Short study title: Brivaracetam for the treatment of partial-onset seizures (focal seizures) in people from 16 to 80 years old with epilepsy

Full study title: A randomized, double-blind, placebo-controlled, multicenter, parallel-group study to evaluate the efficacy and safety of brivaracetam in subjects (≥16 to 80 years old) with partial onset seizures

Thank you	UCB would like to thank all of the participants of this clinical study. Participation in clinical studies like this one directly contributes to the discovery of new medicines for people with epilepsy.
Background	• Seizures are caused by too much electrical activity in groups of cells (called neurons) in the brain. People with epilepsy have seizures that happen again and again. • Partial-onset seizures (also called focal seizures) happen in just one part of the brain. Sometimes focal seizures can spread to both sides of the brain. There are other types of seizures (generalized seizures) that happen in both sides of the brain at once[1].
Purpose of the study	In this study, researchers compared a drug called brivaracetam with placebo. Brivaracetam and placebo are both called study drugs in this summary. • The main purposes of the study were: o To see if people who are already taking anti-seizure medicines have seizures less often when they also take brivaracetam than when they also take placebo. o To get more information about the safety of brivaracetam in people with focal seizures.
Study participants	• Some of the requirements to get into the study were that participants: o Were 16 to 80 years old (in some countries, participants had to be at least 18 years old) o Had at least 2 focal seizures each month in the 3 months before the study. o Were taking 1 or 2 other anti-seizure medicines, but did not have control of their seizures. • A total of 764 people got into the study and took study drug at least once: o 396 were females and 368 were males. o Ages were from 16 to 80 years. The average age was 40 years. • Participants continued their 1 to 2 anti-seizure medicines as their doctor had told them to during the study.

Study design and research methodology

- The study was run in the following countries: Austria, Belgium, Brazil, Bulgaria, Canada, the Czech Republic, Estonia, Finland, France, Germany, Hong Kong, Hungary, India, Italy, Japan, Latvia, Lithuania, Mexico, the Netherlands, Poland, Russia, South Korea, Spain, Sweden, Taiwan, the United Kingdom, and the United States (including the territory of Puerto Rico).

- The study started in Dec 2010 and ended in May 2014.

- The study was double-blind to make sure the results were not influenced by participants, doctors/assistants, or researchers knowing what study drug or amount of study drug participants were taking.

- Before study participants began taking study drug, they were in an 8-week Baseline Period. During this period, they took their usual anti-seizure medicines and kept track of how many focal seizures they had.

- If participants had at least 8 focal seizures during the Baseline Period and also had at least 2 seizures every 4 weeks during the Baseline Period, they could start taking study drug in the 12-week Treatment Period.

  Participants were put into 1 of 3 study drug groups by chance (randomized) by a computer. They had an equal chance of being put into each group. The groups are shown here:

Group 1	**Group 2**	**Group 3**
Placebo every day	Brivaracetam 100mg every day	Brivaracetam 200mg every day

  Study drug tablets were taken by mouth. The participants also took their usual anti-seizure medicines while they were taking study drug.

- During the 12-week Treatment Period, study participants kept track of the number of seizures they had. This was to see if the number of focal seizures was reduced in participants taking brivaracetam compared with participants taking placebo.

- Doctors collected information about participants' medical problems during this study. This was done to look at the safety of the participants and to understand the safety of the study drugs. The medical problems that the doctor thought were due to the study drug are called side effects. Side effects are described in 2 different ways:

  - They can be mild, moderate, or severe.

  And

  - They are either serious side effects or not serious. The doctor used a set of rules when deciding whether or not a side effect was serious.

- At the end of Treatment Period, participants could choose to:

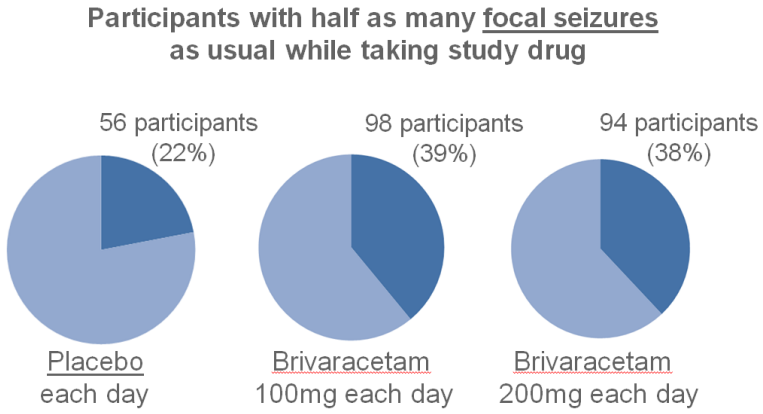
  Go straight into an additional study (called a “long-term follow-up study”) where they could receive brivaracetam along with their other anti-seizure medicines. The results for this study are not included in this summary since it is a separate study.

  OR Have their amount of study drug slowly made lower over a 4-week period then have 2 weeks of no study drug before leaving the study. Participants were to take their usual anti-seizure medicines during all of these weeks.

Key findings

- The first picture below shows the number and percentage of participants in each group whose focal seizure count dropped to at least half of what it was before starting study drug. The results were measured during the 12-week Treatment Period. Results for placebo and 2 different doses of brivaracetam are shown. Participants were also taking 1 to 2 other anti-seizure medicines.

