Multi-arm Optimization of Stroke Thrombolysis (MOST) Stroke

Study Information Sheet

What is this Document?

You have agreed to participate in a research study called Multi-arm Optimization of Stroke Thrombolysis (MOST) Study. This document will give you some additional information about the MOST study. This is not another consent form. You do not need to sign it. It just provides you with additional information about the MOST study.

What is the Study About?

The MOST study includes patients who have had strokes caused by a blood clot in their brain (also called ischemic stroke) and are receiving standard treatments. Standard treatment for strokes caused by clots is to try to dissolve or to remove the clot. The standard medicine used to try to dissolve a clot is called tissue plasminogen activator (tPA). A device may also be used to try to remove the clot. This procedure is called thrombectomy. All participants in the MOST study will receive whichever standard treatments are available and felt by their doctors to be appropriate to treat their stroke.

The main purpose of the MOST study is to examine the safety and the effectiveness of adding one of two blood-thinning medicines to standard treatment with tPA. The blood thinning-medicines are eptifibatide (ep TIF I ba tide) or argatroban (ar GAT ro ban). Both are FDA-approved blood thinners, but they are not approved for treating strokes. We are studying whether these medicines are safe and help stroke patients.

Previous studies have shown that the combination of tPA plus argatroban or eptifibatide might help to keep blood vessels open and decrease stroke severity and impact of the stroke when compared to tPA alone, and seem to be safe. However, those studies were small and did not include enough people to know for sure whether tPA plus argatroban or eptifibatide worked better than tPA alone. There should be enough people in the MOST study to answer this important question.

StrokeNet- The MOST study is being done as part of the StrokeNet network. StrokeNet is a group of hospitals around the country dedicated to stroke research and improvement of stroke care. This hospital is one of the sites participating in this study. Up to 1,200 patients will be enrolled in the MOST study nationwide. There is some more information about StrokeNet at the end of this document.

What Happens During the Study?

Screening and Entry into the Study

Before you were asked to be in the study, the study team and doctors reviewed your medical records in order to determine whether you were eligible to be in the study.

After getting permission (informed consent) to include you in the study, the study team asked you some questions and did a physical exam to assess your stroke.

Investigational Treatments

Most of your treatment is not affected by being in the MOST study. Everyone in MOST is treated with tPA, monitored very closely, and treated with all of the medicines or procedures that are standard treatment for stroke (just like people who are not in the study). The only way that the MOST study affects treatment is whether you *also* receive argatroban or eptifibatide, the medicines studied in MOST.

The MOST study has three investigational treatment groups.

- Group A receives standard treatment plus an IV placebo (salt water) solution that does not have eptifibatide or argatroban in it.
- Group B receives standard treatment plus IV argatroban.
- Group C receives standard treatment plus IV eptifibatide.

You will not know which group you are in. Everyone in each group will have an investigational treatment given through the vein (IV) for a 12-hour period.

Assignment to a Study Group

A computer randomly places you into 1 of the 3 study groups. This means the computer puts you into group A, B or C by chance. Your doctor does not choose which group you are in, and you will not know which group you are in. This makes sure the groups are similar so that any differences in results between the groups can be detected.

Monitoring While Getting the Study Medicine

You are closely monitored while getting the study medicine. Blood tests may be done to measure how long it takes for your blood to clot at 2 and 6 hours depending on which group you are in. The dose of study medicine may be changed based on these results.

If at any time during the study there is a concern that you might be having a side effect (bleeding, for example), you will be assessed. If appropriate, the study medicine will be stopped and you will receive whatever tests or treatments are necessary at that time.

What are the Benefits of Being in the MOST Study?

The MOST study is testing whether either argatroban or eptifibatide (when added to standard treatment with tPA) help to reduce the impact or severity of stroke. However, it is not known for sure whether they do. It is possible that these drugs may help to reduce the impact or severity of your stroke, but you may or may not benefit from being in this study. The knowledge gained from this study will help doctors learn more about what treatments are most effective for stroke.

What are the Risks and Side Effects?

The main risk associated with tPA (the standard stroke treatment) is bleeding. Sometimes that bleeding is minor, like along the gums or where IVs are placed. There can, however, be internal bleeding, which can be serious. The most serious form of bleeding is bleeding into the brain. This can worsen stroke or cause disability or even death. This risk is present for everyone who receives tPA, which is the primary treatment for stroke regardless of whether you are part of the MOST study.

If you are assigned to standard treatment plus placebo (Group A) in the MOST study, there are no added treatment-related risks.

If you are assigned to argatroban or eptifibatide (Group B or C), these drugs may increase the risk of bleeding seen with tPA, including bleeding into the brain. Earlier, smaller studies did not show increased bleeding with these drugs when combined with tPA. These studies showed the chance of bleeding into the brain while receiving tPA alone or with argatroban or eptifibatide, is between 3 to 10 people out of 100.

Additional potential risks of combining argatroban or eptifibatide with tPA include worsening of your stroke and increasing your risk of dying. These risks were not higher in previous studies than they are in patients who are treated with tPA alone.

Other possible side effects of Argatroban include:

- Other kinds of bleeding, such as blood in your stool or urine
  - Easy bruising or bleeding from IVs
  - Coughing up or vomiting blood
- Allergic reaction
- Unusual symptoms while the drug is being given. These are rare and usually go away after the drug is stopped.
  - Stomach discomfort, nausea, or diarrhea
  - Chest discomfort or shortness of breath
  - Unusual heartbeats
  - Fever or headache

https://www.mayoclinic.org/drugs-supplements/argatroban-intravenous-route/side-effects/drg-20072368

Other possible side effects of Eptifibatide include:

- Other kinds of bleeding, such as
  - Blood in your stool or urine
  - Easy bruising or bleeding from IVs or
  - Coughing up or vomiting blood
- Allergic reaction
- Unusual feelings while the drug is being given. These are rare and usually go away after the drug is stopped.
  - Stomach discomfort, nausea, or constipation
  - Feeling like you might pass out
  - Headache

https://www.mayoclinic.org/drugs-supplements/eptifibatide-intravenous-route/side-effects/drg-20074896

What Kinds of Follow-up does the MOST Study Involve?

1 day after enrollment:

You will have a repeat CT scan or MRI to take a picture of your brain. These are part of standard treatment for stroke, but we will record the results for the study.

The study team will also perform a physical exam called National Institutes of Health Stroke Scale (NIHSS). The NIHSS measures specific abilities, which are used to measure the severity a stroke.

The rest of your hospital stay:

In-hospital assessments (physical exams and questions about how you are doing) will occur daily for 3 days or until you go home, whichever comes first.

30-day follow-up:

After 30 days, the MOST study team will follow up with you either over the phone or in person if you are being seen in clinic for another reason around that time. At this visit, we will ask you a series of questions (like you were asked when you were first treated) called the modified Rankin Scale or mRS. These questions ask what you are having trouble with and how your recovery is going. The mRS measures how people who have had a stroke are doing in their daily activities. It is the most common way that researchers judge whether stroke treatments are helpful.

90-day follow-up:

This visit should be in person. We will perform the mRS questions again to measure how you are doing and will ask about your recovery. We will also video record this

assessment, and we will ask you some questions (a set of questions called the EQ-5D) about your quality of life and how you think your health is.

Schedule of Study Events			
Day 0 In hospital	Day 1-3 In hospital	Day 30 By phone or in person	Day 90 Should be in person
Physical exam and questions about your stroke	Physical exam and questions about your stroke	Questions about your stroke and your recovery	Video-recorded visit and questions about your stroke and recovery
Treatment- tPA and other parts of standard stroke care	Treatment- Standard care after stroke (medicines and rehab)	Treatment- Standard rehab and outpatient care	Treatment- Standard rehab and outpatient care
Study treatment- treatment with argatroban, eptifibatide or placebo for 12 hours			

Protection of Confidentiality of Your Study Records

A study number, rather than your name, will be used on study records when possible. Your name and other identifying information will not appear when we present or publish the study results.

This study has a Certificate of Confidentiality which allows the researchers to use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except if information is obtained in the research related to child abuse, or intent to hurt self or others. Study records can be opened by court order. They may also be provided in response to a subpoena or a legally required request for the production of documents.

Additional Financial Information

The costs of your standard treatment will be billed to you or your insurance. Whether you have copayments, deductibles or co-insurance will depend on your plan. You will not be billed for the cost of the argatroban, eptifibatide, or placebo.

If you have any questions or concerns about the study, please contact the study doctor or as described in the informed consent document.

More Information About StrokeNet

The NIH has created the NIH StrokeNet to conduct small and large clinical trials and research studies to advance acute stroke treatment, stroke prevention, and recovery and rehabilitation following a stroke. This network of 29 regional centers across the U.S., which involves more than 300 hospitals, is designed to serve as the infrastructure and pipeline for exciting new potential treatments for patients with stroke and those at risk for stroke. In addition, NIH StrokeNet will provide an educational platform for stroke physicians and clinical trial coordinators.