CONSENT FORM

SUNY Downstate Medical Center

Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT)

Sponsor: National Institute of Neurological Disorders and Stroke (NINDS)

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We are asking if you want to be in a research study. This study is for people who just had a TIA (transient ischemic attack) or a minor stroke.

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?

A TIA seems like a stroke with sudden weakness on one side of the body or trouble speaking, but gets better. People who have had a minor stroke can have a stroke in a few days. Treating a TIA may prevent a stroke. Medicines that prevent blood clots from

forming are often used to help prevent another stroke in people with blockage of one of the arteries in the brain. Two commonly used drugs are being used in this study along with a placebo:

- Clopidogrel stops platelets from sticking together. This helps blood flow more easily, and may prevent a future heart attack or stroke. These drugs are also known as blood thinners. Clopidogrel is approved by the Food and Drug Administration (FDA) for preventing stroke or TIA, and is taken once per day.

- Aspirin also may prevent a second stroke or TIA

Placebo is a pill that has no medication in it.

The purpose of this study is to see if *low-dose aspirin and clopidogrel taken within 12 hours of time last known free of new ischemic symptoms* lowers the risk of a stroke, or heart attack after a TIA. This study compares the risks of the combination of aspirin and clopidogrel with the risks from aspirin alone. A single study in China studying patients with stroke and TIA suggested that the combination of clopidogrel and aspirin was safe and effective. However, there are differences in the treatment of patients, the types of stroke, and the design of the study, so it is not clear whether these results would apply to you.

2) *Who is doing the study?*

Adrian Marchidann, MD is in charge of this study at this location. About 250 people will be in the study at this location. 5,840 people will be in the study at about 350 hospitals. This study is sponsored by the National Institutes of Health (NIH) and the National Institute of Neurological Disorders and Stroke (NINDS).

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

You and/or your insurance company will be responsible for payment of all medical costs that are not related to the study (co-payments or deductibles required under your insurance for any tests and procedures, and for routine follow-up imaging and clinical examinations).

The study drug (clopidogrel and placebo) and all follow-up visits to the study doctors will be paid for by the study. The brain scans, EKG and blood tests performed at baseline and if you have another TIA or stroke are considered part of the standard evaluation for patients with a diagnosis of TIA or stroke. These costs are not covered by the study.

4) *You cannot be in this study if you:*

- Are on clopidogrel and cannot stop taking it (determined by the study doctor).
- You need Warfarin, dipyridamole or NSAIDS (ibuprofen, naprosyn, COX-2 inhibitor, etc) treatment.
- Are allergic to clopidogrel or aspirin
- Are pregnant or breast feeding

5) Pregnancy:

These drugs that are used in this study can harm a developing fetus or a baby. If you are a woman of childbearing age, you must not be pregnant and/or currently nursing a child. You must use an acceptable method of birth control to avoid pregnancy while in this study. Acceptable methods of birth control include hormonal contraceptives, intrauterine device, abstinence or spermicide and barrier method (ie. condom). If you should become pregnant while in the study, you should notify your study doctor immediately.

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

Before you begin the study...

If you agree to take part in this study and sign this consent, you will be screened to see if you are eligible to participate in the study. A study physician will check whether or not you are eligible by reviewing the results of the following tests and procedures that were done as part of your routine care:

1. *A complete physical examination and **medical history** including any medications you are currently taking, since there are some medications you cannot take while you are in this study.*
2. *Neurological evaluation using the NIH Stroke Scale (NIHSS) or the ABCD^2 score.*

   (If you have already had a physical examination and neurological assessment as part of your routine care, they may not need to be repeated for the study. If they were not done, or need to be repeated, the examination and neurological assessment will be done at no cost to you.)
3. *If you are female and not post-menopausal or have not had a prior hysterectomy, you will undergo a blood or urine test to determine if you are pregnant. The drugs in this study can affect a fetus, so pregnant women may not participate in this study.*

You may not be in this study until all of these tests and procedures have been reviewed.

During the study... (Day 1 – about 2 hours)

If you are found eligible to be in the study, you will be randomized. Randomization means that you are put into a group by chance, like a flip of a coin. You will have an equal (a

50:50) chance of being placed in group 1: clopidogrel/aspirin group or group 2: placebo/aspirin group.

This is a double-blind study, which means that neither your study doctor nor you will know which of the study drug groups you are in. However, this information will be available in the case of an emergency. Everyone will take 8 tablets on day 1 and 1 tablet daily for the next 89 days plus a daily dose of aspirin.

- Group 1 takes 8 tablets of 75 mg of clopidogrel each (600 mg total) on day 1, and then takes 75 mg (1 tablet) of clopidogrel each day for the next 89 days. Group 1 aslo takes 50-325 mg of aspirin every day for 90 days.

