# CONSENT FORM

## *SUNY Downstate Medical Center*
## *Kings County Hospital Center*

## *ARTSS-2: A Pilot, Phase IIb, Randomized, Multi-center Trial of Argatroban in Combination with Recombinant Tissue Plasminogen Activator for Acute Stroke*

We are asking if you want to be in a research study. This study is for people who have had a STROKE ("Brain Attack").

## What you should know about research studies:

- This consent form gives you information about the study. It tells you about the purposes, risks, and benefits of this research study.
- ***Regular care*** is based on the best-known treatment. The main goal of regular care is to help the individual patient. The main goal of ***research studies*** is to learn more so that we can help future patients. You might benefit from being in the study, but we cannot promise this.
- There may be risk to participating in this study.
- Your participation is voluntary. You don't have to be in this research study. You can agree to be in the study now and change your mind later. Your decision will not affect your regular care. Your doctor's attitude toward you will not change.
- Please read this consent form carefully. Ask any questions you have before you make a decision. The study doctor will answer your questions. You may consult with your family or friends.

## *1) Why is this research being done?*

Most strokes are caused by a clot that blocks a blood vessel in the brain. When people have a stroke, the normal blood flow decreases, which can cause brain damage. This can cause weakness or lack of feeling to one side of the body, changes in vision, or troubles in speaking or understanding.

The Food and Drug administration (FDA) has approved the use of a drug called rt-PA. This drug breaks up the clots that cause stroke. Patients can get this drug within 3 hours of the start of their stroke symptoms. A European study showed that this drug can be helpful even after 3-4.5 hours. The American guidelines now agree with that.

Although the body may break up the blood clots on its own, rt-PA helps the body in the

process. However, rt-PA is not always enough.

Argatroban is a drug that stops clots. In Japan it is already used for stroke. In the United States it is used for other diseases caused by clots. Animal studies have shown that using Argatroban with rt-PA is better than using rt-PA alone. We completed a study treating 65 stroke patients with Argatroban and rt-PA. There were no apparent safety issues. In fact, using the drugs together seemed more effective in breaking up clots.

The purpose of this study is to see if combining the standard treatment (rt-PA) with Argatroban improves disability in stroke patients at 90 days.

## *2) Who is doing the study?*

Dr. Steven Levine is in charge of this study at this location. About 10 people will be enrolled in the study from SUNY Downstate and at Kings County Hospital Center. About 105 people will be in the study around the world.

This study is being supported by the National Institutes of Health (NIH and the University of Texas – Houston).

## 3) Will it cost me money to be in this study?

The study drug Argatroban will be provided to you free as part of this study.

While participating in this study, there are certain procedures, tests and/or drugs that may be given to you as part of standard medical treatment for your medical condition, but are NOT free of charge. We will bill your insurance provider for these costs. However, if your insurance provider decides that you are responsible for paying any of these costs, such as copayments and deductibles, we will bill you.

You should know that your insurance coverage may legally refuse to pay any study-related costs for a number of different reasons. For example, if the insurance provider believes that the treatments are not medically necessary and/or are not proven effective for your condition, the coverage may deny payment.

It is the research investigator's responsibility to find out in detail what portion, if any, of the study-related procedures your insurance will cover for your participation in the study. If your insurance denies an insurance claim for any study-related procedures, the investigator will assist in the appeal of the denial.

If you have Medicare, you may visit the National Institutes of Health (NIH) website at www.cancer.gov/clinicaltrials/digestpage/medicare for further information about study-related expenses Medicare is required to cover. If you do not have internet access, please use any public library or ask a family member to help you.

## 4) You cannot be in this study if:

- You are not at least 18 years old.
- You are pregnant.
- You have a history of bleeding in the brain, known blood vessel defect, or untreated brain aneurysms.
- You have had a significant bleeding episode [e.g. gastrointestinal (GI) or urinary tract] in the last 3 weeks.
- You have had a major surgery or serious trauma in the last 2 weeks.
- You have had a stroke or heart attack in the last 3 months.
- You have a history of liver problems or liver disease – including a current history of alcohol abuse (Your response will be recorded in the study record, and, in the case of a judicial summons, this information may be released to the authorities).
- You have had a brain tumor.
- You have participated in a drug or device study in the last 30 days.
- You are allergic to Argatroban or its agents.
- **If you arrive at the hospital between 3 – 4.5 hours after your symptoms began, you cannot be in this study if**:
    - You are greater than 80 years old
    - You are taking blood thinners
    - You have a history of stroke and diabetes.

## 5) What will happen to you if you decide to be in this study?

This study involves the following three parts:

1) Screening and treatment through the first 48 hours
2) After treatment through the first 7 days or just before you leave the hospital
3) Follow-up at 3 months

<u>Screening and treatment through the first 48 hours:</u>

This part of the study will take place in the emergency room or in the intensive care unit (ICU).

- As part of your routine care, your doctor will take your medical history and check your blood cell count and the salts in your blood (electrolytes). If you are a woman of childbearing age, your doctor will give you a pregnancy test. Also as part of standard care, your doctor will check your heart with an ECG test, and your brain with a CT scan.
- For the study, if you have a mild to moderate stroke (NIH Stroke Scale score of less than 10) the doctor may image the blood vessels in your brain with a CT-angiogram to determine whether there is a clot.

The activities we will ask you to do are:

- Talk about the informed consent form
- Sign the informed consent form
- Go over the reason for being in the study
- If you can be in the study, a computer will randomly put you in one of three groups. You will have an equal chance of being in each group.
    - Group 1: we will give you the standard of care drug (rt-PA) and no study drug.
    - Group 2: we will give you rt-PA and a low dose (100 ug/kg bolus followed by a 48 hour drip at 1 ug/kg/min) of the study drug.
    - Group 3: we will give you rt-PA and a high dose (100 ug/kg bolus followed by a 48 hour drip at 3 ug/kg/min) of the study drug.
- We will give you the study drug as an IV for up to 48 hours.
    - We will change the amount to make sure your blood is still clotting correctly.
- We will give you another CT-angiogram of your brain 2-3 hours after you receive the study medicine if you received a CT-angiogram prior to receiving the medication.
- We will take blood tests 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours after you receive the study medicine.
    - If we change your dose, we will also take a blood test 2-4 hours after the change.
- We will ask you questions (NIH Stroke Scale) 2 hours, 24 hours, and 48 hours after you receive the study medicine to see if your symptoms are improving.
- We will take another CT scan of your brain after 48 hours.
- We will go over your medical records to look at:
    - Your medical history of stroke or other brain issues
    - Results of your lab tests and ECG
    - Medicines you have taken in the past or are taking now
    - Results of your CT scans
- We will copy this information from your medical records and record it in the study database
- We will not let anyone else know any personal details about you

After you get treatment with the study drug through day 7 or right before you leave the hospital (whichever happens first):

The activities we will ask you to do at this time are:

- We will give you a physical examination, where we will check to see how your stroke has affected you by administering a stroke scale
- We will ask you questions (modified Rankin Scale and Montreal Cognitive Assessment) to see how your stroke affected you.

Follow-up: 3 months after your stroke:

Visit with a doctor at 3 months (this is standard care for stroke patients)

- The study doctor will give you a physical examination, where they will check to see how your stroke has affected you by administering a stroke scale.
- They will administer an exam to see if you have any disabilities by asking you about the things you have been doing everyday.
- The doctor will see if you are having any side effects or problems with your health.
- We will ask you questions (Montreal Cognitive Assessment) to see how your stroke affected your thinking.

## 6) *What are the possible risks of being in the study?*

There may be unwanted side effects or risks from the study drug. Since Argatroban stops clotting, it may increase bleeding. Bleeding may occur anywhere, even in the brain. Previous studies have suggested a 6.2% chance of bleeding when taking Argatroban. We will review safety throughout the study. We will stop the study if there is too much bleeding.

Both rt-PA and Argatroban can increase the risk of bleeding. Using them together might cause more bleeding than using rt-PA alone (6.4% chance). However, the risk of bleeding could also stay the same. In our last study, the low-dose Argatroban plus rt-PA seemed safe. However, the safety of the high-dose Argatroban is still unknown.

Many stroke patients receive a head CT and a CT-A of the head and neck as part of their standard care. These are considered normal X-ray tests for stroke patients. They tell the doctor what kind of stroke you had.

Patients who receive a CT-A may be allergic to the dye. Small allergic reactions (for example, nausea or hives) occur 1 in 200. Bigger allergic reactions like very low blood pressure can occur in 1 in 10,000 people. Also, there is a small risk (1%) of kidney failure. This may be higher if you already have kidney problems or diabetes. The second CT-A produces a small amount of radiation like other X-Rays. This second CT-A is extra for the study to see if treatment helped. The amount of radiation from a CT-A is about the same

as the amount you get in 10 months of day to day life.

You may have a risk or side-effect we don't know about yet. You might develop a new condition or suffer an injury. If you do, you should tell the study doctor immediately.

## 7) What are the possible benefits of being in the study?

We cannot promise that you will benefit from being in this study. However, ***possible*** benefits include better recovery with use of Argatroban with rt-PA. Our study results may also help other people who have a stroke.

## 8) What are your other choices?

The alternative to being in this study is to not participate. You will still receive standard of care.

## 9) If you have any questions or problems, whom can you call?

If you have any questions about this study, you can call Steven Levine at (917) 252-0462. If you think you have been injured because of the research, you should call Steven Levine at (917) 252-0462.

If you have questions about your rights as a research subject, you can call the IRB office at (718) 613-8480, or you can contact the SUNY HSCB University Hospital Medical Director's Office at (718) 270-2401 or the Kings County Hospital Center Medical Director's Office at (718) 245-3921.

Call (718) 270-2121 24 hours a day and ask for Steven Levine for study-related emergencies.

## 10) What information do we keep private?

In this study we will keep your personal information confidential. We will hold your identity confidential and all data will be kept in a secure, limited access location. We will not reveal your identity in any publication or presentation of the results of the study. However confidentiality cannot be guaranteed; your personal information may be disclosed if so required by the Federal Privacy law.

Federal law protects your right to privacy concerning Individually Identifiable Health Information (IIHI). There are certain things you need to know, IIHI is any information from your medical record, or obtained from this study, that can be linked to you, and that refers to your mental or health conditions in the past, the present or the future.

For this study we will create, use or report the following IIHI:

- Information from your medical records including treatment received and service dates
- Information obtained from this study, including results of physical examinations, laboratory tests, CT scans, and CT-angiograms

The researcher, Dr. Steven Levine, his staff and the staff of SUNY Downstate Medical Center and Kings County Hospital Center participating in the research will use your protected IIHI for this research study.

Your IIHI will be shared with the following persons or agencies for purposes related to the conduct of the research:

- The sponsors of the study: the National Institutes of Health (NIH) and the University of Texas – Houston
- The Food and Drug Administration
- The Data Safety Monitoring Board that reviews the safety of this study
- The Institutional Review Board of SUNY Downstate Medical Center, the applicable DMC and KCHC officials, and the federal Office for Human Research Protections.
- Glaxo Smith Kline Inc. that provides the Argatroban

We will have to use and report your health information for an indefinite period of time.

You need to know that some of the individuals or groups mentioned above are <u>not</u> obligated to protect the privacy of your IIHI. For example, NIH and University of Texas – Houston do not have the same obligation to protect your IIHI under the federal privacy laws.

Some IIHI that is obtained in this study will not be shared with you. This includes results from blood tests, CT scans, CT-angiograms, and ultrasounds. This information can be shared with you at the end of the study.

You can withdraw this authorization for the use or reporting of your IIHI. You have to write to us to withdraw:

Steven Levine
SUNY Downstate Medical Center, Box 1213
450 Clarkson Ave.
Brooklyn, NY 11203

If you withdraw we will stop collecting and accessing your IIHI, but we will collect and report any adverse event (bad effect) that you had in the study. Your IIHI collected before you withdraw your authorization will still be used and reported.

If you withdraw your authorization you can no longer be in the study.

If you are not eligible to participate in this study due to the exclusion criteria, the reason for your exclusion will be noted. This information will, however, be kept confidential.

## *11) Can your being in the study end early?*

Being in this study is voluntary. You do not have to be in the study if you don't want to. You can agree to be in the study now and change your mind later. If you want to quit the study, you should talk to Steven Levine or one of the study staff members.

Steven Levine or the University of Texas - Houston can take you out of the study without your permission. Possible reasons for this are:

- if you have an adverse reaction to the study drug.

Also, the University of Texas - Houston may end the study early. If your being in the study ends early, we may ask you to visit the study doctor for some end of study procedures.

## *12) What else do you need to know?*

If we find out any new information that might affect your decision to stay in the study, we will give it to you.

You might be injured by being in this study. If you are, emergency care will be available. If your study visit(s) take place at SUNY Downstate Medical Center, it does not have a policy to pay you if are injured by being in the study.

If your study visit(s) take place at Kings County Hospital Center, New York City Health and Hospitals Corporation does not provide financial compensation for injury or illness from participation in research. Payment for medical treatment, both standard and experimental, as well as treatment of any side effects will be assumed in the usual manner by you personally or through your medical insurance; unless a Sponsor, such as a pharmaceutical or device manufacturer agrees to compensate you for treatment costs for a research related injury not covered by your insurance. However, medical care for any injury or illness resulting from patient participation is available regardless of ability to pay.

## 13) Subject Consent

By signing this consent form you accept that you read this form, or had it read to you. You agree to be in the study and authorize the use and reporting of your individual identifiable health information (IIHI) as explained in this form. You will not be giving up any of your legal rights by signing this consent. We will give you a copy of this form and of DMC's Notice of Privacy Practice.

| Signature of Subject or Legally Authorized Representative (LAR) | Date | Time | Print name |
|---|---|---|---|

If LAR, state relationship to subject

| Signature of Person Obtaining Consent | Date | Time | Print name |
|---|---|---|---|

| Signature of Witness (if applicable) | Date | Time | Print name |
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