Cover page for VIGAB-STAT

Sponsor Name	American Heart Association
NCT number	NCT04772547
Official Title of Study	A phase IIa feasibility trial of irreversible GABA-transaminase inhibition as adjunct treatment of status epilepticus after cardiac arrest
Document date	8 September 2021

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

If you are the legally authorized representative for the subject, as you read the information in this Consent Form, you should put yourself in the subject's place to decide whether or not to allow us to collect research information about the subject and to allow the subject to take part in this study. Therefore, for the rest of this form, the word "you" refers to the subject (adult participant).

If you are an adult participant reading this form, the word "you" refers to you.

Name of person seeking your consent: _____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. **Name of Participant ("Study Subject")**

   _____

2. **What is the Title of this research study (this "Research Study")?**
   VIGAB-STAT IIa: Vigabatrin in post-anoxic status epilepticus – Phase IIa

3. **Whom do you call if you have questions about this Research Study (the "Study Team")?**

   Principal Investigator: Carolina B. Maciel, MD, MSCR (352) 273-5550

   Other research staff: Study Coordinator at (352) 273-5554

4. **Who is paying for this Research Study?**

   The sponsor of this study is American Heart Association.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved? Cardiac arrest claims millions of lives annually, and even after the heart is restarted patients have a high risk for death and disability due to brain damage. Up to one in three unconscious patients that survives a cardiac arrest may experience uncontrollable seizures (or status epilepticus); nearly 100% of these patients ultimately die from the degree of brain injury associated with these seizures. Recent studies showed that early and aggressive treatment of these uncontrollable seizures could vastly improve survival and the degree of disability. These seizures may appear with convulsions such as body jerk or without any obvious outward sign, therefore, continuous monitoring of the electrical activity of the brain to detect uncontrollable seizures and monitor response to treatment is used as standard of care.

   This study aims to understand the possibility of using a medication called vigabatrin as an early treatment for uncontrollable seizures after cardiac arrest. This medication is FDA approved as an add-on medication therapy for patients with refractory epilepsy, a condition that renders patients at risk for recurrent seizures over their lifetime, but has never been studied in uncontrollable seizures after cardiac arrest. This study will look at the ability to provide the drug within a specific time period and learn how the drug is absorbed into and eliminated from the body in patients that have survived a cardiac arrest. Your involvement will last 6 months, during your ICU stay until discharge, and a brief visit 6 months after discharge.

b) What is involved with your participation, and what are the procedures to be followed in the research? While undergoing standard general clinical care for uncontrollable seizures: you will receive a one-time dose of 4,500 mg of vigabatrin in addition to a dose of an antiseizure drug chosen by your treating physician. This dose will be adjusted downward if your kidney function is significantly impaired. Blood levels of vigabatrin will be monitored before giving you the drug and at the following intervals after drug administration: 0.5h, 1h, 2h, 3h, 6h, 12h, 24h, 48h, 72h, and 7d (168h) We will also measure daily levels of any other antiseizure drugs you might be taking when applicable. In addition, blood work will be obtained once daily for 5 days to check for evidence of damage to the brain cells potentially caused by seizure activity. As soon as you are conscious and able, some tests will be given to you. You will also have follow-up appointments at which time you will be given more tests at 6 months after you leave the ICU.

c) What are the likely risks or discomforts to you? All of the usual risks and discomforts of a stay in the ICU after a cardiac arrest will remain present.

The drug will be administered via a feeding tube, which you will already have in place as means for providing nutrition during your ICU stay. Visual loss has been reported with chronic use of vigabatrin and may be permanent. This is why all patients that use vigabatrin must be part of a mandatory registry that is required by the FDA, regardless of participating in a study. As such, we will be using a specific eye exam called the Goldmann perimetry exam to monitor any potential changes to your vision after you get discharged from the hospital at the six-month follow-up visit. Further description of this specific exam is explained later in the document. Prolonged vigabatrin therapy has also been associated with bright spots in some areas of the brain seen on the MRI scan; these changes usually go away with time and are unlikely to represent a risk for damage to the brain long-term. The risk of developing visual loss and these changes in the brain on imaging after one dose of vigabatrin is unknown as there have been no cases reporting these complications after a single dose. Any antiseizure medication can cause confusion, dizziness, somnolence, fatigue during its use, and these side effects have also been reported with vigabatrin. The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure. Vigabatrin also has a number of potential side effects and these are detailed under Question 12 of this form

d) What are the likely benefits to you or to others from this research;

The participation study may provide benefit to you: as vigabatrin is a strong antiseizure medication, it may help control your seizures even after just one dose. Controlling seizures after a cardiac arrest is important as it may prevent brain cells from dying. This study could provide a helpful treatment for patients suffering from uncontrollable seizures in the future. The Principal Investigator may benefit from publications based on results from this study.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

If you choose not to participate you will still receive the standard treatment options for cardiac arrest and uncontrollable seizures during your stay in the ICU.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website 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.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

General critical care, support of your vital organs such as blood pressure and breathing, artificial nutrition and hydration, and management of abnormal blood work results, and treatment for seizures will be according to local protocols and standard of care, whether or not you participate in the study. You may require special devices to be inserted while you are in the ICU, such as an arterial line (a special type of catheter that allows the medical team to monitor your blood pressure and draw blood), a central line (a special type of IV that travels to your heart), or a feeding tube placed through your nose or mouth. You will receive treatment for your cardiac arrest in the standard way.