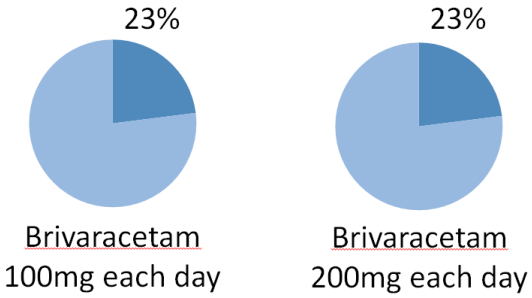
  The picture shows that a higher percentage of participants who took brivaracetam (either amount) every day than participants who took placebo every day had their focal seizure count drop to at least half of what it was before starting study drug.



The next picture shows the decrease in the number of focal seizures in each brivaracetam group compared with the placebo group. The placebo group is not shown in the picture. This is because the picture shows the difference between the decrease in seizure numbers in each brivaracetam group compared with the placebo group.

This picture shows that both brivaracetam groups had decreases in focal seizures compared with the placebo group and the decreases were about the same.

Decrease in focal seizures compared with placebo



For both ways of comparing brivaracetam with placebo, the researchers concluded that the fewer focal seizures shown for brivaracetam 100mg compared with placebo and for brivaracetam 200mg compared with placebo likely did not happen just by chance. They also concluded that the improvement was similar whether the participants took brivaracetam 100mg every day or took brivaracetam 200mg every day.

- Two participants had serious side effects during the study (see below).
  - Of the 261 participants in the placebo group, 2 had serious side effects. One participant had a serious side effect of postictal state. The other participant had grand mal convulsion.
  - Of the 503 participants in the brivaracetam groups, 7 had serious side effects. Some participants had more than one serious side effect. One participant had fall and humerus fracture, and another participant had fall and craniocerebral injury. The other 5 participants with serious side effects each had one serious side effect. These serious side effects were agitation, conversion disorder, epileptic psychosis, psychotic disorder, and status epilepticus.
- Two participants died during the study. One participant died due to sudden unexpected death in epilepsy. The exact cause of death for the other participant was not known. Both participants were in the brivaracetam 200mg group.
- Fifty-eight of the 261 participants in the placebo group (22%) and 207 of the 503 participants in the 2 brivaracetam groups combined (41%) had side effects that started during the Treatment Period. Most side effects were mild or moderate. Some participants had more than 1 type of side effect. All participants were taking 1 to 2 other anti-seizure medicines.

  The list below shows side effects that were reported for at least 2 of every 100 (2%) participants in any of the 3 study drug groups during the Treatment Period. Only those side effects that started during the Treatment Period are shown. For this list, participants in the 2 brivaracetam groups are combined. For each column, the number of participants with the side effect is on the left and the percentage of the group with the side effect is on the right in parentheses.

Side effects in at least 2% of the participants in any of the 4 study drug groups

	Study drug given with 1 or 2 other anti-seizure medicines	
	Placebo	**Brivaracetam (100mg or 200mg each day)**
Somnolence	19 (7%)	83 (17%)
Dizziness	7 (3%)	54 (11%)
Fatigue	5 (2%)	41 (8%)
Headache	6 (2%)	15 (3%)
Nausea	4 (2%)	12 (2%)
Irritability	1 (<1%)	11 (2%)
Vertigo	2 (1%)	8 (2%)
Anxiety	3 (1%)	6 (1%)
Constipation	1 (<1%)	6 (1%)
Insomnia	1(<1%)	6 (1%)

Dizziness and fatigue were reported by a higher percentage of participants on the higher amount of brivaracetam (200mg every day) than the lower amount (100mg every day) (not shown in the list above). Other side effects were about the same in the 2 brivaracetam groups.

- Overall, 696 participants who were put in a study drug group completed the study. A total of 676 participants planned to enter the long-term follow-up study and 20 participants did not plan to enter the long-term follow-up study.

- For more information about this study, please visit https://clinicaltrials.gov/ct2/show/results/NCT01261325?term=N01358&rank=1. For information about other studies for people with epilepsy who have partial-onset seizures (focal seizures) including brivaracetam studies please visit clinicaltrials.gov.

Comment on the outcome of the study

In this study, adding 100mg or 200mg of brivaracetam every day to 1 or 2 other anti-seizure medicines lowered the number of focal seizures more than adding placebo. The improvement drop in focal seizure number was about the same for the higher amount of brivaracetam (200mg every day) compared with the lower amount (100mg every day) of brivaracetam.

A higher percentage of participants in the 2 brivaracetam groups combined had side effects (41%) than participants in the placebo group (22%). In this study, the most common side effects for brivaracetam (those reported by 5% or more of the participants in the 2 brivaracetam groups combined) were somnolence, dizziness, and fatigue. Dizziness and fatigue were reported by a higher percentage of participants in brivaracetam 200mg group than in the brivaracetam 100mg group. The percentage of participants with somnolence was about the same in both brivaracetam groups.

Peer-reviewed publication

Klein P, Schiemann J, Sperling MR, Whitesides J, Liang W, Stalvey T, et al. A randomised, double-blind, placebo-controlled, multicentre, parallel-group study to evaluate the efficacy and safety of adjunctive brivaracetam in adult patients with uncontrolled partial-onset seizures. Epilepsia. 2015;56(12):1890–98.

References:

1. Epilepsy Research UK. What is epilepsy? https://www.epilepsyresearch.org.uk/wp-content/uploads/2014/04/whatisepilepsy.pdf. Accessed 19 Jan 2018.

Last update on 19 Jan 2018.

This summary is provided for informational purposes only.

This summary only shows the results from this one study. Other studies may find different results. The overall results of the study may not reflect the experience of an individual participant of the study. If you need medical advice about your own health or situation, please contact your physician.

Thank you again to all participants!!!