  OR

- Group 2 takes 8 tablets of placebo on day 1, and then takes 1 tablet of placebo every day for the next 89 days. Group 2 also takes 50-325 mg of aspirin every day for 90 days.

In both groups the dose of aspirin will be determined by your study doctor.

Just before you leave the hospital, we will schedule your next visit in about 90 days from the day you enrolled. Information about how to contact the study doctor in case of an emergency will be given to you on a card to keep in your wallet. This wallet card tells everyone that you are in a study using blood thinners.

After you have signed the consent form, you can decide if you will give us permission to contact your regular doctor to inform him or her that you are in this study. If you decide not to give us permission to contact your study doctor, this will not affect your medical care. You will be asked for your contact information, such as your email address and any alternative contacts, so that we can keep in touch with you throughout the study. You can choose not to provide alternative contacts.

Study Visits:

One Week (about 15 minutes)

About 1 week after you enroll, we will call you to ask if you've been taking your study medications. You will be asked about any side effects or possible *adverse events* (any undesirable experiences associated with the use of the study medication). We will also ask you about your other drugs and question you about any symptoms you may have had since your discharge from the hospital.

30 Day Telephone Contact (about 15 minutes)

About 30 days after your first dose, a member of the study team will contact you to assess your condition, ask whether you've been taking your study medications, and whether you are experiencing any side effects or adverse events.

Event Visit (about 2 hours)

If you feel a stroke, TIA or heart attack, go to the nearest emergency department and tell them you are in a study. They or you can call the study number listed on your wallet card as soon as possible. If it is thought that, based on information you provide, you might have had a stroke, a TIA or a heart attack, you will be scheduled for an evaluation.

At the visit, you will:

- have your blood pressure and heart rate checked
- have tests performed as part of your regular care, including a CT or MRI of your head, an ECG and blood tests
- answer any questions about your study medications and any side effects or adverse events
- be evaluated using two scales, the modified Rankin Scale (mRS) and the NIH Stroke Scale (NIHSS)
- complete the Stroke-Free Questionnaire, which asks about any neurological symptoms you may have had since enrolling in the study, and the Morisky Questionnaire which asks about your adherence to your prescribed medications

If the visit is done by telephone, you will:

- answer questions about your study medications and any side effects or adverse events
- be evaluated using the modified Rankin Scale
- complete the Stroke-Free and the Morisky Questionnaire

90 Day Visit or Telephone Contact (about one hour)

- You will need to come back to the Neurology Office. This follow-up visit may be done either in person or by telephone and will include the same questions and tests described under the Event Visit

If the visit is conducted in-person, you will:

- have your blood pressure and heart rate checked
- answer questions about your study medications and any side effects or adverse events
- be evaluated using the modified Rankin Scale and the NIH Stroke Scale
- complete the Stroke-Free and the Morisky Questionnaires

Other tests may be performed as part of your regular care, including a CT or MRI of your head, an ECG and blood tests.

If this visit is done over the telephone, (visit will take less than 1 hour) then you will:

- answer questions about your study medications and any side effects you may have had.
- be evaluated using the modified Rankin Scale
- complete the Stroke-Free and the Morisky Questionnaires.

At the end of the study, we and your doctor will discuss with you the best choice for drugs you should continue. You will not be told which drug you were on until the study is finished and the results are known.

If for some reason we are unable to locate you for the 90 day follow up visit, we will ask your alternate contact and/or review you medical chart to find out if you have been seen by another doctor within your hospital. We will also check to see if you have had a stroke, TIA , or heart attack during the 90 day follow up period. In order to make sure that we include the full 90-day period in our review, we will need to review your chart after the 90 day study period has ended. This means that we may continue to collect information about you up to 150 days from your enrollment.

How long will I be in the study?

About 3 months. About 5 months after you have joined the study, the researchers will no longer collect information about you. If you decide you want to the study team to stop collecting information about you before then, then you must write to the study doctor (Dr. Adrian Marchidann) and ask to be removed from the study. The researchers will use the information that they collected about you up until that point.

Can I stop taking the study medication?

Tell the study doctor if you are thinking about stopping or decide to stop; your study doctor will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so that your study doctor can evaluate any risks from the study drugs, and discuss what alternative follow-up care and testing could be most helpful for you. Even if you stop the study medication we would like to continue to contact you at day 7, day 30, and day 90.

If you decide to stop participating or are withdrawn from the study, information about whether you had a stroke, heart attack or other complication during the 90 days of the study will still be helpful to the research. Giving consent will allow study personnel to collect this information by asking you or your alternative contact on the phone, asking you in-person, accessing your medical record and/or performing a chart review for up to 150 days from your enrollment.

The study doctor may stop you from taking part in this study at any time if he/she believes

it is in your best interest, if you do not follow the study rules, or if the study is stopped. The entire study could also be stopped on the recommendations of a safety committee that will monitor this study or by the sponsors of the study.

7) What are the possible risks of being in the study?

You may have side effects while in the study. You should talk to your study doctor and your doctor who usually takes care of you about any side effects you experience while taking part in the study.

Risks and side effects related to the study drugs include:

a. **Placebo risks:** If you are in the group that receives placebo, you will not have clopidogrel for about three months.

b. **Side effects from study drugs**: People who have a known allergic reaction to any of the study medications should not participate in this study. Many side effects go away soon after you stop taking the medicine. In some cases, side effects can be serious, long lasting, or may never go away.

c. **Side effects from clopidogrel:** Clopidogrel thins the blood in order to help blood flow more easily. Blood clotting may take longer than normal while taking clopidogrel. You may have longer bleeding from cuts, and you may also bruise more easily. Superficial and internal bleeding, including bleeding into the brain, are also side effects of clopidogrel. Internal bleeding and bleeding into the brain are serious conditions that can result in death.

The most common (3% to less then 1%) side effects of clopidogrel include:

- abdominal or stomach pain (<1%),
- diarrhea (<1%)
- skin reactions (rash, itching) (3%)
- aching muscles and/or joints (<1%)
- dizziness (<1-3%)
- fever (<1%)
- headache (<1%)
- a decrease in the number of a type of white blood cell called a neutrophil (<1%)

In rare cases, clopidogrel may cause stomach bleeding. Symptoms of stomach bleeding include darker, tarry (black) stools, stomach pain and sometimes vomiting blood or "coffee grounds". There have also been rare reports of a serious bleeding disorder called thrombotic thrombocytopenic purpura (TTP). This side effect is most likely to occur during the first two weeks of treatment.

Please call right away: During the study, you must immediately tell your study doctor and your doctor about any abnormal or unexpected events, and in particular about:

- Any warning sign of brain attack (feeling weak, or numb on one side, blurry vision, or no vision usually in one eye, unable to talk clearly, dizziness or falling, or severe headache)
- Any anginal pain (chest pain during rest or exercise)
- Any bleeding, spontaneous bruise, bleeding from an unusual site or that takes a very long time to stop)
- Infection (fever, shivering, sore throat, extreme tiredness)
- Skin rash
- Severe diarrhea
- Jaundice (yellow discoloration of the skin), or
- Feeling generally unwell

If you are hospitalized or go to an Emergency Room where the study doctor does not work, whatever the reason is, you (or one of your relatives) should inform your study doctor as soon as possible. You must tell the doctor treating you at the hospital or Emergency Room that you are taking part in this study. You can show him or her the wallet card that explains the study and gives a phone number to call for questions.

d. Side effects from aspirin: Aspirin has two main types of side effects: it can cause gastrointestinal upset and it can increase bleeding. The feelings include stomach pain, heartburn, nausea and/or vomiting. Like clopidogrel, it may cause stomach bleeding. Symptoms of stomach bleeding include darker (sometimes black), tarry stools, stomach pain and sometimes vomiting blood or "coffee grounds" (black or brown material). In rare cases, more serious effects, such as bleeding, have been observed in people who take aspirin for a long time. Even less commonly, hemorrhagic stroke (bleeding in the brain) can occur. The side effects of aspirin are generally dose-related, and tend to occur more often in doses that are higher than the dose of aspirin taken in this study.

e. Side effects from aspirin and clopidogrel: Both drugs thin the blood. Combining them is likely to increase that risk of bleeding. This combination has not been tested right after a TIA. It is likely, based on results of studies from strokes and heart attacks, that clopidogrel combined with aspirin has a little higher risk of major bleeding. The combination of aspirin and clopidogrel may increase the risk of complications with surgeries or other procedures, or may delay the performance of these procedures (due to concerns about bleeding risk). A delay could increase your risk of stroke.

f. Side effects from discontinuing medications for study purposes: If you are currently taking a drug that blocks platelets (such as clopidogrel or dipyridamole) or blocks clotting (such as warfarin), your regular doctor may not want you to enroll in this study. Please try to discuss this study with your regular doctor before you consent. Other medications may be changed if they interfere with aspirin or clopidogrel. These changes will be discussed with you and the doctor who usually takes care of you. Also,

some doctors treat patients with TIA with clopidogrel and aspirin together.

