



CLINICAL TRIAL RESULTS

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medicine works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Pregabalin

Protocol Number: A0081042

Dates of Trial: 16 September 2014 to 13 March 2018

Title of this Trial: A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month Through <4 Years of Age With Partial Onset Seizures

Date of this Report: 27 November 2018

– *Thank You* –

Pfizer, the Sponsor, would like to thank you and your child for participating in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your child's study site.

WHY WAS THIS STUDY DONE?

A seizure is a sudden increase in electrical activity in the brain. Epilepsy is when 2 or more seizures occur that are separated by at least a day, and for which there is not cause for the seizure which can be corrected. Seizures can take on many different forms, can cause many different symptoms, and vary from person to person.

Seizure symptoms can include a feeling or warning that a seizure is about to occur, a temporary loss of consciousness, or a feeling of being confused. The initial symptoms may also progress to shaking of the arms and legs. “Partial onset seizures”, also known as focal seizures, are a common type of seizure. This type of seizure begins in only one part of the brain. This study included children with partial onset seizures.

There are medicines that are available that can be used to stop or control seizures in children, but these medicines may not work well for all children and they may not be tolerated well. Therefore, researchers are interested in finding additional treatment options for children with epilepsy (seizures).

Pregabalin is a medicine that may be used as an “add-on” treatment for children with epilepsy, which means that the medicine is given along with other epilepsy medicines that the child is already receiving. Pregabalin is currently approved in the United States only for older children (at least 4 years of age) with partial onset seizures. Pregabalin is not approved in any country for the add-on treatment of partial onset seizures in children 1 month to younger than 4 years of age. This study was done to learn more about using pregabalin as add-on therapy in these younger children with partial onset seizures.

For this study, researchers wanted to answer the following question:

- Would pregabalin reduce the frequency of partial onset seizures, compared to placebo?

WHAT HAPPENED DURING THE STUDY?

This study compared 3 groups of children to find out if those taking 1 of 2 different doses of pregabalin would have less frequent seizures, compared to children taking a placebo. A placebo does not have any medicine in it, but looks just like the medicine.

The study included children who were at least 1 month old but younger than 4 years old when the study started. All children in this study had partial onset seizures and were currently taking medicine for epilepsy. The children received 1 of 3 treatments in this study randomly (like flipping a coin) and none of the patients, parents, or researchers knew who took pregabalin and who took the placebo. This is known as a “blinded” study.

First, the study doctor checked each child to make sure that they met the requirements to join the study. This was called screening. Children who were found to be a good fit for the study came to a baseline visit that lasted 2 to 3 days, where they were given a test called a video EEG. A video EEG measures brain activity and is used to provide a measure of seizure frequency. Children who had at least 2 partial onset seizures during the baseline video EEG could continue in the study.

Children were then randomly assigned to 1 of 3 treatments during the study:

- Pregabalin 7 milligrams (mg) per kilogram (kg) of weight per day (71 children)
- Pregabalin 14 mg per kg of weight per day (34 children)
- Placebo (70 children)

The dose of study medication was gradually increased from a starting dose to the study dose over the first 5 days of the study. Next, the dose of study medication was kept the same over the next 9 days. The children then came to another visit at which the video EEG testing was repeated over 2 to 3 days. Last, study medication was gradually decreased. Children continued taking their other medications for epilepsy throughout the study.

The chart below shows what happened during the study.



Each individual child was in the study for about 3 weeks. Overall, the entire study took about 3 ½ years to complete because the children did not all start at the same time. Children joined the study at 1 of 113 locations in 29 countries in Africa, Asia, Europe, North America, and South America. It began 16 September 2014 and ended 13 March 2018. A total of 103 boys and 72 girls were enrolled in the study.

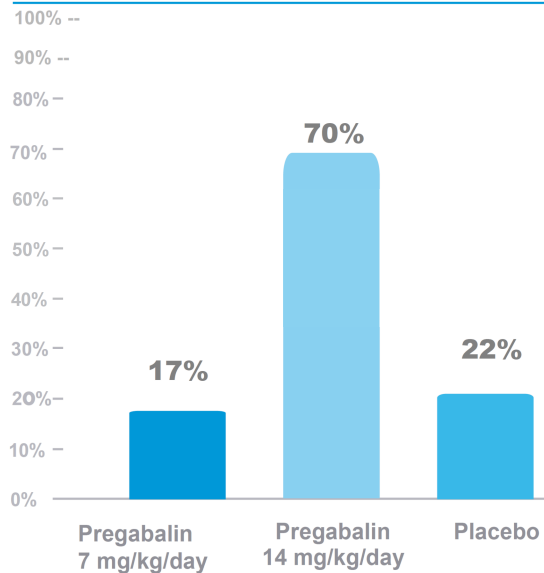
Out of the 175 children who started the study, 169 children (97%) finished it. A total of 6 children (3%) left before the study was over, either because the parent/guardian chose for the child to leave, or because a doctor decided it was best for the child to stop the study. When the study ended in March 2018, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

WHAT WERE THE RESULTS OF THE STUDY?

Did pregabalin reduce the frequency of partial onset seizures, compared to placebo?

To answer this question, the researchers determined each child's 24-hour seizure rate (the number of partial onset seizures in a 24-hour period) from the video EEG tests. Pregabalin at the 14 mg per kg per day dose significantly reduced the frequency of partial onset seizures compared to placebo. Pregabalin at the 7 mg per kg per day dose did not significantly reduce the frequency of partial onset seizures compared to placebo. The comparison to placebo is how researchers determine if a new medicine works for epilepsy. The chart on the following page shows the average reduction in 24-hour seizure rate for children in each treatment group.

Average Reduction in 24-Hour Seizure Rate



WHAT MEDICAL PROBLEMS DID CHILDREN HAVE DURING THE STUDY?

The researchers recorded any medical problems the children had during the study. Children could have had medical problems for reasons not related to the study (for example, caused by an underlying disease). Or, medical problems could also have been caused by a study treatment, or by another medicine the child was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what the side effects of an experimental drug might be.

Out of 175 children in this study, 51 children (29%) had at least 1 medical problem. The most common medical problems reported in children in this study are listed on the following page.

Most Common Medical Problems (Reported in More than 5% of Children)

Medical Problem	Pregabalin 7 mg/kg/day (71 Children Treated)	Pregabalin 14 mg/kg/day (34 Children Treated)	Placebo (70 Children Treated)
Drowsiness	8 (11%)	6 (18%)	4 (6%)
Infection of the nose, throat, and airways	5 (7%)	4 (12%)	8 (11%)
Fever	4 (6%)	2 (6%)	4 (6%)
Vomiting	1 (1%)	0 (0%)	6 (9%)
Common cold	1 (1%)	2 (6%)	3 (4%)
Infection of the lungs (pneumonia)	1 (1%)	2 (6%)	0 (0%)
Infection caused by a virus	2 (3%)	2 (6%)	2 (3%)
Seizure	1 (1%)	2 (6%)	3 (4%)

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered “serious” when it is life-threatening, causes lasting problems, or needs hospital care.

Out of 175 children in this study, 5 children (3%) had serious medical problems. There were 4 children in the placebo group and 1 child in the pregabalin 14 mg per kg per day group who had a serious medical problem. No children died during the study.

WHERE CAN I LEARN MORE ABOUT THIS STUDY?

If you have questions about the results of your study, please speak with the doctor or staff at your child's study site.

The full scientific report of this study is available online at:

www.clinicaltrials.gov

Use the study identifier **NCT02072824**

www.clinicaltrialsregister.eu

Use the study identifier **2013-003420-37**

www.pfizer.com/research/research/clinical_trials/trial_results

Use the protocol number **A0081042**

Please remember that researchers look at the results of many studies to find out which medicines work best and are safest for patients. Other studies of pregabalin are ongoing.

**Again, thank you for volunteering.
We do research to try to find the
best ways to help patients, and you
helped us do that!**