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 # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

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

Who is funding this study?

This study is funded by the Berne Cardiovascular Research Center at the University of Virginia

Key Information About This Research Study

Principal Investigator:	Antonio Abbate, MD, PhD Berne Cardiovascular Research Center 415 Lane Rd (MR5); PO Box 801394 Charlottesville, VA 22908-1394 Phone (434) 297-9449
Funding Source:	Cardiovascular Research Center, University of Virginia

You are being asked to take part in a research study. You do not have to take part in this study. You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What is the purpose of this study?

The purpose of this study is to assess whether a drug that we commonly use for the treatment of gout, namely colchicine, can reduce inflammation in the setting of heart failure (a clinical condition in which the heart is weakened and unable to function properly). Several studies have shown that reducing inflammation may benefit patients with heart failure. A recent study performed here at University of Virginia has shown that treatment with colchicine in the setting

of gout was associated with better short-term outcomes in patients with heart failure. We hypothesize that the reduction of inflammation may be the link between colchicine treatment and improved outcomes.

You are being asked to take part in this study because you have been admitted for heart failure and may meet the criteria for this trial.

Why would you want to take part in this study?
You might like to take part in this study because by participating you may help to understand the mechanism of heart failure and how colchicine works. In this study, by chance (like flipping of a coin) half of subjects will be assigned to receive colchicine and the other half will receive placebo (a look-alike pill that has no activity). If you are assigned to receive colchicine which will likely reduce the inflammation in your body. If you are assigned to receive placebo, then we would not expect you to experience any change in your heart condition. Even if you do not receive colchicine, the information gained by participating in this study may help others in the future.

Why would you NOT want to take part in this study?
You might not want to take part in this study because participating in the study may require some additional visits to the hospitals and additional bloodwork. We will, however, try to limit these additional visits and blood draws and try to make them coincide, as much as possible, with your standard of care of visits.

If you have certain medical conditions with your heart, kidneys, blood, or liver it may not be safe for you to participate. Your study doctor will discuss your medical history with you and determine if it is safe for you to be part of the study.

Colchicine does not mix well with many different kinds of medication. These medications include certain antibiotics, antiviral and pain medications. Your study doctor will review all of your medications with you to be sure it will be safe for you to be in the study.

Colchicine may also cause adverse effects, like diarrhea and abdominal pain, muscle pain and fatigue, and changes in blood cell count. These adverse events with colchicine are generally mild and reversible, meaning they resolve when stopping the treatment.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form. If you agree to take part in this study, you will:

1. Taking Colchicine or an inactive pill (placebo) once or twice per day (depending on your kidney function) for 14 days. Subsequently, you will take colchicine or placebo once per day (or every other day) for 76 days. In case your research doctor determines you have kidney disease, the above-mentioned doses will be cut in half (i.e., one pill per day the first 14 days then one pill every other day). You may also be taking additional medications prescribed by your doctor for your heart condition that are considered standard care.
2. We will analyze your blood to assess inflammatory function. We will take blood (1 tube – approximately one teaspoon each time) at the following timepoints:
    a. Before starting the treatment
    b. After 24±12 hours
    c. After 48±12 hours
    d. After 72±12 hours
    e. After 14±7 days
    f. After 90+7 days
3. One of the members of the research team will periodically assess your chart for 90 days (full treatment duration) to see whether you have had any issues with any symptoms of heart failures or side effects from the medications. You will be asked to return on day 90 with the pill bottle to exit the study.

What is the difference between being in this study and getting usual care?
You will receive all standard of care treatments per your heart doctor's advice. The usual treatment would include:

- Various kinds of medications that act on the heart to help it pump more efficiently, or stronger, and at a more normal rate)
- Diuretics (fluid pills) that help eliminate excess fluid in your body to relieve heart congestion
- Medications that prevent and treat a heart rhythm that's too fast or irregular

If you choose to be in the study, you will receive the study drug called **colchicine** in addition to the medications and treatments recommended by your heart doctor. ***Colchicine*** is a drug that has been used for centuries in the treatment of gout.