Standard of care procedures such as blood work, brain imaging with CT or MRI, and monitoring for hidden seizures (those without jerking) with continuous brain wave monitoring (EEG) will be performed and data from these procedures will become part of this study.

7. What will be done only because you are in this Research Study?

As part of this study, you will receive a one-time dose of 4,500 mg of vigabatrin (or lower depending on your kidney function). The study drug will be given by itself, and when allowed by your normal clinical care, no other drugs will be given within 15 minutes of administration. Drug level will be monitored before giving vigabatrin and afterward at, 0.5h, 1h, 2h, 3h, 6h, 12h, 24h, 48h, 72h, and 7d (168h) along with daily levels of antiseizure drugs you may be taking, each of these blood draws will consist of 1cc of blood. In addition, blood work for tests that suggest damage to brain cells will be collected once a day for 5 days after receiving the drug, collectively these blood draws will consist of 1-2 teaspoonfuls of blood per day. The study team will collect these blood samples from your arterial line that was placed as part of your normal clinical care whenever possible. If for any reason the study team cannot collect blood from your arterial line, we will collect blood through venipuncture.

The study team will perform neurological assessments daily while you are in the ICU. As part of the neurological assessments, the study team will take measurements of the size of your pupils and how quickly they react to light, called pupillometry. Pupillometry is performed with a special device called a pupillometer. It uses a camera to take a video of each of your eyes and to calculate your pupil size and how quickly your pupils react to light. This test takes 1-2 minutes and does not hurt. As soon as you recover from the coma and are able, some tests will be given to you that include questionnaires summarizing your level of disability and visual assessment to screen for potential visual loss. You will also have formal follow-up appointments at which you will be given more tests at 6 months after you leave the ICU.
A table of scheduled events is included at the end of this form.

The following tests will be administered and data gathered at the following timepoints.

Baseline
The following subject characteristics and medical information will be collected
• Criteria for entry into the study
• Demographics
• Drugs administered
• Medical history
• Home medications
• Factors leading to seizure (e.g., prior traumatic brain injury or other structural injury, history of epilepsy, congenital defects)
• Results of FOUR-score assessment during admission. This assessment assesses the severity of coma.
• Neurological assessments
• Signs of uncontrollable seizures prior to EEG monitoring
• vigabatrin levels in your blood
• antiseizure drug levels
• Results of blood tests done upon admission

Data that will be collected during drug administration:
• FOUR-score – data will be collected on the severity of your coma
• Neurological assessments
• Pupillometry
• Drug levels and results of monitoring labs

Data collected daily during your stay in the intensive care unit
• FOUR-score
• Neurological assessments
• Pupillometry
• Serious adverse events (SAEs)
• Levels and results of labs
• Data will be collected on details of uncontrollable seizures and the times associated with the administration of vigabatrin
• EMSE – epidemiology based mortality score – this will be used to track severity of seizures

Data to be collected at ICU discharge
• FOUR-score
• You will be asked to obey verbal commands
• Data will be collected on the amount of time on mechanical ventilation
• ICU length of stay
• Neurological assessments

Data to be collected at hospital discharge
• FOUR-score
• Discharge status (e.g., good, fair, stable, poor, critical, dead)

• Neurological assessments
• Discharge destination

Data to be collected on Day180
You will return to the Neuromedicine Hospital and the following data will be collected and assessments performed
• Survival status
• Neurological Assessments
• MoCA – this is a cognitive assessment which will ask you 9 questions to test your memory, math calculations, orientation to date and time and concentration
• Goldmann perimetry– you will be scheduled at the Neuro-Ophthalmology Clinic at the Oaks Mall. This is a visual test to determine your range of peripheral vision and may take 5-15 minutes to complete
• VFQ-25 – you will be asked 25 questions about your eyesight and may take 5-10 minutes to complete
• SF-36 – you will be asked questions about your quality of life and general health and may take 5-10 minutes to complete