Taking other medications while on the study: Certain medications may make clopidogrel less effective. If you receive any new prescriptions while you are on the study, you should tell the study doctor.

g. **Risks of blood draws:** The risks and discomforts of drawing blood include temporary discomfort from the needle stick, the possibility of pain or bruising at the site of the blood draw, occasional feelings of lightheadedness and, rarely, infection at the site of the blood draw.

h. **Unknown Risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study. For more information about risks and side effects, ask your study doctor.

i. **Confidentiality:** Participation in research means a loss of confidentiality. Information about you will be handled as confidentially as possible. The study doctors and researchers conducting this study and health care workers providing services to you in connection to the study will have access to your medical and your study records.

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.

8) What are the possible benefits of being in the study?

We can not promise that you will benefit from being in this study. However, possible benefits may be that clopidogrel could stop a stroke or heart attack from happening to you. What we learn from this study may help us figure our how to prevent a stroke in patients with a TIA or a minor stroke. The knowledge gained from this research may help other people with TIA in the future.

9) What are your other choices?

If you do not want to join this study, you will get the usual treatment for a TIA. There are several drugs approved by the Food and Drug Administration to stop a stroke. Aspirin is available without a prescription, and clopidogrel is available from your doctor. Other drugs are available to you from your doctor without being in this study.

You may also choose not to receive any drugs. You may wish to discuss your treatment with your doctor before you decide to be in this study.

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

- Adrian Marchidann MD, Richard Sinert DO, or their staff.
  - 718-270-1259 (Dr. Marchidann)
  - 718-245-2793 (Dr. Sinert)
  - 718-270-2121 and have operator page the doctors
- If you think you have been injured because of the research, you should call Adrian Marchidann, MD; Richard Sinert, DO or staff
  - 718-270-1259 (Dr. Marchidann)
  - 718-245-2793 (Dr. Sinert)
  - 718-270-2121 and have operator page the doctors
- If you have questions about your rights as a research subject, you can call the IRB office
  - (718) 613-8480
- Or you can contact the SUNY HSCB University Hospital Medical Director's Office
  - (718) 270-2401

11) 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 name, age, sex, race, and medical history.
- Information obtained from this study, including physical examination, laboratory tests, ECG heart tracing, brain scan including CT or MRI.

The researchers (including Dr. Adrian Marchidann, Dr. Pia Chatterjee, Dr. Steven Levine, Dr. Richard Sinert, Dr. Helen Valsamis, Dr. Ethan Brandler, Dr. Lorenzo Paladino, and Dr. Jennifer Martindale), their staff (including Sarah Zelonis and Saroj Kunnakkat), and the staff of SUNY Downstate Medical 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 sponsor of the study, NIH/NINDS
- The Data Safety Monitoring Board that reviews the safety of this study,
- The Institutional Review Board of SUNY Downstate Medical Center, the applicable DMC officials, and the federal Office for Human Research Protections,
- Study monitors from the POINT CRC Coordinating Center (The EMMES Corporation, Rockville, Maryland) and the NETT(University of Michigan)
- Staff from the Neurological Emergencies Treatment Trials Network (NETT) (University of Michigan),
- Staff from Statistical Data Management Center (Medical University of South Carolina)
- The University of California at San Francisco (UCSF)

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 not obligated to protect the privacy of your IIHI. For example, the sponsor NIH or the Emmes Corporation does 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 which study arm you are in. 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: Attention: Sarah Zelonis; 450 Clarkson Ave, Box 1213, 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.

12) 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 Adrian Marchidann, MD; Richard Sinert, DO, or one of the study staff members.

Adrian Marchidann, MD; Richard Sinert, DO, research staff or the sponsor can take you out of the study without your permission. Possible reason for involuntary withdrawal would be continuing on the study would be harmful, adverse harmful event, or pregnancy.

Also, the sponsor of the study may end the study early. If your being in the study ends

early, we may ask you to visit the study doctor for a final visit for information about which drugs to continue.

13) What else do you need to know?

You will not be paid for taking part in this study.

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. It will be very difficult to distinguish an injury caused by treatment of your condition from one caused by taking part in a study. If you are, emergency care will be available and you will be treated as immediately and appropriately as you would for usual treatment of similar medical issues. It is important that you tell your study doctor about the injury. SUNY Downstate Medical Center does not have a policy to pay you if you are injured by being in the study.

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. There are no plans for this hospital or the Sponsor to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

14) 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	Date	Print name
Signature of Person Obtaining Consent	Date	Print Name
Signature of Witness (if applicable)	Date	Print name

Permission To Contact My Regular (Primary Care) Doctor:

Do you give permission for the study doctor to contact your regular (primary care)

physician to tell him or her that you are in the study?

Sign One:

Yes_____ No _____
Signature Signature

Alternative Contacts

Please indicate whether you wish to allow alternative contacts to be contacted regarding your participation in this study by signing your name in the "Yes" or "No" line.

Sign One:

Yes_____ No _____
Signature Signature