Colchicine is approved by the U.S. Food and Drug Administration (FDA) for several diseases, but not for heart failure. However, the FDA has allowed ***colchicine*** to be used in this research. So far, preliminary studies performed at the University of Virginia have suggested that the use colchicine may be associated with better hospital outcomes among patients with heart failure**.** Whether this is due to colchicine is not currently known.

If you take part in the study, you will be assigned to take either colchicine or placebo (a look-alike pill that has no activity) for 90 days in addition to the medications prescribed by your heart doctor. In this timeframe we will assess your blood work to look for signs of improved inflammatory function.

How many people will take part in this study?
Approximately 30 subjects will be in this study at UVA.

How long will this study take?

The study will last approximately two years. Your participation in the study will last for a total of 90 days.

What will happen if you are in the study?

SCREENING (visit will last about 15 minutes)
Visit 1*):*

If you agree to participate, you will sign this consent form before any study related procedures take place.

Before you can start the study, the research team will perform a screening review of your medical chart to assess the presence of inclusion and exclusion criteria. In addition, a screening blood test may be added onto your morning labs. If you did not have blood drawn on that day, we will draw a tube specifically for the screening test. We will measure a blood level of inflammation called high-sensitivity C-reactive protein (hs-CRP). If the hs-CRP will come up elevated (i.e., >2 mg/L), and you have the inclusion criteria and none of the exclusion criteria, you will qualify to take part in the study. At that point we will collect a tube of blood (approximately a teaspoon) to measure further markers of inflammation.

BASELINE, RANDOMIZATION and STUDY TREATMENT (Each visit will last about **15 minutes)**
Visit 2
If you are found to be eligible, 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 doctor can choose which treatment you are assigned. Neither you nor your doctor will know which study treatment you will get until the study is done. But if your doctor needs to know, the people doing this study can find out.

GROUP 1: Colchicine.

If you are assigned to this group, you will receive a capsule containing 0.6 mg of colchicine twice per day (or once if you have kidney disease) for 14 days. Subsequently, you will be taking colchicine 0.6 mg once per day (or once every other day if you have kidney disease) for 76±14 more days to complete treatment.

GROUP 2: Placebo
A placebo is a harmless substance that looks like the study drug, but which should have no effect. If you are assigned to this group, you will receive a capsule that does not contain any active drug, using the same regimen you would if you were receiving Colchicine.

You will continue to receive heart failure medications and treatments prescribed by your doctor as part of your medical care regardless of group assignment.

At baseline you will also have blood sample drawn.

Study Visits 3, 4, 5, and 6:
The study includes 4 further visits for lab work to analyze the levels of inflammation in your blood. The blood samples will be collected at approximately 24, 48 hours, 72 hours and 14 days after the initiation of study treatment. If you are still a patient in the hospital at any of those timepoints, a research tube will be collected as part of your morning lab work and will be sent to the research lab. If you are already discharged, the research team will schedule an appointment to collect your blood at the University of Virginia Heart and Vascular Center outpatient facility.

FOLLOW UP
You will continue taking the study medication to complete approximately 90 days of treatment in total. The research team will monitor your chart in the interim to assess whether you will be experiencing any adverse clinical event.

END OF STUDY Visit:
You will be asked for a follow-up visit at around 90 days. At that time, the study team will assess whether you have experienced any significant heart failure related events or other health conditions. You will be asked to return the experimental medication tube for the study team to assess your compliance with the study treatment. In addition, lab work will be performed to analyze the levels of inflammation in your blood.

After you have completed this visit, the study is over and you will have no interactions with the study team and no longer receive the study drug.

Study Schedule

	Visit 1 (Screening)	Visit 2 (Baseline)	Visit 3	Visit 4	Visit 5	Visit 6	Follow-up	End of Study
Study day	-1	0	1	2	3	14 +/- 7 days	90 +/- 7 days	After 90 days of study treatment
Informed Consent	x							
Review study eligibility	x							
Medical History	x							
Vital signs	x							
Physical Exam	x							
Blood draw (for laboratory testing)	x	X	X	X	X	X		X
Study Medication Dispensed		X						
Chart review							X	
In-person visit with Study Medication collection								X

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety. These responsibilities are listed below:

- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Ensure that the study drug is taken as instructed, keep the study drug in a safe place away from other children, return any unused study drug at the final visit, and report any lost or missed tablets.

- Ensure that the study drug is taken only by you, the person for whom it has been prescribed.
- Answer all of the study-related questions completely.
- You must not eat grapefruit or drink grapefruit juice during the course of your participation in this study.
- Inform your **Primary Care Practitioner (PCP) that you are in a clinical research study and you may be taking Colchicine**. You may want to show them this informed consent which will provide the PCP with details related to the study, and contains a list of medications that should not be taken with the study drug. This information may help guide medication selection. In addition, it can provide the PCP with information on how to contact the study PI or study team if one of those medications is deemed necessary for your care, which will assist with the coordination of stopping and restarting the study medication.
- **Inform the study doctor or study staff as soon as possible if you have to take any new medications**, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor or study staff will let you know if you can take these medications. In case one of the medications that should not be taken is deemed necessary, the study team will coordinate stopping and restarting the study medication.
- **In the event you start experiencing any of the following symptoms related to the study drug**, such as blood in stools and urine, hives or rash, severe cramping with dark urine or significant weakness of a limb, **stop taking the medication and immediately call 911 or go to the nearest emergency room**.

Please note the following numbers and instructions:

- 911 or go the nearest emergency room, if any of the above serious side effects occur.
- Please contact the study team at (434) 982-1058 if you start a new drug. They will assist you in coordinating the stopping and restarting the study medication.
- Please call the study team at (434) 982-1058 if you have any questions about any side effects listed below or any questions about the study.

Blood Testing

We will take (or "draw") up to 1 teaspoon of blood for the first 4 visits of the study**.** There is a remote probability we will need an additional 1 teaspoon of blood for the screening hs-CRP as explained above, if you did not have clinical labs that specific morning. The total amount of blood we will take will be 4 to 5 teaspoons. The blood we take will be tested to measure the levels of inflammation in your blood.

When these tests are done any left-over sample will be thrown away or they will be de-identified. This means there is no information that could be used by anyone to determine who the sample came from.

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 of the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

A risk of allowing us to collect information about you is a potential loss of privacy. The University of Virginia will do its best to protect your records so that facts about you and your health will be kept private. The chance that information identifying you will be given to someone else is very small. However, we cannot *guarantee* it will be safe.

Risks and side effects related to the treatment with colchicine include:

Common

- Diarrhea
- Nausea
- Abdominal discomfort

Less Common

- Vomiting

Rare but serious

- Black or tarry stools
- Blood in stools or urine
- Numbness or pain in hands and feet
- Rash or peeling of the skin
- Hives and swelling of face and mouth
- Headache
- Reduction of your blood cells
- Rhabdomyolysis: damage to muscle cells
- Neuromuscular toxicity: damage to the nerves that activate muscles

- Reversible azoospermia in males: reversible loss of male fertility

Please stop the study medication and seek appropriate medical care, as well as notify the study team immediately if you experience any symptoms potentially indicative of serious side effects, such as blood in stools and urine, hives or rash, severe cramping with dark urine or significant weakness of a limb.

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.

Risks from Placebo

Risks associated with the placebo are generally minimal. There is a very remote possibility that you may be allergic to the components of the capsule or of the inert content.

Risks associated with blood draws

Likely:

Potential for minimal discomfort, minor bleeding at venipuncture site.

