Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____**Medical Record #** _____

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Sponsor: University of Virginia Department of Nephrology – Nephrology Clinical Research Center

What is the purpose of this form?

This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this form.

Who is funding this study?

This research study is being conducted by the University of Virginia Department of Nephrology – Nephrology Clinical Research Center. Astra Zeneca will be paying the University of Virginia, Nephrology Clinical Research Center to conduct this study.

Why is this research being done?

The purpose of this study is to see if a medication called Ticagrelor (Brilinta®) is safe and effective compared to placebo in preventing vascular access failure for patients with End Stage Renal Disease (ESRD) on hemodialysis who have a vascular access (arterio-venous fistulae).

This space is reserved for IRB Approval Stamp. DO NOT CHANGE OR DELETE

The main renal replacement therapy for End stage renal disease (ESRD) in the USA is hemodialysis (HD). Hemodialysis is a lifesaving treatment when you have kidney failure. To keep up a regular dialysis schedule, you need a sturdy dialysis access where blood can flow in and out of the body. It must have a good, steady blood flow. Vascular access for hemodialysis can be provided by means of an autogenous fistula, arteriovenous graft, or central venous catheter. A functioning vascular access is crucial for hemodialysis. Vascular-access failure is when your access is no longer working. Vascular-access failure (VAF) is common and is a major source of complications for hemodialysis patients. VAF is also the most common reason for hospitalization among hemodialysis patients.

Ticagrelor (Brilinta®) is a prescription antiplatelet medication. Platelets can stick together and form a clot. This medication works by making the platelets in your blood less likely to stick together and form a clot.

Ticagrelor (Brilinta®) is approved by the Food and Drug Administration (FDA) for use in patients with acute coronary syndrome to reduce the rate of certain cardiovascular events. It is not, however, approved for use in hemodialysis patients for the purpose of preventing clotting and is therefore considered investigational for the purpose of this study.

So far, the drug Ticagrelor (Brilinta®) has been given to thousands of people who have acute coronary syndrome. **This will be the first study that the drug Ticagrelor (Brilinta®) will be given to hemodialysis patients suffering from end stage renal disease (ESRD).**

You are being asked to be in this study, because you are on hemodialysis and have a vascular access.

Up to 88 people will be in this study at UVA.

How long will this study take?

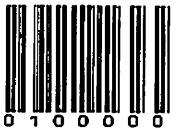
Your participation in this study will require 19 study visits over a 12 and a half month period of time. Each visit will occur while you are here for your regularly scheduled dialysis session and will last about 30 minutes.

What will happen if you are in the study?

SCREENING VISIT (this visit will take 1 ½ hours to complete and this will take place while you are at your regular dialysis session):
Visit 0

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening visit. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- Review of your medical history and dialysis history to include type and place of you access
- Current medication review



- Physical exam and vital signs (blood pressure, heart rate)
- Review of your history of access issues/problems
- For women of child bearing potential we will collect a serum blood sample to perform a pregnancy test

If you are eligible, you will start on the study treatment at one of your dialysis treatments within a week of the screening visit. If you qualify for the study the study team will schedule you for a visit to start study treatment.

RANDOMIZATION and STUDY TREATMENT: (Visits 1-12) (Twice a month study visits for the first 6 months)
***(Each* visit will last about 30 minutes and will occur during your regular dialysis session)**

You will be randomly assigned (like the flip of a coin) to 1 of 2 study treatment groups. You have an equal chance of being assigned to any one of the groups. Neither you nor your study doctor can choose which treatment you are assigned to; however once you have been assigned a treatment the study team will know which treatment you are on. You will be able to find out which study treatment you have been assigned when the study is done.

GROUP 1: Ticagrelor (Brilinta®) 180mg (90mg twice a day)

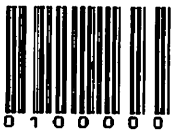
GROUP 2: Placebo (taken twice a day)
* A placebo is a harmless substance that looks like the study drug, but which should have no effect.

For the purpose of this study, we will refer to both Ticagrelor and placebo as the "study drug"

- You will be taking the study drug once in the morning and once in the evening.
- You must take the study drug as directed with or without food every day for 6 months.
- You should take your morning and evening doses around the same time each day, but you may adjust those times if you have a change in your schedule that requires taking the study drug at a different time. You can discuss with your study doctor how to arrange this.
- At each study visit, you will be asked about how you are tolerating the study drug
- You must bring all study drug in to one of your twice monthly visits and you must bring the study drug to the final treatment day visit which is Visit 12

During the study treatment period you will have the following study related procedures:

- You will also have a physical exam at Visit 12 (Month 6).
- We will be recording your hemoglobin levels that are currently being obtained twice a month for standard of care. Hemoglobin in the blood carries oxygen from the respiratory organs (lungs) to the rest of the body through our red blood cells. The weeks you have your standard of care labs drawn we will be gathering your hemoglobin results from your dialysis record.



- The study team will also be collecting your bleeding time each week while you are on study medication. If you have prolonged bleeding the nursing staff will be notified and they will send you for further evaluation.
- Vital signs, including your weight and other dialysis visit information will be obtained from your dialysis record which will be done at your normal dialysis session and is part of your standard of care; the results will be recorded for research purposes.

FOLLOW UP: (Visits 13-Visit 18) (Once a month study visits for 6 months)
***(Each* visit will last about 30 minutes or less and will occur during your regular dialysis session)**
After you have been on study treatment for 6 months you will have a follow up period for 6 months (Visits 13-18). For this period you will be seen once a month.

During the follow up period you will have the following study related procedures:

- You will also have a physical exam at Visit 18 (Month 12).
- The study team will also be collecting your bleeding time each week during the follow up period.
- Vital signs, including your weight and other dialysis visit information will be obtained from your dialysis record which will be done at your normal dialysis session and is part of your standard of care; the results will be recorded for research purposes.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

Study Schedule

	Screening Visit	Visit 1 to Visit 12	Follow Up Visits Visit 13 to Visit 18	Weekly Visits
Study Visits		Day 1 to Month 6 Visits twice a month (+/- 5 days)	Month 7 to Month 12 Visits once a month (+/- 5 days)	
Informed Consent	X			
Review Study Eligibility	X			
Medical History/Dialysis History	X			
Bleeding Time	X	X	X	X
Changes in Medical History & Medications		X	X	
Vital signs	X	X	X	
Physical Exam	X	X (Visit 12 Only)	X (Visit 18 Only)	
Study Medication Dispensed/Collected		X Dispensed-Visit 1 Collected-Visits 3, 6, 9 & 12)		

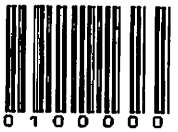
What are the risks of being in this study?

Ticagrelor (Brilinta®) has been safe and effective for people with acute coronary syndrome. **This medication has not been tested in people with end stage renal disease on hemodialysis.**

The following bulleted risks were noted in previous trials using Ticagrelor (Brilinta®).

Frequent complaints (seen in at least 3% of study participants) that have been reported during studies:

- Bleeding
- Dyspnea (Shortness of Breath)
- Cough
- Dizziness
- Nausea
- Atrial Fibrillation (Heart Rhythm Disorder)
- Hypertension (High Blood Pressure)
- Non-Cardiac Chest Pain
- Diarrhea
- Back Pain
- Hypotension (Low Blood Pressure)
- Fatigue



- Chest Pain
- Headache

More Frequent complaints (seen in at least 6 to 7% of study participants) that have been reported during studies:

- Bradycardia (Slow Heart Rate)
- Elevated Serum Creatinine

There have also been cases of increased uric acid levels for subjects taking ticagrelor. A high uric acid level, or hyperuricemia, is an excess of uric acid in your blood. Uric acid is produced during the breakdown of purine, a substance found in many foods. Once produced, uric acid is carried in your blood and passes through your kidneys, where most of it leaves your body when you urinate. A high uric acid level may result in attacks of gout, but not everyone who has high uric acid gets gout, and not everyone with gout has high uric acid. Increased uric acid may also increase the chances of kidney stones.

There is also an increased risk of severe bleeding for subjects taking ticagrelor. Due to the increase risk of severe bleeding there may be a risk of delay in any surgery that you may need while taking this study medication.

Risks of Sharing the Drug
Do not share the study drug with anyone. It is prescribed only for you and could hurt someone else. Keep it out of reach of children and people not able to read or understand the label.

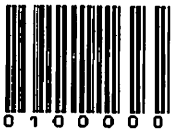
Blood Donation
If you participate in this study it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks for women:
If you are pregnant now, or get pregnant during the study, please tell us. Being in this study might hurt your unborn baby, so you will not be able to join or stay in the study. Also, you should be sure you do not get pregnant during the entire study including follow up period (visits 13 to 18) which are the monthly visits. You must agree to use an effective method of birth control during the study. If you have questions about birth control, please ask the study leader.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You may benefit from being in this study. Possible benefits include: less problems with your vascular access so that you would be able to avoid having to go through the usual treatments for vascular access failure (usual treatments listed below). In addition, information researchers get from this study may help others in the future.



What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatments for dialysis access failures are listed below. If blood flow is blocked, your doctor may be able to clear it with a tiny balloon or tube (stent). Sometimes a blood clot can be cleared with blood thinner medicine.

- If your access is infected, your doctor will remove all or part of it. You will have antibiotic treatment for the infection.
- If your access needs time to heal, you will have a temporary catheter placed for about 3 weeks or less. For longer use, a temporary catheter called a "permacath" may work for a few months.
- If you need a new permanent access, talk to your doctor about your options. If you aren't a candidate for a fistula, your doctor can create another graft.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $415.00 for finishing this study by check from the University of Virginia.
You should get your payment about 2 weeks after finishing the study. The income may be reported to the IRS as income.

If you do not finish the study, you will be paid $25.00 for any visit completed for screening through visit 12.
You will be paid $15.00 for any visit completed for visits 13 through visit 18.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, and child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

By agreeing to be in this study, you are donating your blood for research, and giving up any property rights you may have in them. The results of this research using your donated materials may have commercial value. However, you will not receive any payments.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: serum pregnancy testing (if applicable), study drug, and physical exams.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given

to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study.
Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

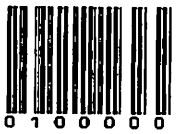
How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?



- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. We ask them to protect your privacy. However, they may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

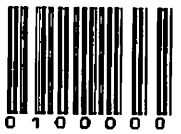
What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your records will be able to find out that you are in this study. This is done so your regular doctors will know what drugs or treatment you are getting in the study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study



Emaad Abdel-Rahman
Internal Medicine, School of Medicine
University of Virginia
Nephrology Division
PO Box 800133
Charlottesville, Virginia 22908 Telephone: (434) 924-5820

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Consent From Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the subject and the subject had the opportunity to ask any questions he/she had about the study. I also agree that the subject freely gave their informed consent to participate in this trial.

IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE