What is EFIC?

The US Food and Drug Administration (FDA), an agency of the federal government that oversees human research involving investigational medicines, has issued regulations to allow clinical studies for emergency research for life-threatening conditions where the current treatment is unproven or unsatisfactory, in order to improve patient outcomes. This type of research, or study, is called Exception from Informed Consent (EFIC) and is when a patient or their legally authorized representative (LAR) is unable to provide consent for their participation at the time of enrollment in the study.

There have been over 40 EFIC studies over the past two decades with over 45,000 patients for use in situations where a patient is unable to give consent to be enrolled in a clinical study. EFIC can only be used when:

- The person is experiencing a life-threatening medical condition
- The best treatment is not known, or current treatments are unsatisfactory
- The study might provide direct benefit to the person
- It is not possible to get permission from the person because of their medical condition nor from the person's guardian because there is a very short amount of time required to treat the medical problem
- There is no way to identify who is at risk for this condition ahead of time

The information provided in this brochure is intended to inform the community about the **RESET (Researching Established Status Epilepticus Treatment) study** and obtain feedback. To learn more information about the study, EFIC, or to request an opt-out bracelet, please visit our website, **TheRESETStudy.com**. If you have any questions, comments or concerns about this study, you may participate in an online survey or focus group to provide your feedback. Space is limited for the focus group and a $50 gift card will be provided for your participation.

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MARINUS

Marinus Pharmaceuticals Inc, a pharmaceutical company dedicated to the development of innovative therapeutics to treat seizure disorders, is sponsoring the RESET (Researching Established Status Epilepticus Treatment) study using Exception from Informed Consent for emergency research. The purpose of the RESET study is to determine how safe and effective ganaxolone (an investigational medicine) is when used in addition to the current medicines for the treatment of prolonged seizures.

RESET

Learn about how a clinical study for individuals with potentially life-threatening seizures, the **RESET study**, may impact you or someone you know!

What is status epilepticus?

Status epilepticus (SE) is the most severe form of epilepsy and is a neurological emergency that requires urgent treatment to avoid possible permanent brain damage, death or other lasting problems. The diagnosis of SE is considered when someone has a seizure for longer than five minutes OR has two or more seizures occurring within a five-minute time span without returning to a normal level of consciousness between the seizures.

Based on SE duration and response to treatment, it is divided into four stages: early, established, refractory and super-refractory status epilepticus. For this clinical study, the **RESET study**, investigators are looking at the second stage of SE, **established status epilepticus (ESE)**, which is defined as SE that persists despite the first-line treatment (usually with benzodiazepine).

Why is this study being done?

Status epilepticus is the second most common neurologic emergency in the US and there are over 150,000 patients in the US that have experienced status epilepticus.

Based on a variety of factors such as cause, age, and duration of the seizure, approximately 3% – 26% of patients with SE do not survive. Since longer seizures lead to greater risk of injury and death, it is important to treat patients experiencing SE as quickly as possible to try to stop the seizures.

There is a significant proportion of both children and adults with SE that have prior history of epilepsy, however, it is not possible to predict who will have SE or identify who is at risk since as many as half (50%) of patients with SE have never had it before.

What is the purpose of this study?

The purpose of the RESET study is to determine the safety and effectiveness of ganaxolone (an investigational medicine) when administered in addition to current medicines used to treat prolonged seizures.

Investigational means ganaxolone has not been approved by the FDA for use outside of clinical studies like this one and it is important to evaluate if a disease or medical condition improves while taking it as part of the clinical study.

When a patient arrives at a hospital's emergency department experiencing prolonged seizures or SE, the standard practice is to administer a benzodiazepine (first-line treatment) followed by an IV antiepileptic drug (second-line treatment). If the seizures have not stopped after the first- and second-line treatment have been given, the patient then moves into the third stage of SE, also known as refractory status epilepticus (RSE).

Because current medications used to treat ESE have been shown to be ineffective in over 50% of patients, the RESET study is trying to evaluate if adding ganaxolone to the second-line treatment (an IV antiepileptic drug) would improve seizure control in more patients.

What if I do not want to participate?

If you wish to opt-out of future participation in this study, please contact our study team to receive an opt-out bracelet or visit the study website to request your opt-out bracelet be sent to you.

How is the RESET study different from other studies?

Normally, doctors get permission (consent) from a person before they can be included in a clinical study. However, due to their seizure condition, the patients in this study may be unconscious and unable to consent for themselves. Because the patient is experiencing a neurological emergency that requires urgent treatment to avoid possible permanent brain damage, death or lasting problems—there is a small window of time to give that patient the study medication that may potentially help them.

When a potentially eligible patient arrives at the hospital, the study team will try to see if there is a family member or legally authorized representative (LAR) they can contact to get consent for the patient to receive the treatment for the study. If they are unable to reach someone, and the patient meets the eligibility requirements for the study, they may be enrolled in the study without their legal representative's or family member's consent.

Who is eligible to participate in this study?

This study will be performed in the emergency department. Anyone 18 years or older who continues to seize despite the first-line seizure treatment, a benzodiazepine, could potentially participate in the study. The first-line treatment may be administered prior to arriving at the emergency department and those patients would still be eligible to participate.