Ascension Providence Hospital
16001 West Nine Mile Road, Southfield, MI

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

AND

AUTHORIZATION TO USE OR DISCLOSE PROTECTED HEALTH INFORMATION

FOR RESEARCH TO BE CONDUCTED AT PROVIDENCE HOSPITAL,

PROVIDENCE PARK HOSPITAL AND MEDICAL CENTERS

Title: Efficacy and Safety of Cilostazol-Nimodipine Combined Therapy on Delayed Cerebral Ischemia after Aneurysmal Subarachnoid Hemorrhage (SAH): A Multicenter, Randomized, Double-blinded, Placebo-controlled Trial

Principal Investigator:

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Co-Investigators:

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Please read the following material to ensure that you are informed of the nature of this clinical research study and how you will participate in it. Signing this form will indicate that you have been informed and that you give your consent to participate in a free manner. Federal regulations require written informed consent prior to participation in this clinical research study.

INTRODUCTION

This is an important form. Please read it carefully. It tells you what you need to know about this research study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and any applicable risks. Your signature on this form also means that you want to take part in this study. This is a randomized multi-center double-blinded controlled clinical trial. Your doctor will explain the clinical research study to you. Research studies or clinical trials only include people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this research study because you recently underwent either a surgical or endovascular intervention for the treatment of intracranial hemorrhage and are being seen at Ascension Providence Hospital.

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BACKGROUND

This research study is designed to evaluate the effects of the combination between Cilostazol and Nimodipine on delayed cerebral ischemia due to cerebral vasospasm after anterior circulation aneurysmal subarachnoid hemorrhage. Cilostazol is a selective phosphodiesterase-3 inhibitor which exerts a vasodilatory and antithrombotic effect. Nimodipine is a dihydropyridine calcium channel blocker which is recommended for the postoperative treatment of aneurysmal subarachnoid hemorrhage. We seek to compare the incidence of delayed cerebral ischemia when treated with Cilostazol and Nimodipine versus when treated with Nimodipine alone. The researchers will compare two different groups. With your consent, you will be randomly assigned to a group who receives conventional post-intervention treatment with Nimodipine or to a group who receives conventional post-intervention treatment with Nimodipine in addition to 100mg Cilostazol twice daily for 14 days after your intervention. Your chances of being in one group are 1 in 2, much like flipping a coin. This is a double-blind study, which means neither you nor your doctor will know which group you are in until the study is completed.

Imaging will be taken 1 day after your intervention, 7 ± 2 days after your intervention, approximately 1 month and 6 months after discharge as part of your standard of care. More imaging, including but not limited to CTA or MRI scans, may be needed depending on the individual care management plan.

PURPOSE OF THE STUDY

- To demonstrate that the combined use of Cilostazol and Nimodipine when compared to Nimodipine alone will decrease the rate of delayed cerebral ischemia during your hospital stay

- To demonstrate that the combined use of Cilostazol and Nimodipine when compared to Nimodipine alone will not lead to significant increase in bleeding disorders

- To demonstrate that the combined use of Cilostazol and Nimodipine when compared to Nimodipine alone, will lead to significant improvement in the following:
    - The rates of symptomatic vasospasm
    - The rates of angiographic vasospasm
    - Quality-of-life outcomes: Modified Rankin Scores (mRS) at Pre, 1, 3 and 6 months postoperatively and SF-12 at 1, 3 and 6 months postoperatively
    - Length of hospitalization
    - Length of stay in the intensive care unit (ICU)
    - Duration of ventriculostomy use

How many people will take part in this study?

Approximately 120 men and/or women of at least 18 years of age will be in this study.

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How long will I be in this study?

You will participate in this study for 6 months. Your part in the study is completed once you have completed your 6-month follow-up visit with your surgeon including completion of the modified Rankin Scores and SF-12 questionnaires.

What will happen if I take part in this research study?

You have recently undergone either a surgical or endovascular intervention for the treatment of intracranial hemorrhage and your surgeon has determined that you meet eligibility criteria to participate in this research study.

After your enrollment, you will receive the necessary post-intervention care. If you are randomly selected into the treatment group, you will receive the drug Cilostazol in addition to your standard care regimen. If you are not, you will receive the standard care regimen plus a placebo. However, your knowledge of which group you are assigned to, as well as the administration of that drug will not be known to you. Throughout your hospital stay, data will be collected including any Cilostazol-related adverse events, occurrence of symptomatic vasospasm, and length of stay, among others. This all will be collected from either your electronic medical record or directly from you by a blinded member our staff. You will follow-up in clinic with your surgeon for standard post-interventional evaluation which includes 1, 3, and 6-month follow-up visit along with completion of modified Rankin Score and SF-12 questionnaires.

Risk to patients

Important risks and side effects of 100mg Cilostazol may include:

Frequent side effects:
- Headche
- Abnormal stools
- Diarrhea

Infrequent side effects:
- Abdominal pain
- Back pain
- Infection
- Palpitation
- Tachycardia
- Flatulence
- Nausea
- Peripheral edema
- Myalgia
- Dizziness
- Cough increased
- Pharyngitis
- Rhinitis

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Rare side effects:

- Chills
- Vertigo
- Other rare side effects

***Frequent* (occurs in 10-25% of people – 10 to 25 out of 100 people)**
***Infrequent* (occurs in 1-10% of people – 1 to 10 out of 100 people)**
***Rare* (occurs in less than 1% of people – less than 1 out of 100 people)**

Every effort will be made to minimize any discomfort and these risks. There may be other risks that are unknown at this time.

