

Short study title: Brivaracetam for the treatment of partial-onset seizures (focal seizures) in people from 16 to 70 years old with epilepsy

Full study title: A multicenter, double-blind, parallel-group, placebo-controlled, randomized study: evaluation of the efficacy and safety of brivaracetam in subjects (≥16 to 70 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	<ul style="list-style-type: none">• 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.• <u>Partial-onset seizures</u> (also called <u>focal seizures</u>) 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 (called generalized seizures) that happen in both sides of the brain at once¹.
Purpose of the study	<p>In this study, researchers compared a drug called brivaracetam with <u>placebo</u>. Brivaracetam and <u>placebo</u> are both called study drugs in this summary.</p> <ul style="list-style-type: none">• The main purposes of this study were:<ul style="list-style-type: none">○ 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 <u>placebo</u>.○ To get more information about the safety of brivaracetam in people with <u>focal seizures</u>.
Study participants	<ul style="list-style-type: none">• Some of the requirements to get into the study were that participants:<ul style="list-style-type: none">○ Were 16 to 70 years old (in some countries, participants had to be at least 18 years old).○ Had at least 2 <u>focal seizures</u> each month in the 3 months before the study.○ Were taking 1 or 2 other anti-seizure medicines, but did not have control of their seizures.• A total of 398 people got into the study and took study drug at least once:<ul style="list-style-type: none">○ 227 were males and 171 were females.○ Ages were from 16 to 71 years. The average age was 37 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 Belgium, Finland, France, Germany, Hungary, India, Italy, the Netherlands, Poland, Spain, Switzerland, and the United Kingdom.
- The study started in September 2007 and ended in February 2009.
- 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, they could start taking study drug for the 12-week Treatment Period.

Participants were put into 1 of 4 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:

<u>Group 1</u>	<u>Group 2</u>	<u>Group 3</u>	<u>Group 4</u>
<u>Placebo</u> every day	Brivaracetam 20mg every day	Brivaracetam 50mg every day	Brivaracetam 100mg 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, participants kept track of the number of seizures they had. This was to see if the number of focal seizures was lower 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 2-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.

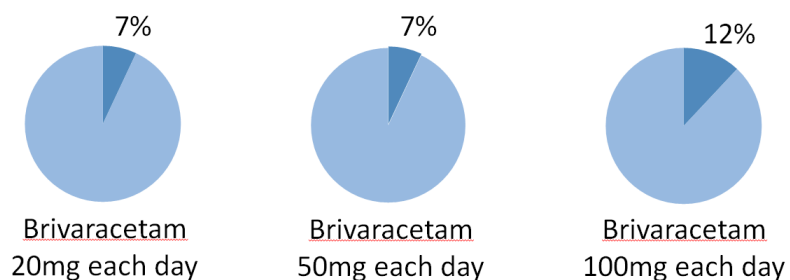
Key Findings

- The picture below shows the comparison of focal seizures each week during the Treatment Period for each brivaracetam group versus the placebo group. Participants were also taking 1 to 2 other anti-seizure medicines. 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.

The picture shows that the brivaracetam 50mg group had 7% fewer focal seizures each week than the placebo group, but the researchers concluded that the difference shown was likely just due to chance.

No conclusions could be made about the other brivaracetam amounts compared with placebo. This was because of rules made before the study began. The rules said if the difference shown between the brivaracetam 50mg and placebo group was likely due to chance, no other comparisons could be made.

Decrease in focal seizures each week compared with placebo



- Two participants had serious side effects during the study. One participant reported grand mal convulsion and the other reported psychotic disorder. Both participants were in a brivaracetam group.
- Two participants died during the study. One participant died due to sepsis. The participant was taking placebo. The other participant died before starting study drug.
- Thirty-one of the 100 participants in the placebo group (31%) and 102 of the 298 participants in the 3 brivaracetam groups combined (34%) had side effects

that started during the Treatment Period. Some participants had more than 1 type of side effect. Most side effects were mild or moderate. All participants were taking 1 to 2 other anti-seizure medicines.

