Consent and Authorization Form

Principal Investigator: **Saketh Guntupalli, MD**
COMIRB No: **15-0187**
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Study Title: **The Safety of Oral Apixaban (Eliquis) versus Subcutaneous Enoxaparin (Lovenox) for Thromboprophylaxis in Women with Suspected Pelvic Malignancy; a Prospective Randomized Open Blinded End-point (PROBE) Design**

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
This study plans to learn more about a new oral medication option (Apixaban) for preventing venous thrombus events following gynecologic surgery. A venous thrombus event is a blood clot. Women having gynecologic surgery for cancer have about a 10% risk of a blood clot in the 1-month following surgery. In some, this may be fatal. Anti-coagulation treatment following surgery decreases your risk for blood clots.

The new medication (Apixaban) will be compared to the current medication Enoxaparin, which is commonly called Lovenox. Lovenox is an injectable medication taken for 28 days, used to prevent blood clots.

You are being asked to be in this research study because:

- You are having surgery for your suspected or confirmed gynecologic cancer,
- You have no history of blood clots, and
- You have no history of any bleeding disorder.

Other people in this study
Up to 500 people from your area will participate in the study.

What happens if I join this study?
If you join the study, you will be asked to complete a screening visit where you will provide your medical history and demographic data to the study doctor. Your medical chart may also be accessed for review of your health history. The study doctor will use this information to determine if you are eligible.

If you are determined eligible to continue in the study, you will be scheduled for a pre-operative exam. This exam will be completed as part of your routine clinical care. In addition to the routine clinical procedures at this visit (pregnancy test, physical exam, etc.), you will be asked to complete a survey as part of the research study which will evaluate your quality of life. This should take about 10 minutes to complete.

Either before or after your procedure you will be randomized (like flipping a coin) to receive either the oral study medication (Apixaban) or the current standard of care medication (Enoxaparin). You will take the medication for 28 days following your surgery. Your prescription will be filled by the University of Colorado Hospital inpatient pharmacy before you leave the hospital. On each of the 28 days you will be asked to record the time you take the medication, as well as all other medications you are taking, in a diary provided to you. The study team will provide instructions on taking your medication and completing the diaries before you leave the hospital. You will be asked to keep all medication bottles, even those that may be empty or unused, during the course of the study.

You will return to the clinic for your routine post-operative visit approximately 2 weeks after your surgery. In addition to the routine clinical procedures at this visit, you will review your diaries and return your empty medication bottles/syringes to a member of the study team. Your medical chart will also be accessed for review of your health history. Approximately 28-35 days after your procedure you will be asked to come in for a research visit. At this visit a member of the study team will collect all medication bottles/syringes, unused medication, and a physical exam will be conducted. You will also be asked to complete a survey which will evaluate your quality of life, and your medical chart will be accessed for review of your health history. The survey will take about 10 minutes to complete.

Approximately 90-97 days after your procedure you will return to the clinic for your routine post-operative visit. Your medical chart will be accessed by the study team for review of your health history. At this time participation in the study will end.

If at any time during the course of the study you experience any symptoms of a blood clot, you will be asked to contact your doctor and schedule a clinic visit for evaluation of your symptoms. These symptoms include: pain in leg, warmth in skin, visible veins not normally visible, leg fatigue, severe chest pain, or coughing up blood. If a blood clot is suspected, you may be asked to stop taking the study medications and your study participation will end.

What are the possible discomforts or risks?

Risk of surgical procedure (not study related): Women having gynecologic surgery for cancer have about a 10% risk of a blood clot in the 1-month following surgery. In some, this may be fatal. Symptoms of a blood clot include: pain in leg, warmth in skin, visible veins not normally visible, or leg fatigue. Contact your doctor if you are experiencing these symptoms.

Risks of study procedures:

- Medication: Like all medicines, Apixaban can cause side effects. The negative events that are the most likely to happen to you if you receive Apixaban are listed below. You may not get any of them, but it is important to know what to do if they do occur.

