

MODEL INFORMED CONSENT DOCUMENT

Version Date: 5 January 2015



Title of Study:

Established Status Epilepticus Treatment Trial (ESETT):

A multicenter, randomized, blinded, comparative effectiveness study of fosphenytoin, valproic acid, or levetiracetam in the emergency department treatment of patients with benzodiazepine-refractory status epilepticus.

Why am I being asked to participate?

If you are acting as a representative for another person to participate in this study, “you” throughout this document refers to that person.

You have received a copy of this form because you had a long seizure that would not stop on its own. This is called status epilepticus. You needed immediate treatment in the hospital Emergency Department. The doctors and nurses had to give you a medicine quickly to stop the seizure. Three common, similar medicines that are used to treat seizures are being studied here to see which medicine works best. You qualified for this emergency research study and were enrolled. Permission was not possible because you were unable to tell us your preference at the time.

Now, you are being asked to continue to take part in this research study. Continuing to participate in the study is voluntary, which means you can choose whether or not you want to continue. Before you can make your decision, you will need to: know what the study is about, the risks and possible benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study and this consent form. This form gives you important information about the study. Please take time to review this information carefully. You may find some of the medical words hard to understand. Please talk

to the study doctor or the research team about this form and ask them any questions you have. You may also decide to discuss it with your family, friends, or family doctor. If you decide to continue your participation in the study, you will be asked to sign this form.

A description of this clinical trial is available on www.Clinicaltrials.gov as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. Please use NCT01960075 to find the study on this site.

What is the purpose of this research study?

Most seizures either stop on their own without treatment or stop with initial emergency treatments (medications such as valium). Seizures that persist despite emergency treatments are very dangerous. The purpose of this study is to find out which of three commonly used medicines is best in patients who have seizures that continue despite initial emergency treatments. The study will find out which is safer and more effective at stopping seizures.

The three medicines are fosphenytoin (also called Cerebyx or Dilantin), levetiracetam (also called Keppra) and valproic acid (also called Depacon or Depakote).

All three medications are approved by the Food and Drug Administration for the prevention of seizures. All three drugs are considered investigational drugs in this study. Levetiracetam and valproic acid have not yet been approved to stop long seizures. Fosphenytoin has been approved by the FDA to stop seizures in adults, but not in children. Doctors have used all three of these medications to safely stop ongoing seizures in adults and children for many years. Doctors are allowed to, and commonly do, use approved medications like this, even if the medicines are not labelled by FDA for that particular use.

How long will I be in the study? How many other people will be in the study?

Children and adults who continue to have seizures despite treatment with a benzodiazepine medication (such as valium) are enrolled in this study. Children are included in this study because the treatments being studied are used to treat prolonged seizures in both children and adults.

About 795 subjects at more than 40 hospitals across the United States will participate in this study. Enrollment will take place over 4 or more years. Approximately 20 subjects will be enrolled here at <<Site Name>>. No one will be included or prevented from participating based

on gender, race, color, economic status, or national origin.

If you decide to continue participating in this study, the researchers will continue to collect your medical information only until you are discharged from the hospital.

What happens in this study?

Everyone in this study gets medicine for their seizure given into a vein. Everyone will be randomly assigned to receive one dose of one of the study medicines. Random means assigned by chance, like the flip of a coin. Initially 1 in 3 patients will get fosphenytoin, 1 in 3 get levetiracetam, and 1 in 3 get valproic acid. As the study goes on, if one drug does not appear to be as effective as the others, it will be given less frequently.

Because we could not delay treating your seizures, you already were treated with the study medicine.

Here is what has happened so far:

A doctor examined you and treated you medically. The doctor found that you did not have another reason for having a seizure that could be treated easily, like low blood sugar.

After the doctor determined you were eligible for the study, you received one dose of the three study medicines (either fosphenytoin, levetiracetam or valproic acid) at random. Neither you or your doctor will know which study medicine you received. The doctors caring for you in the hospital will be told what medicine you received if needed to guide your subsequent care. Some medical information about you and your condition has been collected. Two blood draws, up to 5 ml total of blood, may have been collected for study purposes.

No other aspect of your routine medical care was affected by enrollment in the study. As part of your regular medical care, you may have later been treated with one or more of the three medicines being studied, or different medicines, but not as part of the study.

What am I being asked to do?

Now, you are being asked to decide whether or not to continue participating in this study.

Continuing in the study does not involve getting any further medications or tests. If you decide

to continue participating, you allow us to collect some medical information about you and how you are doing until you are discharged from the hospital. The information that we have or will collect includes demographics, your condition and treatment in the emergency department, medical history, whether your seizures have recurred in the hospital, some tests and findings during your hospitalization, adverse events, and the dates of hospital admission and discharge.

There is no time commitment being requested from you. Your participation in the study is over when you are discharged from the hospital.

What are the possible risks and discomforts?

The medical risks and discomforts of being in the study are similar to the risks of getting standard care. Having prolonged seizures is associated with substantial medical risks. These risks are not affected by participation in the study.

The study medicines, fosphenytoin, levetiracetam and valproic acid, are all anti-convulsants, but they work in different ways, and have different risks. The risks of the study medicines are the same whether they are given in the study or for treatment of seizures outside of this study.

Risks and possible side effects of any of the study medicines include drowsiness, dizziness, an allergic reaction, or pain, discomfort, or inflammation where you got the injection in the vein. In addition, fosphenytoin may cause low blood pressure, slow heart rate, vasculitis, or skin rash. Levetiracetam may cause behavior changes such as nervousness, confusion, or aggression. Valproic acid may also cause a skin rash and liver or pancreas problems. There may be other unknown risks as well.

There may be other risks if you are pregnant. Having seizures may cause risk to the fetus, and all of these drugs may cause damage to the fetus in sustained use. There is no known risks to the pregnancy of a single dose of any of the study medicines . There may be risks of the study medicines to a pregnant woman or a fetus that are not yet known. Women who are known to be pregnant will not be enrolled in the study, but it will not be possible to obtain the results of a pregnancy test before enrollment. This is because prolonged seizures are dangerous. If you are currently pregnant, you should inform the study team and your doctor.

There is also a risk of breach of confidentiality related to participation in the study. We will do our best to keep all of your medical information that we collect confidential. We will keep your study information in a secure location during and after the study. Only the members of the study team and the persons and entities listed below will have access to your medical information for the study.

What are the possible benefits?

Because we do not know which of the study drugs is better, you may benefit from receiving a better medicine, but this is not guaranteed. Depending on when you are enrolled in the study, there may be an increased likelihood of being given the best medication. You may not get any benefit from being in this research study. However, the information that we obtain from this study may benefit patients in the future. The information may help us to provide more effective treatments in the future for patients with seizures.

What happens if I choose not to continue in the study?

The alternative to continuing is to no longer take part in the study. If you decide not to continue, your decision will not affect your current or future medical care in any way. If you choose not to continue, no further information will be collected about you.

Being in this study is entirely voluntary. You are also free to withdraw your consent to continue in the study at any time with no impact on your care now or in the future. You may ask and will receive responses to any questions during the course of the study.

New Information:

You will be informed of any new information discovered during your participation that may affect your choice to continue in the study. We may contact you when the study is completed to share the results.

What happens if I am injured or hurt during the study?

If you suffer any injury as a result of taking part in this research study, standard medical care will be available. However, neither this hospital, the NIH, nor the study sponsor or his delegates are able to offer financial compensation or to absorb the costs of medical treatment for such an injury. You will not be giving up any of your legal rights by signing this consent form.

You should report any injury to **SITE PI, MD** at **SITE PI PHONE NUMBER** or to the **SITE Institutional Review Board** at **IRB PHONE NUMBER**.

Costs and compensation:

You will not be paid to be in the study. The study medicines will be provided free of charge. If you received a bill that you believe is related to your taking part in this research study, please contact the study team.

Confidentiality:

To protect your privacy, the information about you gathered for this study will be coded with a special study number. Your name and information that could identify you will be stored securely at the site where you were enrolled or in the study database. Information in the medical record and the study database will be reviewed by monitors and others from the study team or other groups with oversight or regulatory responsibilities. These include:

- **SITE NAME**
- University of Michigan study personnel
- University of Virginia study personnel
- Data Coordination Unit of the Medical University of South Carolina
- National Institutes of Health and affiliates
- Food and Drug Administration
- ESETT Data and Safety Monitoring Board

In addition, records can be opened by court order or produced in response to a subpoena or a request for production of documents.

Identifying information includes your name, address, telephone number, medical record number, and any other information that could directly identify you. Links between your study number and your identifying information will be kept in a secure location.

Health information about you collected for the study may be stored electronically or on paper. The information stored on the computer is kept in password protected files that are maintained on password protected computers. The information stored on paper is stored in a locked file cabinet in a locked office. Health information about you collected for the study may include copies of part of your chart, which are used to check that information put in the study data base is correct. It may also include information recorded while you were in the Emergency Department. The study team may keep a copy or have a facsimile sent and kept in a secure

location at **SITE NAME**.

Your records will be kept for as long as necessary for purposes of the research study. During that time they will be kept confidential to the extent permitted by law. The results of this study could be published in an article, but would not include any information that would let others know who you are. Study results will be published by group only and no data shared publicly will include your name or identifying information.

QUESTIONS: If you have further questions concerning matters related to this research, please contact:

Investigator's Name: SITE PI, MD
Telephone Number: PHONE NUMBER
Research Nurse Coordinator: STUDY COORDINATOR
Telephone Number: PHONE NUMBER

Informed Consent to Continue Participation

SIGNATURES:

Sign below only if you understand the information given to you about the research and choose to continue. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at (XXX)XXX-XXXX. If you decide to continue in this research study, a copy of this signed consent form will be given to you.

We are interested in your experience with this consent process and may ask to talk to you about it further now, or in the future, to ask you a few questions about it.

Participant's Name

Signature and Date/Time

OR

Name of Legally Authorized Representative

Signature and Date/Time

Name of Person Obtaining Consent

Signature and Date/Time

Informed Withdrawal Addendum

(Attach to informed consent document only when a participant chooses to withdraw.)

SIGNATURES: Sign below if you understand the information given to you about the research and choose **not** to continue. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at (XXX)XXX-XXXX.

Although you are opting not to continue in the study, we are interested in your experience so that we can learn more about how patients feel about this type of medical research. We may ask to talk to you about your experience further now, or in the future, to answer a few questions about it. Check here if you do not want to be asked.

Participant's Name

Signature and Date/Time

OR

Name of Legally Authorized Representative

Signature and Date/Time

Name of Person Obtaining Withdrawal

Signature and Date/Time