RESEARCH CONSENT FORM

Project Title: Pilot study of the neuroprotective effects of hydrogen and minocycline in acute ischemic stroke
Principal Investigator: Kamil Stefanowski, MD
Co-Investigators: Dennis Choi, MD, PhD; Michael Guido, MD, Jason Mathew, DO; MD; Alison Caruana, MD; Lauren DeNiro, MD; Yuehjien Gu, MD; Ethan Brandler, MD
Department: Neurology, Emergency Medicine

You are being asked to be a volunteer in a research study.

You are encouraged to take your time in making your decision. You may want to discuss this study with your friends and family.

PURPOSE

The purpose of this study is:

- To test the effect of two drugs (hydrogen and minocycline, given together) on recovery after an acute stroke
- Adult patients with symptoms of acute stroke in the past 24 hours can be in the study.
- While there are a few drugs that can directly reduce brain damage after stroke in lab animals (neuroprotective drugs), no such drug has yet worked in humans. We hope that the combination of hydrogen and minocycline will be effective as neuroprotective drugs in human stroke.
- Hydrogen can protect brain cells from damage by stroke in animals. Hydrogen is present in low amounts in normal air. Hydrogen is considered experimental in this study as it is not approved by the US Food and Drug Administration (FDA) for use as a drug.
- Minocycline is a widely used antibiotic drug that can also protect brain cells from damage by stroke in animals. Minocycline is experimental in this study as it is not approved by the FDA to treat stroke.
- We aim to enroll 100 subjects from Stony Brook University in this study.

PROCEDURES

If you decide to be in this study, your part will involve:

- Your baseline brain function and vital signs will be obtained from your medical record.
- You will be assigned by chance to either the treatment group to receive the real drug, or the placebo group. There is an equal chance of being in either group like flipping a coin. The placebo group will receive an inactive substance that looks like the real drug.
- Hydrogen will be given 2-3 times a day for 3 days, dissolved in drinking water or intravenous (IV) fluid. If you are found to be unable to swallow, a tube can be inserted through your nose to your stomach (called a “nasogastric tube”). This is part of routine care for many patients after a stroke. The tube provides a route to administer fluids, nutrition, and medicines. We can administer the hydrogen water through the tube. If you cannot have a nasogastric tube inserted, the hydrogen water will be administered IV. If you can swallow but cannot tolerate thin liquids, you can use pre-thickened water like Hormel Thick & Easy or thickener.
- Minocycline will be given once a day for 5 days, by IV fluid or capsules.
- If you are discharged before completing the treatment, you will be given the study medications to take with you. Study staff will call to see if you are able to finish the treatment.
- Study staff will call you on study day 45 and day 90 to ask a few questions about your brain function. The phone call will take 10 minutes. If you have a clinic visit at day 90, the questions will be asked in person.
- After the study, your data will be saved on a secure Stony Brook server which can only be accessed by study staff. In the future, the study staff may submit a new proposal to obtain approval from the Stony Brook Institutional Review Board to use this data.
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RISKS / DISCOMFORTS

The following risks/discomforts may occur as a result of you being in this study:

- We do not expect any major side effects from hydrogen. Mild side effects reported in earlier small studies were headache, heartburn, and loose stools.

- Minocycline has been taken by many people and is usually safe. However, any drug can produce side effects in an individual. Uncommon side effects of minocycline include sensitivity to sunburn, skin itching, joint aching, light-headedness, dizziness, ringing in ears, or an allergic reaction. When side effects occur, they usually stop when the drug is stopped.

- Enrolling in this study may lead to somewhat earlier insertion of the nasogastric tube. The potential risks of nasogastric intubation include discomfort, and injury of the tissue inside of the nose, sinuses, throat, esophagus, or stomach. Rare risks

include internal bleeding, abdominal cramping, abdominal swelling, diarrhea, nausea, vomiting, regurgitation of medicine, and aspiration.

- The potential risks of IV drug delivery include discomfort, bruising, and pain at the site of injection. Rare risks include inflammation of the vein used for injection, phlebitis, metabolic disturbances, and injury. Very rarely will there be severe reaction, anaphylaxis, cardiac arrest, or death.

- **Being a part of this study while pregnant may expose the unborn child to risks that are not justified, given the purpose of the study. Therefore, pregnant females will be excluded from the study. If you are a female who can become pregnant, a pregnancy test must be done and must be negative before you can enter this study. If you are sexually active, you or your partner must agree to use appropriate contraceptive measures while you are taking study drug. These measures include:**
  - **Abstinence**
  - **Barrier methods (such as condom or diaphragm) used with a spermicide, or**
  - **an intrauterine device (IUD).**

  Birth control pill is not recommended as the study drug (minocycline) may cause it to be less effective. If you do become pregnant while taking study drug, you must inform your study staff immediately.

Since this is a research study, not all risks may be known at this time. There may be unforeseen risks associated with study participation.

BENEFITS

The following benefits may occur as a result of being in this study, but this cannot be guaranteed:

- The study drug may protect your brain from damage and thus improve your recovery.
- This study will help researchers develop better treatments for stroke.

PAYMENT TO YOU

You will not be paid for your participation.

CONFIDENTIALITY

We will take steps to help make sure that all the information we get about you is kept confidential. Your name will not be used wherever possible. We will use a code instead. All the study data that we get from you will be kept locked up. The code will be locked up too. If any papers and talks are given about this research, your name will not be used.

We want to make sure that this study is being done correctly and that your rights and welfare are being protected. For this reason, we will share the data we get from you in this study with the study team, Stony Brook University's Committee on Research Involving Human Subjects, applicable Institutional officials, and certain federal offices, including the Office for Human Research Protections (OHRP), and, where applicable, the Food and Drug Administration (FDA). However, if you tell us you are going to hurt yourself, hurt someone else, or if we believe the safety of a child is at risk, we will have to report this.

In a lawsuit, a judge can make us give him the information we collected about you.

While you are in this study we will get data about your health from your medical record. We will also get health data from the results of the tests you will have done in this study. You have a right to privacy but the data we get about your health in this study can be shared with the people referenced above (the study team, those who work for Stony Brook University's Committee on Research Involving Human Subjects, applicable institutional officials, and federal offices such as OHRP, FDA) as well as:

- your medical doctor
- A board that reviews the safety of the study on an on-going basis.

Your health data are shared to make sure the study is being done correctly, costs are charged correctly, and to make sure your rights and safety are protected. Not all of these people are required by law to protect your health data. They might share it with others without your permission.

Some of the health information we get from you in this study cannot be shared with you until the end of the study.

You have the right to stop allowing us to use or give out your health data. You can do this at any time by writing to Dr. Stefanowski (Department of Neurology, 101 Nicholls Road, Health Sciences Center T12-020, Stony Brook, NY 11794-8121). If you do this, we will stop collecting any new health data from you, except if we need to keep an eye on a bad side effect you were having in the study. We will use any data we collected before you wrote your letter. When you sign the consent form at the end, it means:

- That you have read this section.
- That you will allow the use and reporting of your health data as described above.
- You have received a form from the University Hospital. It is called the Notice of Privacy Practices form.

Clinical Trial Registry

A description of this clinical trial will be available on http://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".

COSTS TO YOU

The study drugs will be given to you without cost. There are no other costs to you or your insurance company for medications or treatment given in this study.

ALTERNATIVES

Your alternative to being in this study is simply not to participate.

IN CASE OF INJURY

If you are injured as a result of being in this study, please contact Dr. Stefanowski at 631-444-2599. The services of Stony Brook University Hospital will be open to you in case of such injury. However, you and/or your insurance company will be responsible for payment of any resulting treatment and/or hospital stay.

CONSEQUENCES OF WITHDRAWING

You may choose to withdraw from the study at any time. There are no risks associated with withdrawing from the study.

REMOVAL FROM STUDY

Your participation in the study may be stopped by study staff at any time. You will be removed from the study if: you become pregnant; your medical condition or current medications change; the study staff deem that it is in your best interests to withdraw from the study; or you do not follow study procedures.

YOUR RIGHTS AS A RESEARCH SUBJECT

- Your participation in this study is voluntary. You do not have to be in this study if you don't want to be.
- You have the right to change your mind and leave the study at any time without giving any reason, and without penalty.
- Any new information that may make you change your mind about being in this study will be given to you.
- You will get a copy of this consent form to keep.
- You do not lose any of your legal rights by signing this consent form.

QUESTIONS ABOUT THE STUDY OR YOUR RIGHTS AS A RESEARCH SUBJECT

- If you have any questions, concerns, or complaints about the study, you may contact Dr. Stefanowski at 631-444-2599. Address: Department of Neurology, 101 Nicholls Road, Health Sciences Center T12-020, Stony Brook, NY 11794-8121.
- If you have any questions about your rights as a research subject or if you would like to obtain information or offer input, you may contact Ms. Lu-Ann Kozlowski, Committee on Research Involving Human Subjects, (631) 632-9036, OR by e-mail, lu-ann.kozlowski@stonybrook.edu.
- Visit Stony Brook University's Community Outreach page, http://www.stonybrook.edu/research/orc/community.shtml for more information about participating in research, frequently asked questions, and an opportunity to provide feedback, comments, or ask questions related to your experience as a research subject.

If you sign below, it means that you have read (or have had read to you) the information given in this consent form, and you would like to be a volunteer in this study.

☐ Subject able to provide consent

_____	_____	
Subject Name	Signature	Date
_____	_____	
Name of person obtaining consent	Signature	Date

☐ Subject unable to provide consent

_____
Subject name

_____	_____	
Legally authorized representative (LAR) name	Signature	Date

_____
Relationship to Subject

_____	_____	
Name of person obtaining consent	Signature	Date

"My signature below attests to the fact that I am a qualified professional and I have interviewed (name of patient) on _____ (date). I have determined that s/he does_____ does not_____ have the capacity to consent to participation in this research activity, in that s/he is____ is not____ capable of appreciating a) that the activity described in this consent document constitutes research, not standard treatment, b) the risks and benefits of this study c) the alternatives that are available if s/he chooses not to participate, and d) that the decision to not participate will be accepted without penalty, i.e., without jeopardizing his/her clinical care."

_____	_____	
Professional Providing Attestation Name (Printed)	Signature of Professional providing Attestation	Date