UF | Institutional Review Board
UNIVERSITY of FLORIDA

University of Florida – Jacksonville

SUBJECT INFORMATION AND CONSENT FORM

TITLE: Pharmacodynamic and pharmacokinetic profiles of switching between cangrelor and ticagrelor following ticagrelor pre-treatment: The Switching Antiplatelet -5 (SWAP-5) study

PROTOCOL NO.: SWAP-5
IRB Protocol #20203948

SPONSOR: University of Florida

INVESTIGATOR: Francesco Franchi, MD
655 West 8th Street
Jacksonville, Florida 32209
United States

STUDY-RELATED PHONE NUMBER(S): Francesco Franchi, MD
904-244-2060
904-244-0411 (24 hours)

Name of person seeking your consent: _____

Place of employment & position: _____

Name of Participant ("Study Subject")

_____

In general, what do you need to know about this Research Study?

The purpose of this form is to seek your consent to participate in research.

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved? The purpose of this study is to rule out that there would be a drug to drug interaction when Ticagrelor is given before a Cangrelor infusion
b) What is involved with your participation, and what are the procedures to be followed in the research? Your involvement will require receiving a dose of Ticagrelor and an infusion of Cangrelor or placebo along with 7 blood draws at different time points. This will occur twice at two different visits.
c) What are the likely risks or discomforts to you? There are risks of pain or discomfort from the blood draw, and there are risks to all the medications, which are discussed in detail below.
d) What are the likely benefits to you or to others from the research? There is no guarantee of direct benefit.
e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you? The alternative is to not participate.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

WHAT WILL BE DONE AS PART OF YOUR NORMAL CLINICAL CARE (EVEN IF YOU DID NOT PARTICIPATE IN THIS RESEARCH STUDY)?
If you choose not to participate in this study, you will be treated and followed by your primary care team per normal standard of care.

WHY IS THIS RESEARCH STUDY BEING DONE?
You are being asked to participate in this study because you have coronary artery disease for which you are taking aspirin. You must be informed so you can decide whether you want to participate.

Platelets are parts of your blood that stick together to help form a clot. The stickier your platelets are, the greater your chances of having heart attacks or strokes. Platelets from patients with heart disease tend to stick together more, increasing the risk of having a heart attack or stroke. To prevent a heart attack, there are antiplatelet drugs (blood thinners) to keep your platelets from sticking together. Ticagrelor (Brilinta), is one of the oral antiplatelet drugs used in the treatment of patients with coronary artery disease like yours and are typically used in association with baby aspirin.

For patients who are suffering from a heart attack and require a stent, it is likely the doctor would give the patient Ticagrelor after a stent has been placed. However, ticagrelor is sometimes administered immediately at hospital presentation before the procedure. The doctor might also use another blood thinning medication called Cangrelor during the stent procedure, which is given through an IV. Cangrelor is used during the procedure to potentiate the blood thinning effects and can be administered before or at the same time of ticagrelor. However, there have been no studies that test how cangrelor and ticagrelor work in patients that receive cangrelor after have already received Ticagrelor.

The purpose of this pilot study is to test the presence of drug to drug interactions when adding Cangrelor to patients already on Ticagrelor. For this study we will be looking at patients who are not currently having a heart attack or on any blood thinning medications, besides aspirin. The results of this pilot study will help inform if it is therefore safe to treat patients who are having a heart attack with Cangrelor if they have already received Ticagrelor. Cangrelor is approved by the FDA for patients undergoing coronary artery stenting; however, as used in this research study, it is considered investigational.

HOW MANY PEOPLE ARE EXPECTED TO TAKE PART IN THIS RESEARCH STUDY?
Up to 30 people are expected to take part in this study.

HOW LONG WILL YOU BE IN THIS RESEARCH STUDY?
If you are eligible, you will be expected to take part in the research for up to 33 days.

WHO CAN PARTICIPATE IN THIS STUDY?
Your study doctor will determine if you are able to participate in this research study. Please feel free to ask the study doctor about the study requirements for participation.

WHAT WILL BE DONE ONLY BECAUSE YOU ARE IN THIS RESEARCH STUDY?
Your study doctor will fully explain the study, other possible treatments, and any known or possible side effects of participating in this study. If you consent to participate in this study, your study doctor will collect data from your medical records. You will be evaluated to see if you meet criteria to enter into the research protocol. If you are a woman of childbearing potential, a pregnancy test will be done prior to taking any study medication. If you are found to be pregnant, you will not be randomized and your participation in this study will end.

Once consented, you will be randomized (like the flip of a coin) to receive a loading dose of Ticagrelor, which is 180mg, and either a 2 hour infusion of Cangrelor or placebo. Laboratory assessments will be performed to measure how your body is responding to the two medications. There will be 7 blood draws that will occur at baseline, at the start of infusion, 30 min after start of infusion, 1 hour after start, 2 hours after start, 3 hours after start, and 4 hours after start.

You will then enter a washout phase for 1-4 weeks. This will allow time for all of the medication to leave your system. After that period is complete, you will return to receive another loading dose of Ticagrelor and then based on if you received the Cangrelor or placebo in your first infusion, you will switch over to the opposite group. The same laboratory assessments will be completed at the same time points.

After these two visits your participation in the study will be complete.

Most of your blood samples will be processed immediately. However, others will need to be stored and processed after the end of the study. Only laboratory staff will have access to these samples and your identity will be protected.

WHAT ARE THE POSSIBLE DISCOMFORTS AND RISKS?
Your study doctor will be responsible for reviewing and monitoring your well-being.

The following are potential risks:

i. Blood drawing. There is the discomfort of blood drawing and you may experience bruising, and/or bleeding where the needle is inserted. Occasionally some people become dizzy or feel faint.
ii. The most common side effects of Cangrelor are: bleeding, dyspnea (shortness of breath), worsening renal (kidney) function and hypersensitivity.
iii. The most common side effects of Ticagrelor are bleeding, shortness of breath, headache, cough, dizziness, and nausea.
iv. It is unknown whether using Cangrelor and Ticagrelor together will increase these risks.

If you are a woman:

- You cannot take part in this study if you are pregnant or breastfeeding a child
- You must agree not to become pregnant while you are in this study
- If you are heterosexually active and able to get pregnant you must use birth control during the study. The type of birth control you use must be discussed with the study doctor before you begin the study. The study doctor must approve the method you use before you can enter the study
- If you get pregnant during the study, you must tell the study doctor immediately. You will have to stop taking the study drug. The study doctor will advise you about your medical care and will ask you to allow him/her to collect information about your pregnancy, your delivery and the health of your baby. There may be risks to a fetus or breastfeeding child that are currently not known.

If you are a man:

- If your partner becomes pregnant in the time between when you start taking the study drug until your last dose of study drug, you must tell the study doctor immediately. The sponsor may ask you and your partner to allow them to collect information about her pregnancy, delivery, and the health of the baby

i. **Loss of confidentiality**.

To protect you from above concerns:

i. The blood tests will be drawn by experienced personnel.
ii. Patients who are known to have bleeding problems will not participate in this study to reduce this risk.
iii. The data will be stored as secured coded access.

This study may include risks that are unknown at this time.

Taking part in more than one research study or project may further increase the risks to you. If you are currently enrolled or have recently taken part in another research study, you must tell the person reviewing this consent form with you.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, you may ask questions now or call the Principal Investigator or contact person listed on the front page of this form.

WHAT ARE THE POSSIBLE BENEFITS TO YOU?
There is no guarantee that you will personally benefit by participating in this research study.

HOW COULD OTHERS POSSIBLY BENEFIT FROM THIS RESEARCH STUDY?
Your participation in this study may help the investigators to learn more about the effects of administering Cangrelor after the patient has already been given with Ticagrelor, and may help other people in the future.

HOW COULD THE RESEARCHERS BENEFIT FROM THIS RESEARCH STUDY?
The sponsor is paying the University of Florida for conducting this research study. In general, presenting research results helps the career of a scientist. Therefore, the study doctor may benefit if the results of this study are presented at scientific meetings or in scientific journals.

CONFLICT OF INTEREST
Dr. Franchi is a paid consultant for AstraZeneca pharmaceutical the maker of Ticagrelor, which is used in the study. Please feel free to ask any questions you may have about this matter.

IF YOU CHOOSE TO TAKE PART IN THIS STUDY, WILL IT COST YOU ANYTHING?
Ticagrelor and either Cangrelor or placebo and its infusion will be provided at no cost to you while you are participating in this study.

The Sponsor will pay for all medical services required as part of your participation in this study as described above in the section of the consent form headed by the question "What Will Be Done Only Because You Are In This Research Study". This may include some medical services that you would have received if you were not in this study. If you receive a bill for these services, please contact Francesco Franchi, MD at 904-244-2060.

All other medical services provided to you that are note directly required by this study will be billed to you or your insurance company in the usual manner. You will be responsible for paying any deductible, co-insurance, or co-payments for those services, and for any non-covered or out-of-network services.

Some insurance companies may not cover costs associated with research studies. Please contact your insurance company for additional information.

