KESETT CC/PD Content

Website content

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Website content - Landing page

Ketamine in Established Status Epilepticus Treatment Trial (KESETT)

Seizures are a medical emergency that can occur in children and adults. Most seizures are short and stop on their own. These are scary, but are not usually dangerous. Prolonged seizures that do not stop on their own, however, are dangerous and may be life-threatening. Paramedics and emergency doctors give a class of medicines called benzodiazepines to stop prolonged seizures. This usually works but in one or two out of every five patients with prolonged seizures, additional medicines are needed to stop the seizures. Several additional medicines can be used by paramedics and emergency doctors to stop prolonged seizures, but it is unknown which medications work best. We are performing a study to learn if a combination of two existing anti-seizure medicines will stop seizures better than just the medicine most commonly used. Everyone enrolled in the study will receive the most common drug used, levetiracetam, and two thirds of the people enrolled will be given the drug in combination with ketamine.The study is called KESETT. This study is being performed at hospitals around the country in both children and adults, including [insert name(s)] in your community.

In patients who continue to have seizures, additional medications to try to stop the seizures must be given as soon as possible after arrival in the emergency department. People included in KESETT are unconscious because of their seizure, and so cannot be asked about their consent to be in a study. Therefore, this emergency study will enroll participants without their consent.

This study is being conducted at about 60 sites across the US and will enroll no more than 770 people.

Website content - Frequently Asked Questions (FAQ) page

{text condensed to show questions, and expand to show answer when clicked)

Why is KESETT being performed?

The KESETT study is being performed so that doctors can know the best medications to use in the emergency department to treat people with prolonged seizures. KESETT will compare the anti-seizure medication most commonly used in those with prolonged seizures, called levetiracetam (also known as Keppra), with a combination of levetiracetam and another anti-seizure medication, called ketamine.

Are the medications used in this study experimental?

Levetiracetam is currently the most common medication given in usual care for patients with prolonged seizures in the emergency department. Ketamine is also sometimes used to stop seizures, but is used much less commonly for this purpose. Ketamine is commonly given as usual care to treat pain or to provide sedation. Although both medications are FDA approved, and both are routinely used in the emergency department, neither are approved by the FDA for treating prolonged seizures. In this study, therefore, both are considered investigational for treating prolonged seizures and this is the first known study comparing the two medications combined together for seizure treatment.

Who will be included in the study?

People with prolonged seizures are included in this study. This condition is called status epilepticus. Status epilepticus is a life-threatening situation in which the brain is in a state of persistent seizure. The condition is usually defined as a seizure, or rapidly recurring seizures, lasting longer than five minutes without stopping or without the person waking up. This study includes only those who remain in status epilepticus in the emergency department even after receiving a full dose of a benzodiazepine medication (like diazepam, also called Valium). Seizures affect people of all ages, so adults and children down to one year of age are included in this study. Many who develop status epilepticus are people with epilepsy, but others may have never had a seizure before.

What happens in the study?

Every person coming to the emergency department who is eligible will be included in the study. Everyone in this study gets one of three types of study medicine to try to stop their seizure. As the study goes on, if one study medication does not appear to be as effective as the others, it will be given less frequently. Neither the study participant nor their doctor will know which study medicine they received while in the emergency department. If the study medication is effective, it is expected to stop seizures within 10 to 15 minutes. If the seizure does not stop, doctors will give whatever additional medications are needed as part of usual care. A rapid EEG headband may be placed on the study participant's head to detect if silent seizures are occuring. The EEG headband stays on for one to four hours. After the study medicine is given, blood samples may be taken to measure the amount of study drug in the blood. Medical information about the study participant and their condition will be collected from the medical record until hospital discharge.

Will all patients receive the same study medications?

No. In order for us to be able to determine which study medication or combination of medications are better at stopping seizures, patients will be given one of three possible study medications. Everyone will be randomly assigned to receive a single intravenous administration of study medication as early as possible. Random means assigned by chance, like the flip of a coin. Initially 1 in 3 patients will get study medication including levetiracetam alone. Another 1 in 3 will get study medication including levetiracetam and 1 mg/kg of ketamine. Another 1 in 3 get study medication including levetiracetam and 3 mg/kg of ketamine. As the study goes on, if one study medication does not appear to be as effective as the others, it will be given less frequently.

How can research be done on a person without the person's permission?

Research is normally only conducted with the express permission of the patient or parent/legal guardian. However, it is not possible to obtain patients' or parent's consent to study treatments in life-threatening emergencies like status epilepticus. Yet, emergency research is needed to learn what treatments work best. KESETT is conducted under federal regulations that allow an exception from informed consent (EFIC) for emergency research. Once a participant wakes up, or a parent or representative is located, they will be told about the study enrollment and asked to give their permission to continue in the study.

What is an exception from informed consent (EFIC)?

In 1996, the Food and Drug Administration (FDA) developed specific regulations to permit emergency research without consent, in special circumstances, and with additional safeguards. These regulations recognize that there are situations in which patients or family members cannot give informed consent – but that there is also a need to advance emergency care through research.

What are the benefits of this study?

Usual care with levetiracetam stops seizures about half of the time. Combining levetiracetam with ketamine may stop seizures more often, less often, or the same as levetiracetam alone. People in the study may benefit from receiving a more effective medicine, but this is not guaranteed. Participants may not get any benefit from being in this research study. What is learned in this study may also help us to provide more effective treatment for patients with seizures in the future.

What are possible risks of being in the study?

Prolonged seizures that do not stop on their own is a medical emergency. Most of the risks of this condition are similar in those participating in the study and those not participating. It is possible that we will learn that one of the treatments in the study is better than the others. If this is the case, people in one treatment group may not have as good an outcome as those in the other groups.

The study medicines, levetiracetam and ketamine, 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. However, there could be unknown risks of combining the two medicines together, since this is the first time this has been done as part of a research study.

Risks and possible side effects of any of the study medicines include drowsiness, dizziness, an allergic reaction, or pain, discomfort, or inflammation where the medicine is injected in the vein. Ketamine can cause vivid dreams, and a person can be confused or agitated until it wears off. Rare side effects may also include abnormal heart rhythms, high blood pressure, or vocal cord spasms. There may be other unknown risks as well.

If a blood sample is drawn for the study, it can cause slight discomfort, bruising or infection at the site. The EEG headband used in the study can also cause minor skin irritation.

There is also a risk of breach of confidentiality related to participation in the study. We will do our best to keep all the medical information we collect confidential. Precautions are taken to secure this information.

Who is funding the study?

The National Institute of Neurological Disorders and Stroke (NINDS), part of the United States National Institutes of Health.

Can a person opt out of this research?

Yes. Those who do not want to be enrolled in the study can indicate this on a medical alert. This can be marked on one's own medical alert ID or bracelet or we will provide a medical alert wristband indicating "KESETT study declined" for those people upon request.

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Tri-fold brochure content

Front

Learn about KESETT
a seizure study that may affect you or someone you know.

kesett.org

[KESETT Logo}

Inside

Prolonged seizures that don't stop on their own are dangerous.

Most seizures stop on their own or with an initial dose of medicine, and are not very dangerous. Prolonged seizures that don't stop on their own are dangerous. This condition is called status epilepticus.

Status epilepticus :

- Can happen to people of any age
- Can happen to people with epilepsy or people having their first seizure
- Causes people to be unconscious
- Typically requires hospitalization
- Can cause brain damage or death if not effectively treated

KESETT is a research study about medications to stop status epilepticus if the first standard medication does not work.

Commonly used medicines for status epilepticus in the emergency department only work about half of the time. KESETT is a study to see if a combination of medicines might work better. The study compares three ways of treating seizures that continue after an initial emergency treatment. The study compares the most common medicine used in the emergency department, levetiracetam (or Keppra), with a combination of levetiracetam and another medicine called ketamine. The study will find out what treatment is more effective at stopping seizures, and whether the treatments are safe. In this study people with prolonged seizures will get one of these three treatments.

- Levetiracetam only,
- Levetiracetam and ketamine 1 mg/kg, or
- levetiracetam and ketamine 3 mg/kg

Who will be included?

Children 1 year or older and adults who are brought to the emergency department with prolonged seizures with convulsions and unconsciousness lasting more than five minutes are

eligible for this study. Patients will be enrolled in the trial emergently if they have not stopped having seizures after initial emergency treatment. .

What happens in this study?

Everyone in this study is treated emergently for their seizures, but some will get the usual medicine, levetiracetam, alone, and others will get the usual medicine, levetiracetam, combined with one of two doses of ketamine. Both levetiracetam and ketamine are commonly used in the emergency department for seizures or other indications. Which study medications each person gets is assigned at random and the study doctor and participant do not know which study medicines they received. Study medicine is given once, usually shortly after arrival in the emergency department. After the study medicine is given, blood samples may be taken to measure the amount of study drug in the blood. A rapid EEG headband may be applied for one to four hours to detect if silent seizures are occurring. All other aspects of emergency treatment are the same as usual care of people with status epilepticus.

As the study goes on, a higher proportion of patients will be randomized to the medicine or combination which better stops seizures.

If the seizure does not stop doctors will follow their normal procedure and give extra medication to make it stop.

How is enrollment in KESETT different from other studies?

Normally, researchers get permission before a person can be included in a study. A person having a seizure will not be able to give consent. Since a seizure that will not stop on its own must be treated quickly, there will not be enough time to locate and talk to the person's parent or legal representative about the study. To ensure that emergency treatments are never delayed, patients will be enrolled in the study without their parent or legal representative's consent. This is called an exception from informed consent for emergency research. Once the representative is located or the patient wakes up, they will be told about the study and asked to give their permission to continue in the study.