Test/Lab	Baseline	D0	D1	D2	PASE	VGB Administered (0h)	0.5 h	1h	2h	3h	6h	12 h	24 h	48 h	72 h	96 h	120 h	168 h	D14/ICU Discharge	Hospital Discharge	D180
Review of Eligibility: Inclusion/Exclusion Criteria[b]	X	X	X	X																	
Demographics	X																				
Informed Consent		X	X	X																	
Medical History		X																			
Vitals		X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	X
Cardiac-specific Treatments and Assessments		X																			
Neurological Assessments		X	X	X	X	X							X	X	X	X	X	X	X	X	X
Pupillometry		X	X	X	X	X		X					X	X	X	X	X	X	X		
FOUR		X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	
Medications		X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	X
mRS																				X	X
GOS-E																				X	X
CPC-E																				X	X

MoCA																				X
EMSE																				X	
VGB level						X[c]	X	X	X	X	X	X	X	X	X			X			
Standard Anti-seizure drug level						X[c]		X		X		X	X		X			X			
Routine complete blood cell count, complete metabolic panel, ABG, lactic acid	x	x	x	x	x						x		x	x	x	x	x	x			
Biomarkers: NSE, GFAP, NfL						X							X	X	X	X					
Taurine level						X[c]									X			X			
cEEG		X	X	X																	
MRI Window															X	X	X				
Goldmann perimetry																					X
VFQ-25																					X
Clinical Events		X	X	X	X	X		X		X		X	X	X	X	X	X	X	X	X	
Discharge Summary																				X	

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect medical record data, EEG and MRI data, lab tests, demographic information, questionnaires related to the study and all standard hospital, diagnostic, and treatment related information.

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study. The results of your EEG and visual testing (Goldmann perimetry) will be de-identified and no personal information will be shared with co-investigators at other institutions (Yale University and Tomas Jefferson University, respectively) who are analyzing the data.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- Your insurance company for purposes of obtaining payment

- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

Your participation will last approximately six months consisting of: the length of your ICU stay and treatment, and at 6 month follow up visit after discharge from the ICU.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

12 status epilepticus subjects who suffered a cardiac arrest will take part in this phase of this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

There are risks and discomforts during the admission in the ICU after a cardiac arrest and those will be discussed with you. Damage to your vision (from blurriness to visual loss) have been reported with chronic use of vigabatrin and may be permanent. As such, we will be performing eye exams and assessments upon your regaining of consciousness. We will also perform pupillometry during your ICU admission. There are no risks associated with these tests.

As is commonly seen with any antiseizure medication, the use of vigabatrin may cause fatigue, somnolence, dizziness and imbalance, abnormal eye movement, tremor, memory impairment, weight gain, joint pain, and confusion, all of which go away after discontinuation of use. Using vigabatrin for long periods has also been associated with bright spots in some areas of the brain seen on MRI scan, which go away when vigabatrin treatment is stopped and may not cause any known long-term sequelae. The drug may have risks unknown at this time.

Additionally, the risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure. When possible, the study team will collect blood samples from your arterial line, which you will already have as part of your normal clinical care. Collecting blood from an arterial line does not hurt and there are no additional risks.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

The vigabatrin treatment may help control your seizures and protect your brain cells from dying.

13b. How could others possibly benefit from this Research Study?

This study could lead to a treatment that could improve the outcomes for patients suffering from uncontrollable seizures after cardiac arrest.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

If you choose not to participate in this study you will receive the standard treatment options for uncontrollable seizures (status epilepticus) and post-cardiac arrest recovery.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- The principal investigator believes the study is not in your best interest.
- You are no longer eligible to participate in the study.
- The study ends early.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No, there will be no additional costs to you or your health plan as a result of your participation in this study. The sponsor will pay for all health care costs related to your participation, including all required study items, services and procedures described in this consent form. However, if you feel you have received a bill related to this study, please contact the Principal Investigator.

If you receive any healthcare at UF Health that is not related to this study, this care will be billed as usual.

17. Will you be paid for taking part in this Research Study?

You will be paid a $25 stipend to cover travel expenses for your return to the research clinic for the Day 180 visit. You must complete this visit in order to receive the stipend.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment contact the study coordinator.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the Research Team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this Research Study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

_____

Signature of Person Obtaining Consent & Authorization Date

Consenting Adults. You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

Adult Consenting for Self. By signing this form, you voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____

Signature of Adult Consenting & Authorizing for Self Date

Parent/Adult Legally Representing the Subject. By signing this form, you voluntarily give your permission for the person named below to participate in this study. You hereby authorize the collection, use and sharing of protected health information for the person named below as described above. You are not waiving any legal rights for yourself or the person you are legally representing. After your signature, please print your name and your relationship to the subject.

_____

Consent & Authorization Signature of Legal Representative Date

_____ _____

Print: Name of Legal Representative Print: Relationship to Participant:

_____

Print: Name of Subject:

_____

Print: Name of Subject: