RESEARCH SUBJECT CONSENT FORM

TITLE:	A randomized control trial of furosemide or placebo with usual antihypertensives in the antepartum management of severe hypertension with wide pulse pressure
PROTOCOL NO.:	2020-033 WIRB® Protocol #20203025
SPONSOR:	Pai-Jong Stacy Tsai
INVESTIGATOR:	Pai-Jong Stacy Tsai, MD, MPH 1319 Punahou Street Suite 824 Honolulu, HI 96826 USA
STUDY-RELATED PHONE NUMBER(S):	808-983-6000 (24 hours)

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research?

We expect that your taking part in this research will last about 1 hour. You will continue to be observed while you are in the hospital for any side effects related to your participation in the research.

Why is this research being done?

The purpose of this research is to confirm whether furosemide decreases your blood pressure when it is too high.

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, the general procedures include: when your blood pressure is high and needs to be treated, you will be given furosemide or placebo (no furosemide) with the medication that your doctor orders to lower your blood pressure. Your blood pressure will be checked at least four times (every 15 minutes for one hour) after receiving the medications. Otherwise, the care you receive will not be affected by participating in the study.

Could being in this research hurt me?

The most important risks or discomforts that you may expect from taking part in this research are fluid/electrolyte loss if you are selected to receive furosemide and an increased number of blood pressure checks after you receive furosemide or placebo.

Will being in this research benefit me?

The most important benefits that you may expect from taking part in this research include better control of your high blood pressure, which may lower your risk of stroke, problems with the placenta, and negative effects on your heart.

Possible benefits to others include helping to find effective therapies to control high blood pressure in pregnancy.

What other choices do I have besides taking part in this research?

Instead of being in this research, your choice would be to receive usual care. Not participating in the study will not affect the care you receive.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don’t understand, ask questions.
- Ask all the questions you want before you decide.

Why is this research being done?

The purpose of this research is to see if using intravenous furosemide (also known commonly as a 'water pill' and blood pressure medication) helps to control blood pressure for pregnant women with very high blood pressure.

About 70 subjects will take part in this research.

How long will I be in this research?

We expect that your taking part in this research will last for about 1 hour. After you receive treatment your blood pressure will be checked every 15 minutes for up to 1 hour. You will continue to be observed for any side effects related to your participation in the research while you are in the hospital.

What happens to me if I agree to take part in this research?

If you decide to participate in this research you will be asked to provide informed consent. After consent has been provided you will be put into a study group by chance (like a coin toss/ like drawing straws). You have a 1 out of 2 chance of being placed in each group. You cannot choose your study group. One group will receive a placebo (saline solution) and one group will receive furosemide intravenously. Participants in both groups will also receive the usual care for their high blood pressure.

Furosemide is a drug that has been approved by the Food and Drug Administration (FDA) for the treatment of high blood pressure. However, in this study the use of furosemide is investigational.

After you receive furosemide or placebo your blood pressure will be checked every 15 minutes for up to 1 hour (4 times).

This study is blinded, which means that during the research, you and the study doctor will not know which group you are in. Your study doctor can find out in case of an emergency.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Alert your care providers of any medical issues that you experience.

Could being in this research hurt me?

There are no known side effects associated with saline solution (placebo group).

The most common side effect associated with furosemide is fluid/electrolyte loss.

Rare side effects include:

- Cardiovascular: Low blood pressure, inflammation in blood vessels
- Central nervous system: Dizziness, headache, tingling, restlessness, vertigo
- Dermatologic: Assorted rashes, itching, sensitivity to the sun, skin sloughing
- Endocrine & metabolic: Elevated sugar level in your urine or blood, increased uric acid in your blood, increased serum cholesterol, increased serum fats
- Gastrointestinal: Abdominal cramps, loss of appetite, constipation, diarrhea, upset stomach, mouth irritation, nausea, inflamed pancreas, vomiting
- Genitourinary: Bladder spasm
- Hematologic & oncologic: Decreased white blood cells or red blood cells, bruising, low platelets.
- Hepatic: Mental confusion, increased bile acids in your liver causing jaundice, liver enzymes increased
- Hypersensitivity: Mild or severe allergic reactions
- Immunologic: hypersensitivity reaction that could be characterized by fever, skin rash, lymph node swelling, blood abnormalities and internal organ involvement.
- Neuromuscular & skeletal: Muscle spasm, weakness
- Ophthalmic: Blurred or yellowed vision
- Otic: Deafness, ringing in your ears
- Renal: inflammation in your kidneys
- Miscellaneous: Fever

The FDA has determined that furosemide is a pregnancy category C drug. This means that studies in animals have shown adverse effects of the drug on the fetus, however, the effects on human fetuses are unknown. As a category C drug, the potential benefits of this drug may warrant use in pregnant women despite potential risks.

There may be additional risks that are unknown at this time.

Will it cost me money to take part in this research?

In some cases, insurance does not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

The study sponsor will provide the study drug/placebo. This will not be charged to your insurance.

Will being in this research benefit me?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits to you include improvements in your blood pressure which can reduce your risk of stroke, placenta problems, and negative effects of very high blood pressure on your heart.

Possible benefits to others include improvements in treatment for high blood pressure during pregnancy.

What other choices do I have besides taking part in this research?

Instead of being in this research, your choices may include:

- Routine treatment, which includes intravenous labetalol, intravenous hydralazine, or oral nifedipine.
- Your provider may also treat you with intravenous furosemide unrelated to the study if they feel it is in your best interest.

What happens to the information collected for this research?

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- Government agencies, such as the Food and Drug Administration
- The Institutional Review Board (IRB) that reviewed this research
- Hawai‘i Pacific Health.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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.

