



**University of Florida – Jacksonville**

**SUBJECT INFORMATION AND CONSENT FORM**

**TITLE:** Impact of chronic kidney disease on the pharmacodynamic and pharmacokinetic effects of ticagrelor in patients with diabetes mellitus and coronary artery disease.

**PROTOCOL NO.:** ESR-15-10953  
WIRB® Protocol #20151832  
Clinicaltrials.gov identifier: NCT02539160

**SPONSOR:** The University of Florida

**INVESTIGATOR:** Dominick J. Angiolillo, MD, PhD  
655 West 8th Street  
Jacksonville, Florida 32209  
United States

**STUDY-RELATED  
PHONE NUMBER(S):** Dominick J. Angiolillo, MD, PhD  
904-244-3378  
904-244-0411 (24 hours)

**Name of person seeking your consent:** \_\_\_\_\_

**Place of employment & position:** \_\_\_\_\_

**Name of Participant (“Study Subject”)** \_\_\_\_\_

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. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

**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 are a diabetic patient who had a stent implanted in the artery of your heart due to a blockage and because of this also you are taking a blood thinning medication called clopidogrel, commercially known as Plavix®, in addition to a low dose baby 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. Platelets from the patients with diabetes mellitus tend to stick together more, increasing the risk of having a heart attack. It is also known that if you have both diabetes and kidney disease your platelets are even stickier and your chances of having a heart attack even higher compared to patients with diabetes but without kidney disease. Importantly, diabetes is the most common cause of having kidney disease. In fact, around 20 to 30% of people with diabetes develop kidney disease. To prevent a heart attack, there are antiplatelet drugs (blood thinners) to keep your platelets from sticking together. clopidogrel (Plavix®) and ticagrelor (Brilinta®) are antiplatelet drugs used in the treatment of patients with coronary artery disease like yours. In large-scale clinical investigation, Brilinta® has shown greater clinical benefits than Plavix®. The finding was consistent also in patients with diabetes mellitus or kidney disease. However, it is unknown if Brilinta® could prevent platelets from sticking together in patients with both diabetes mellitus and kidney disease.

In another large-scale clinical investigation, 60mg of Brilinta® was as effective as 90mg of Brilinta®, but with reduced side effects. However, it is unknown if the 60mg dose of Brilinta is as effective on blocking platelets compared with the 90mg dose in patients with diabetes mellitus and kidney disease.

The purpose of this study is to evaluate the effect of Brilinta® according to kidney function in diabetic patients and to evaluate the effects of two dosing regimens of Brilinta® (60mg and 90mg).

**HOW MANY PEOPLE ARE EXPECTED TO TAKE PART IN THIS RESEARCH STUDY?**

Up to 115 people are expected to be consented 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 20 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 antiplatelet medication. If you are found to be pregnant, you will not be randomized and your participation in this study will end. Nursing woman can't participate in this study.

Other study related procedures will include a physical. At the screening visit, if results from blood tests performed in the last 90 days are not available, blood will be collected for determination of complete blood count, HbA1c, and renal function. After undergoing screening, if you are eligible to participate you will come for a total of 3 visits for a total of 5 blood draws. Baseline platelet function tests will be done to see how sticky your platelets are. After this, you will be randomized (chosen, like the flip of a coin) to:

- (1) switch to Brilinta® 90 mg tablet twice daily for 7-10 days or
- (2) switch to Brilinta® 60 mg tablet twice daily for 7-10 days.

After 7-10 days you will be asked to come to our clinical site in the morning 12±2 hours after the last dose of Brilinta®. Blood draws will be performed before and 2 hours after administration of the study drug.

After this first phase you will switch to the different dose of Brilinta® and keep it for 7-10 days (90mg of Brilinta® for 60mg users and 60mg of Brilinta® for 90mg users). After 7-10 days you will be asked to come to our clinical site in the morning 12±2 hours after the last dose of Brilinta®. Blood draws will be performed before and 2 hours after administration of the study drug. After this, the study will be over and you will resume your standard of care therapy.

Approximately 30 cc (one ounce) of blood will be collected from you for the blood samples mentioned above by inserting a needle directly into your vein or from a catheter in your vein.

### **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:

- 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

- **The most common side effects of Brilinta® are:** shortness of breath, headache, cough, dizziness, nausea and bleeding that may be minor or life-threatening or fatal. During treatment with ticagrelor, dizziness and confusion have been reported. Therefore, patients who experience these symptoms should be cautious while driving or using machines.
- Loss of confidentiality.

To protect you from above concerns:

- The blood tests will be drawn by experienced personnel
- Patients who are known to have bleeding problems will not participate in this study to reduce this risk.
- 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?**

Participation in this study may or may not help to improve your condition. It is also possible that your condition may worsen. 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 learn more about the effects of administering ticagrelor (Brilinta®) 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. Angiolillo has received consulting fees from Astra Zeneca, the maker of ticagrelor, in the past 12 months. Please feel free to ask any further questions you might have about this matter.

**IF YOU CHOOSE TO TAKE PART IN THIS STUDY, WILL IT COST YOU ANYTHING?**

The Sponsor will pay for the medical services that you receive as part of your participation in this study which are described 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. All other medical services will be billed to you or your insurance company. 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 \$15.00 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. If the payments total \$600 or more or you are a nonresident alien, payment will be processed through the University of Florida Accounts Payable department and 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.

The study team will provide you with an informational form called the Prepaid Card Facts document. If you have any problems regarding your payment call the HSP Office (352) 392-9057.

**WHAT IF YOU ARE INJURED BECAUSE OF THE RESEARCH STUDY?**

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

If you are injured as a direct result of your participation in this study, only professional medical care that you receive at the University of Florida Health Science Center will be provided without charge. Hospital expenses will be billed to you or your insurance. You will be responsible for any

deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies. Please contact your insurance company for additional information.

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 Dominick J. Angiolillo M.D. at (904) 244-3378 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. You can receive the study drugs without participating in the study.

**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 entitled. If you leave this study for any reason, please contact Dominick J. Angiolillo, M.D., Ph.D. at 904-244-3378 or 904-244-0411 (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 effectiveness of the study drug in treating patients with coronary artery disease and diabetes, with or without kidney disease
- to evaluate a possible new use for the study drug

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 The University of Florida and AstraZeneca Company.
- 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
- Western Institutional Review Board
- Your insurance company for purposes of obtaining payment

Every attempt will be made to protect your right to privacy within legal limits. However, records associated with your participation in the study, including medical histories (case histories) which may identify you, and this informed consent signed by you, will be made available for inspection by the Western Institutional Review Board® (WIRB®), AstraZeneca company or designee (including any persons or companies which are contracted by AstraZeneca company to have access to the research information during and after the study, such as the monitor(s) and auditor(s)), the US Food and Drug Administration (FDA), and state and other local authorities. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. In addition, the results of treatment and laboratory data may be published for scientific purposes, but your identity will not be disclosed. By signing a written informed consent form, you are authorizing such access.

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 Dominick J. Angiolillo, M.D. Ph.D., 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:

Dominick J. Angiolillo, M.D., Ph.D. at 904-244-3378 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:

Western Institutional Review Board® (WIRB®)  
1019 39<sup>th</sup> Avenue SE Suite 120  
Puyallup, Washington 98374-2115  
Telephone: 1-800-562-4789 or 360-252-2500  
E-mail: [Help@wirb.com](mailto:Help@wirb.com)

or

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

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB 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.

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Name of Participant (Print)

Date

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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:

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Printed Name of Person Conducting Informed Consent Discussion    Position

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Signature of Person Conducting Informed Consent Discussion

Date