WILL YOU BE PAID FOR TAKING PART IN THIS RESEARCH STUDY?
You will be paid $100.00 in Visa debit cards for each completed study visit to help cover time and travel. It may take up to 48 hours to process your debit card. If you do not complete all of your visits you will be paid for the visits that were completed.

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to **nonresident aliens** must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment contact the study team at 904-244-5659.

WHAT IF YOU ARE INJURED BECAUSE OF THE RESEARCH STUDY?

If you feel you have a research-related injury, notify the study doctor who will treat you or will refer you for treatment.

If you are injured as a direct result of your participation in this study, only the services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered.

The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the Principal Investigator Francesco Franchi, MD at (904) 244-2060 weekdays between the hours of 8:00 a.m. and 5:00 p.m., after regular business hours, you may call (904) 244-0411 if you experience an injury or have questions about any discomforts that you experience while participating in this study.

WHAT OTHER CHOICES DO YOU HAVE IF YOU DO NOT WANT TO BE IN THIS RESEARCH STUDY?
If you choose not to participate in this study, you will still continue receiving your medical care just as you normally do.

DO YOU HAVE TO BE IN THIS STUDY?
Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you leave this study for any reason, please contact Francesco Franchi, MD or 904-244-2060 (24 hours). They will tell you how to stop your participation safely.

CAN YOU BE WITHDRAWN FROM THIS RESEARCH STUDY?
The FDA, your study doctor, your local institution, has the right to stop your participation in the study, or cancel the study, without your consent at any time. Your study doctor may take you off the study at any time for any of the following reasons:

- if he/she decides it is in your best interest.
- if you do not consent to continue in the study after being told of changes in the research that may affect you;
- or for any reason.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

If you agree to participate in this study, the study doctor will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the study doctor needs your authorization. The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Complete past medical history to determine eligibility criteria
- Records of physical exams
- Laboratory, x-ray, MRI, and other test results
- Records about study medications or drugs

This information will be stored in locked filing cabinets or in computers with security passwords.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will include only information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, or any other photographs, numbers, codes, or so forth that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, throughout your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- to determine the safety of administering Cangrelor after a patient has been pre-treated with Ticagrelor

Once this information is collected, it becomes part of the research record for this study.

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study doctor, and research staff associated with this project
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures
- The University of Florida Institutional Review Board

Your PHI may be shared with:

- the study sponsor
- United States and foreign governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments
- WCG IRB
- Your insurance company for purposes of obtaining payment

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

Your PHI will be used and shared with others until the end of study.

This information will be destroyed 2 years after research is conducted or longer per University of Florida and/or FDA requirements.

You may not be allowed to see or copy certain information in your medical records collected in connection with your participation with this study while the research is in progress if the research includes treatment. When the research study is completed you will have access to inspect or copy your records with certain exceptions under applicable law.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the study doctor.

Your withdrawal must be made in writing and sent to Francesco Franchi, MD 655 West 8th Street, Jacksonville, Florida 32209.

NEW INFORMATION ON THE STUDY DRUG

You will be informed about any new information, such as adverse reactions (side effects) that could affect your decision to continue in this study. You may be asked to sign a new consent form if that should occur.

WHAT IF I BECOME PREGNANT DURING THE STUDY?
If you are pregnant or nursing before you enroll in the study, you may not participate in the study.

WHERE CAN I FIND INFORMATION ABOUT THE STUDY?
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.

WHO WOULD YOU CALL IF YOU HAVE ANY QUESTIONS?
If you have questions about the study, please ask us before signing this form. If you require further general information regarding the research study, if at any time you feel you have had a research-related injury or reaction to the study drug, or if you have questions, concerns or complaints about the research please contact:

Francesco Franchi, MD at 904-244-2060 or 904-244-0411 (24 hours).

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

WCG IRB
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 855-818-2289
E-mail: researchquestions@wcgirb.com

or

The University of Florida in Jacksonville at (904) 244-9478.

WCG IRB is a group of people who perform independent review of research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

CONSENT TO PARTICIPATE IN THIS RESEARCH STUDY

I have been informed about this study's purpose, procedures, possible benefits and risks. I have also been told alternatives to being in the study and how my protected health information will be collected, used, and shared with others. I have been given the opportunity to ask questions. My questions have all been answered satisfactorily. I agree to be in this research study. I have received a copy of this form.

By signing this consent form, I have not given up any of my legal rights.

I authorize the release of my medical records for research or regulatory purposes to those agencies listed under the Authorization section of this consent form.

Name of Participant (Print) Date

Signature of Participant

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study, the alternative to being in the study; and how the subject's protected health information will be collected, used, and shared with others:

Printed name of person conducting informed consent discussion Position

Signature of person conducting informed consent discussion Date