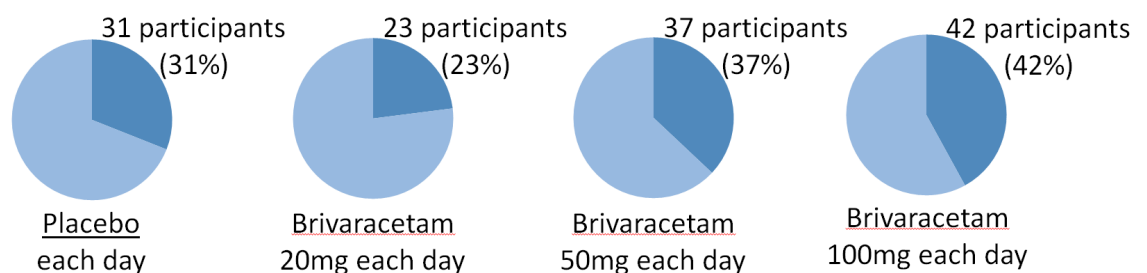
The list below shows side effects that were reported in at least 3 of every 100 participants (3%) in any of the 4 study drug groups during the Treatment Period. For this list, participants in the 3 brivaracetam groups are combined. Only those side effects that started during the Treatment Period are shown. 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 3% of the participants in any of the 4 study drug groups

	Study drug given with 1 or 2 other anti-seizure medicines	
	<u>Placebo</u>	<u>Brivaracetam (20mg, 50mg, or 100mg each day)</u>
<u>Somnolence</u>	6 (6%)	19 (6%)
Headache	3 (3%)	19 (6%)
Fatigue	2 (2%)	14 (5%)
<u>Vertigo</u>	3 (3%)	11 (4%)
Dizziness	4 (4%)	11 (4%)
<u>Asthenia</u>	3 (3%)	6 (2%)
Nervousness	1 (1%)	6 (2%)
<u>Insomnia</u>	1 (1%)	5 (2%)
<u>Nausea</u>	3 (3%)	5 (2%)
<u>Anxiety</u>	0	5 (2%)
Irritability	0	5 (2%)
Disturbance in attention	1 (1%)	3 (1%)
<u>Paraesthesia</u>	3 (3%)	0

The picture below shows the number and percentage of participants with any side effects by group. The percentage of participants with side effects seemed to get higher when the amount of brivaracetam went up.

Participants in each group with side effects



	<ul style="list-style-type: none"> • Overall, 367 participants who were put in a study drug group completed the study. A total of 345 participants entered the long-term follow-up study and 22 did not enter the long-term follow-up study. • For more information about this study, please visit https://clinicaltrials.gov/ct2/show/results/NCT00490035?term=N01252&rank=1. For information about other studies for people with epilepsy who have <u>partial-onset seizures</u> (<u>focal seizures</u>) including brivaracetam studies please visit clinicaltrials.gov.
<p>Comment on the outcome of the study</p>	<p>In this study, adding brivaracetam 50mg every day to 1 to 2 other anti-seizure medicines was not that different from adding <u>placebo</u> every day. No conclusions could be made about adding brivaracetam 100mg every day and brivaracetam 20mg every day compared with adding <u>placebo</u> every day in reducing seizure number.</p> <p>The percentage of participants with any <u>side effect</u> was about the same in the <u>placebo</u> group (31%) and the 3 brivaracetam groups combined (34%). In this study, the most common <u>side effects</u> for brivaracetam (those reported by 5% or more of the participants in the 3 brivaracetam groups combined) were headache, <u>somnolence</u>, and <u>fatigue</u>. The highest percentage of headache was in the brivaracetam 50mg group and of <u>fatigue</u> was in the brivaracetam 100mg group. The percentage of <u>somnolence</u> was about the same for each brivaracetam group.</p>
<p>Peer-reviewed publication</p>	<p>Biton V, Berkovic SF, Abou-Khalil B, Sperling MR, Johnson ME, Lu S. Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: A phase III randomized, double-blind, <u>placebo</u>-controlled trial. <i>Epilepsia</i>. 2014;55(1):57–66.</p>

References:

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

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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!!!