You should tell the person obtaining your consent if you are currently participating in any other medical research studies.

What are the benefits of the study?

There may be no direct benefit to you in participating in the study. However, it is possible that you may have less chance of delayed cerebral ischemia or symptomatic and angiographic cerebral vasospasm following your surgery. You may also experience an improvement in postoperative quality-of-life. In the future, other patients may benefit from the results of this study, when they become known.

What other options are there?

One option is to not participate. You do not have to participate in this research study in order to continue receiving treatment for your condition. Electing to not participate in this study will not affect your care whatsoever.

Do I have to participate in this study?

Your participation in this study is voluntary. Your refusal to participate will cause no penalty or loss of benefits which you would otherwise receive. If you decide to participate, you may change your mind about being in the study and may quit at any time without penalty of loss of benefits regarding your future care. If new information becomes available during the study that may affect your willingness to continue in the study, your doctor and/or his/her associate will discuss this information with you. Also, your doctor may stop your participation at any time if he/she feels it is in your best interest.

Will it cost anything to participate?

We do not expect there to be any additional costs to you if you participate in this study. Besides the drug treatment, the additional care you would receive during this study is considered standard of care and would not otherwise be different.

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Compensation to patients – None

There is no compensation or pay offered for your medical care if you are injured as a result of participating in this study. You and/or your medical insurance may have to pay for your medical care if you are injured as a result of participating in this study. You are not giving up any of your legal rights by signing this consent form.

Confidentiality of Records

The principal investigators will have access to your medical records and your test results. While absolute confidentiality cannot be guaranteed, all research material which could identify you will be kept as confidential as possible within the state and federal laws. You should be aware that your medical records could be examined by the study staff, the Institutional Review Board (a group of people who review the research to protect your rights), or government agencies in order to verify the data collected during this research study. If the results of this study are presented in any public forum, you will not be personally identified.

Participant HIPAA Authorization to Use and Disclose Protected Health Information (PHI)

Your participation in this study will require the use and disclosure of certain medical and other information about you. The information that may be used or disclosed includes any and all health care records such as: laboratory, pathology and/or radiology results, CT scans, MRI, and Protected Health Information (PHI) previously collected for research purposes.

Your PHI will be used in the following ways: To conduct the research and to ensure that the research meets legal, institutional or accreditation requirements.

Your authorization to use and disclose the above information has no expiration date.

Your PHI may be seen, used or disclosed to the following:

- The researchers and members of the research team
- Other health care providers or employees of Ascension Providence Hospital
- Representatives of the Institutional Review Board (IRB), the FDA (Food and Drug Administration), or other governmental agencies involved in research monitoring.
- Other agencies as required by law.

You have the right to review your PHI. However, if you agree to participate in the research study and sign below, you will not be able to look at your research information until the research study is completed.

You do not have to sign this authorization. If you decide not to sign the authorization it will not affect your treatment or eligibility for health benefits. However, if you do not sign this authorization you may not participate in this study.

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You may withdraw your authorization at any time by notifying the principal investigator in writing, but the withdrawal will not affect any information already disclosed. However, you need to be aware that your written withdrawal of this Authorization may result in the termination of the research-related treatment being provided to you.

This study and more information will be available at ClinicalTrials.gov which is a registry and results database of publicly and privately supported research studies conducted in the United States and around the world. Sponsors or investigators of certain clinical trials are required by U.S. law to register their trials on and submit summary results to ClinicalTrials.gov. Each study record includes a summary of the study protocol, including the purpose, recruitment status, and eligibility criteria. Study locations and specific contact information are listed to assist with enrollment. You can visit ClinicalTrials.gov for more information regarding this study.

Who do I call with questions about the study or to report an injury?

If you have any questions regarding a research-related injury, you can contact:
Troy Dawley, DO
22250 Providence Dr Ste 601, Southfield, MI 48075
(214) 886-6111

If you have any questions about your rights as a subject in this clinical research study, you may contact the IRB representative at 248-849-8889 at Ascension Providence Hospital.

CONSENT

You have had the opportunity to fully discuss the purpose of this clinical research study and how it will be carried out. Your questions have been answered. Your participation in this study is fully voluntary and you may withdraw at any time.

Your signature below acknowledges that you voluntarily agree to participate in this clinical research study, and you will receive a signed copy of this form.

_____
Printed Name of Research Subject

_____ _____
Signature of Research Subject Date

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Legally Authorized Representative (if applicable):

_____
Printed Name of Legally Authorized Representative

_____ _____
Signature of Legally Authorized Representative Date

Check Relationship to Subject:*

☐ Legal Guardian or Legally Authorized Representative for Medical Care (LARM)
☐ Spouse

☐ Adult Son or Daughter ☐ Mother or Father ☐ Adult Brother or Sister ☐ Other, explain:

Reason subject is unable to sign for self:

**If a Legal Guardian or Legally Authorized Representative for Medical Care (LARM) has not been appointed, then consent should be obtained from the closest next of kin (in the order listed above). When that individual is unavailable or refuses to act the next in order should be contacted.*
** If there is a disagreement among next of kin regarding the appropriateness of the treatment plan, Clinical Safety Risk Management may be contacted. Outside of business hours, Clinical Safety Risk Management can be contacted through any St. John Hospital operator.*

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

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