of 126 participants.
- 13.6% of participants who took the placebo had adverse reactions during the study. This was 17 out of 125 participants.

What adverse reactions did the participants have?

The most common adverse reaction was having too much protein in the urine. This was the only adverse reaction that happened in 5.0% or more of participants in either of the treatment groups. This means it happened in at least 1 out of every 20 participants in either of the treatment groups. There were other adverse reactions, but these happened in fewer participants.

During the study, the adverse reaction of having too much protein in the urine happened in:

- 7.1% of participants who took levetiracetam. This was 9 out of 126 participants.
- 0.8% of participants who took the placebo. This was 1 out of 125 participants.

How has this study helped patients and researchers?

The results of this study have helped researchers learn more about using levetiracetam in Japanese and Chinese participants 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 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 doctor.

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

At the time 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:

- www.clinicaltrials.gov/ct2/show/study/NCT01228747
- www.clinicaltrialsregister.eu/ctr-search/search?query=2014-004401-32

If you have questions about this study, UCB contact information is available at: www.ucb.com/UCBCares

Study Information

Protocol Number: N01159

Study Sponsor: UCB Japan Co. Ltd. sponsored this study. It is referred to as UCB in this summary. UCB Japan Co. Ltd. is an affiliate of UCB Biopharma SRL.

Full Study Title: A double-blind, multicenter, randomized, placebo-controlled study to evaluate the efficacy and safety of adjunctive treatment with oral levetiracetam (L059) in epilepsy patients aged ≥16 with generalized tonic-clonic (GTC) seizures

National Clinical Study Number: NCT01228747

EudraCT Number: 2014-004401-32

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:
Having too much protein in the urine	"proteinuria". This can be a sign of kidney damage.

This summary was last updated on 26 January 2021
The final clinical study report is dated 15 December 2014