Data collected in this research might be used for future research or distributed to another investigator for future research without your consent, only after it has been de-identified.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

Compensation in case of injury:

No financial compensation or coverage will be routinely provided by the sponsor or study doctor. If you require treatment for any injury or illness related to procedures required by the study, or if you suffer side effects while in the study, you should contact your study doctor, Dr. Stacy Tsai at 808-983-6000, who will give you the necessary medical care and advice. The cost of this medical care and advice will be billed to you or your medical insurance in the usual manner.

By signing this consent form, you will not give up any legal rights.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest
- You have a side effect that requires stopping the research
- You are unable to take the research medication

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What happens if I agree to be in this research, but I change my mind later?

If you decide to leave this research, contact the research team so that the investigator can stop study procedures and collecting data on you.

Will I be paid for taking part in this research?

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

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR A RESEARCH STUDY

A federal law known as the Health Insurance Portability and Accountability Act (HIPAA) sets rules for protecting the privacy of patients' health care records. HIPAA requires health care providers, except in specific circumstances, to obtain written permission from research participants before using and disclosing their health information.

This authorization allows the research team to use and disclose my health information associated with the research described in this consent form.

What is the purpose of this authorization?

By signing this document, I am authorizing or giving permission for the research study doctor and research staff to access, receive, use and disclose Protected Health Information ("PHI") about me. The research will only use the information as described below and as allowed by law.

What Protected Health Information ("PHI") is covered by this authorization?

The PHI that may be accessed, collected, and used by the research team includes:

- Demographic information (e.g., my name, address, date of birth, etc.). This information could be used to identify me;
- All information in medical records, results of physical examinations, medical history, lab tests, or certain health information such as tumor measurements, CT scans, MRIs, x-rays and pathology results relating to your high blood pressure held by providers, clinics, facilities at which you have been treated;
- Information obtained from me in the Study as a result of tests or procedures;
- Information about other medical conditions that may change my treatment;
- Information on side effects (adverse events) I may have, and how these were treated.

I understand my medical records may contain information about AIDS or HIV infection, venereal disease, treatment for alcohol and/or drug abuse, or mental health or psychiatric services and that the research team may have access to that information.

Who may use and disclose my PHI?

By signing this authorization form I give permission to Hawaii Pacific Health, my doctor(s) and other health care providers that have cared for me or performed diagnostic testing and procedures to disclose the above information to the research doctor and the research staff.

I also authorize the research doctor and staff to use and disclose my research-related health information.

Who may receive my PHI?

I authorize the following persons or groups to receive research-related health information about me:

- The research sponsor. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor, or
  - owned by the sponsor.
- Department of Health and Human Services (HHS) agencies,
- The U.S. Food and Drug Administration (FDA),
- Other federal, state, and local agencies having oversight over this research,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported,
- Hawai'i Pacific Health,
- The Hawaii Pacific Health (HPH) Research Institute, HPH Officials, and the HPH Office of Compliance for purposes of overseeing the research study and making sure that my ethical rights are being protected.
- University of Hawai'i,
- Western Institutional Review Board® (WIRB®).

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to monitor the research to be sure it was done correctly.

If the results of this research are made public, information that identifies you will not be used.

Is my PHI protected after it has been given to others?

There is a risk that your information will be given to others without your permission or some of the recipients may not be required to comply with Federal privacy regulations. If this happens, your information may no longer be protected.

Can I refuse to sign this authorization?

You have the right to refuse to sign this authorization. This would prevent those listed above from having access to, using, or disclosing your PHI for this research study. However, by refusing to sign this authorization, you understand that you cannot participate in this research study.

Can I revoke (cancel) this authorization?

You may change your mind and revoke (take back) this Authorization at any time. To revoke this Authorization, you must write to: Dr. Stacy Tsai, 1319 Punahou Street, Honolulu, HI 96826

If you decide to revoke (cancel or "take back") your authorization:

- Your revocation will not become effective until the covered entities affected by the revocation receive or are informed/have knowledge of your revocation;
- No new identifiable information will be accessed, collected or disclosed after the covered entity receives your revocation;
- Information that was already collected may still be used and disclosed to others to maintain the integrity of the research; and
- The researchers in this research study are not required to destroy or retrieve any of your health information that was created, used or disclosed for this research prior to receiving your written revocation.

When will this authorization expire?

Your authorization to use your PHI for this research study will not expire even if you terminate your participation in this research or you are removed from this research by the principal investigator.

Will all recipients of my PHI be required to protect the information?

Some of the persons or groups that receive your study information may not be required to comply with HIPAA privacy laws, and your information may lose its federal protection if those persons or groups disclose it.

OTHER RESEARCH ACTIVITIES:

In addition to the research uses described above, the researchers would like your authorization to store the PHI collected about you in a secured database or central repository for use in future related research. You are not required to authorize this additional use in order to participate in this research study.

Please initial one of the following to indicate your preference regarding the use of your information for future research.

_____ Yes, I authorize the use of my PHI for future research

_____ No, I do not authorize the use of my PHI for future research

If you authorize the use of your PHI for future research, your authorization will remain valid until revoked in writing by you.

Can I revoke my authorization for future research?

You have the right to revoke your authorization for future research at any time. Your revocation must be submitted in writing, either on paper or electronically to: Dr. Stacy Tsai, 1319 Punahou Street, Honolulu, HI 96826, paijong@hawaii.edu. Your revocation will not become effective until the covered entity providers affected by the revocation receives or is informed/has knowledge of your revocation.

Written Permission

By signing this consent form I authorize the release of my PHI in connection with this research study. I understand that this authorization is voluntary. I will receive a signed copy of this form.

Statement of Consent:

Your signature documents your consent to take part in this research.

Signature of adult subject capable of consent	Date
Signature of person obtaining consent	Date