  Common (between one in ten to one in a hundred patients might experience the event)
  - Bleeding in the eye, under the skin, from the nose and gums
  - Bruising
  - Vomiting of blood
  - Blood in stool and urine

  Uncommon (between one in a thousand to one in ten-thousand might experience the event)
  - Sensitivity reaction (e.g. skin rash, difficulty breathing, swelling of the face)
  - Bleeding in the brain, in the lining of the stomach, from the mouth, and from hemorrhoids
  - Blood in sputum (nasal and throat mucus)
  - Abnormal bleeding from injection sites, sites of cuts, sites of injury and vaginal

  Rare (between 1 in 10,000 to 1 in 100,000)
  - Bleeding in the respiratory tract (including the lungs)

  These risks are the same if you are assigned to the Enoxaparin group. Enoxaparin is not an investigational drug. Enoxaparin is the standard of care prescribed to you following gynecologic surgery if you decide not to participate. You would have the same risk as you would if you didn't participate in the study.

- Confidentiality: there is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it can not be guaranteed.

Becoming pregnant: If you become pregnant, the particular treatment or procedures involved in the study may involve risks to the embryo or fetus which are currently unclear. The reproductive risk potential of apixaban in humans has not been fully evaluated. Apixaban has not been studied in pregnant or lactating women. All subjects must agree to use at least one of the following highly effective methods of contraception. Talk to your doctor about the best options for you.

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

What are the possible benefits of the study?
This study is designed for the researcher to learn more about new medication options for preventing blood clots, following gynecologic surgery. An oral medication may provide patients with an easier and more cost-effective option for treatment after surgery.

This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Are there alternative treatments?
There may be other ways to prevent blood clots after surgery. The standard of care is an anticoagulation medication. Some of these medicines are: Heparin, Enoxaparin, or Lovenox. Treatment is taken daily using a self-administered injection. You could also choose to get no treatment at all for prevention of blood clots following surgery.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?
This research is being paid for by Bristol-Meyers Squibb, the manufacturer of the study drug.

Will I be paid for being in the study?
You will not be paid to be in the study. You may be reimbursed for your medication co-pay, or deductible if applicable, as indicated below.

Will I have to pay for anything?
It will not cost you anything to be in the study. Your surgery and the medicines provided to you during surgery will be provided per standard of care. All visits for your gynecologic surgery are standard of care and will be billed to your insurance in the normal manner. If you are randomized to receive the current standard of care medication (Enoxaparin), you may be charged a co-payment for the medication, or a pharmacy charge if you have an applicable deductible which has not yet been met. This will be dependent on your insurance plan. You will be reimbursed the total amount of this co-pay or pharmacy charge. If you are randomized to receive the study medication (Apixaban), you will receive the medication free of charge.

Is my participation voluntary?
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or

rights to which you are entitled. It is important to know that if you stop taking your medication, you may be at a higher risk for major bleeding or a blood clot, than if you stay on the medication. You should talk to your study doctor before stopping the medication.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

Can I be removed from this study?
The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?
If you have an injury while you are in this study, you should call Dr. Guntupalli immediately. His phone number is 303-266-4172.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?
The researcher carrying out this study is Dr. Saketh Guntupalli. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Guntupalli at 303-266-4172. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Guntupalli with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

A description of this clinical trial will be available on http://www.Clinical Trials.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 will see my research information?
The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Saketh Guntupalli, MD
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Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- Bristol-Meyers Squibb who is the company paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available to: Bristol-Meyers Squibb.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (DOB, age, gender, race/ethnicity, phone number, email address, address)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records

What happens to Data that are collected in this study?
Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures

of disease. The data collected from you during this study are important to this study and to future research. If you join this study:

- The data is given by you to the investigators for this research no longer belong to you.
- Both the investigators and the company paying for this research, Bristol-Meyers Squibb, may study the data collected from you.
- If data are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

Agreement to be in this study and use my data
I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____Date:_____

Print Name:_____

Consent form explained by:_____Date:_____

Print Name: _____

Only sign Witness if subject is unable to provide informed consent:
Witness Signature:_____Date:_____

Witness Printed Name:_____