Before researchers may do a study using an exception from informed consent, they must provide information about the study to the community and get their feedback.

How can I share my opinions and feedback about this study?

The research team is interested in your opinions and feedback. You can complete a survey found at this website <insert site url>, or contact the study team directly. You may be able to participate in a focus group as well.

Back.

What if I do not want to be included in the study?

People that do not want to be included in this study when they arrive in the emergency department and have status epilepticus can communicate their desire to opt out of the study by indicating this on some form of medical alert identification. They can add “KESETT Study Declined” to their existing medical alert identification, or they can request a silicone medical alert identification bracelet from the study team.

Those who do not participate in the study, will receive the usual medical treatment provided for people with established status epilepticus at the hospital in your community.

Where can I learn more about the study?

You can learn more about the study online at <insert site url> or by contacting the local study team

<Insert site contact information>.

SIREN & PECARN Networks

The KESETT study is conducted by researchers in the SIREN and PECARN networks. The study is funded by the National Institutes of Health. .

SIREN & PECARN conduct studies to learn how to improve care for children and adults with medical emergencies and injuries, including conditions affecting the brain and nervous system.

The hospitals that will be participating in KESETT in this area include:

<insert site name(s)>

Survey content

The KESETT study is being performed so that doctors can know the best medications to use in the emergency department to treat people with prolonged seizures. KESETT will compare the anti-seizure medication most commonly used in those with prolonged seizures, called levetiracetam (also known as Keppra), compared with a combination of levetiracetam and another anti-seizure medication, called ketamine.

This study is being done before we can obtain subject consent due to the nature of the emergency. Consent will be sought as soon as possible after treatment.

<insert site URL>, click here

<information from website or trifold content>

Do you have any comments you would like to tell the researchers about this study? We would value your feedback via the link below. Your feedback will remain confidential.

First we want to check whether we have communicated clearly about the study. Based on what we have explained, is the following statement true or false? This study is being done without people's consent because there is not enough time to ask their permission and they are in an emergency situation unable to provide their consent.

• True

• False

1. If you had prolonged seizures that did not stop with initial emergency treatments, would you want to be included into this research study, even though you couldn't give consent? We would still try to get consent for continued participation after you are stable and your legally authorized representative can be identified.

• Yes

• No

• I don't know

• I don't want to answer

2. <skip logic, if no / I don't know> What is the reason for your concern?

• Fear about negative effects of the study

• Patients should not lose the right to provide consent for themselves

• Other (please specify)

• I don’t know

• I don’t want to answer

3. If your child or another one of your family members had prolonged seizures that did not stop with initial emergency treatments, would you want them to be included into this research study, even if they or you couldn’t give consent? We would still try to get consent for continued participation after their arrival to the hospital.

• Yes

• No

• I don’t know

• I don’t want to answer

• Not applicable (respondent doesn’t have family members)

4. <skip logic, if no / I don’t know> What do you believe would be the reason for their concern?

• Fear about negative effects of the study

• Patients should not lose the right to provide consent for themselves

• Other (please specify)

• I don’t know

• I don’t want to answer

5. Do you believe that emergency medical research is necessary?

• Yes

• No

• I don’t know

• I don’t want to answer

6. Do you believe that this study should be done in your community?

• Yes

• No

There are a few more questions to ask to make sure that we have a representative sample of your community’s opinions. Your answers will be kept anonymous.

7. What is your age?

8. What is your sex?

• Male

• Female

• I don’t want to answer

9a. Which of the following categories best describes your race?

• American Indian or Alaska Native

• Asian

• Black or African American

• Middle Eastern or North African

• Native Hawaiian or Other Pacific Islander

• White

• I don’t know

• I don’t want to answer

9b. Which of the following categories best describes your ethnicity?

• Hispanic or Latino

• Not Hispanic or Latino

• I don’t know

• I don’t want to answer

10. What is the highest level of education you have completed?

• Less than high school

• High school diploma or GED

• Associate, Technical or Vocational degree

• Some college

• Bachelor’s degree

• Post-graduate degree

• I don’t want to answer

11. Which category best describes your annual household income before taxes:

• Less than $20,000

• $20,000 to less than $35,000

• $35,000 to less than $50,000

• $50,000 to less than $65,000

• $65,000 to less than $80,000

• $80,000 to less than $100,000

• $100,000 or more

• I don’t know

• I don’t want to answer

12. How often do you have someone help you read hospital materials?

• Always

• Often

• Sometimes

• Occasionally

• Never

13. How often do you have problems learning about a medical condition because of difficulty understanding writing information?

• Always

• Often

• Sometimes

• Occasionally

• Never

14. How confident are you filling out medical forms by yourself?

• Always

• Often

• Sometimes

• Occasionally

• Never

15. What is your ZIP code?

16. YOUR OPINION MATTERS GREATLY TO US. Please add any additional comments regarding the KESETT study.