Rare

- bruising and/or infection at venipuncture site.
- Potential for participants to experience lightheadedness and/or nausea (rare).
- Potential for rhythm disturbance of the heart (extremely rare)
- Syncope (extremely rare)

Risks to Confidentiality and Privacy

There are social/psychological risks associated with breaching participants' confidentiality and/or privacy. The likelihood of this occurring, however, is very low, and will be further lowered by storing data in a UVA approved database that does not link patients' identities with their data. To further reduce these risks, except when required by law, patients will not be identified by name, or by any other personal information.

Contraindicated Medications

Some medications should not be taken while on colchicine. The study team will screen your current medications to make sure you are not taking any these medications. However, make sure your PCP and normal care team members are aware that you are in this research study, and know of the list of these medications in case they plan on changing your treatment.

- Protease inhibitors (drugs used to treat viral infections like HIV/AIDS)

- Macrolides antibiotic (Z-pack, Azithromycin, clarithromycin and erythromycin) treat infections like bronchitis, etc.)
- Ketoconazole, Fluconazole and Itraconazole -use to treat fungal (yeast) infections
- Nefazodone (Serzone) used for depression
- Non-dihydropiridine calcium channel blockers (Verapimil, diltiazem, Cardizem Cartia, Dilacor, Diltiax, Taztia Tiazac)
- Aprepitant (also called Emend) used to treat post-op nausea or nausea from chemotherapy
- Ranolazine (ranexa) use to treat chest pain
- Cyclosporine- used to treat autoimmune diseases and helps fight organ rejection post transplant.

Also taking colchicine with statins (drugs that treat bad cholesterol) or fibrates (drugs that lower triglycerides) may increase the rates of a rare complication called rhabdomyolysis. While those medications are not considered contraindicated, be mindful of severe muscle pain and dark urine if you are taking those medications.

Could you be helped by being in this study?

. , .
You may or may not benefit from taking part in this study or taking the study medicine.
If you receive the study medicine and it works for you, your heart disease and/or inflammation symptoms may improve. The information we get from you during the study may help you or other people with heart failure and inflammation 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 treatment would include:

- Guideline directed medical therapy, if appropriate in your case, which includes:
    - Medications called Beta-blockers. These drugs slow your heart rate and reduce high blood pressure
    - Medications called Renin angiotensin aldosterone system inhibitors, such as ACE-inhibitors, Angiotensin receptor blockers or neprylisin inhibitors/ARB combination.
    - Medications called Mineralcorticoid receptor antagonists
    - Medications called Sodium-glucose contransporter type 2 inhibitor (SGLT2i)
- Diuretics to relieve heart congestion
- Medications that prevent and treat a heart rhythm that's too fast or irregular

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 not get any money for being in this study.

By agreeing to be in this study, you are donating your blood samples 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 blood tests related to the research study and the dispensing of the investigational drug will be provided at no cost to you or your health insurance. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

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 your insurance company for an estimate of what these costs might be or if pre-approval is required.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). 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.

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) The side effects of the treatment are too dangerous for you
c) New information shows the treatment will not work or is not safe for you
d) You do not follow your doctor's instructions
e) The study sponsor closes the study for safety, administrative or other reasons

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

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.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

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.

Information obtained from you during this study may be used in future research. Your information may be shared with other researchers inside the University of Virginia. They will not be sent with information that could identify you such as name, address or phone number.

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.

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 or complete the "Leaving the Study Early" part of this form and return it to the researchers. 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 medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the Principal Investigator listed earlier in this form 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

What if you have a concern about this study?

You may also report a concern about this 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 22903
Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the UVA Study Tracking 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.

You may also report a concern anonymously by calling the UVA Compliance Hotline phone number at 1-800-235-8700.

Would you like the study team to communicate with you by email or text message?

If you choose to communicate with the study team by unsecure email (email that is not encrypted) or text message to your personal phone, there is some risk that your health information could be read or accessed by someone else while the information is sent or saved by your email or phone provider.

Your personal email or phone provider may also share or release your information because they do not have to follow the privacy laws that UVA follows. Sometimes email and phone providers release information to marketing companies for use in direct advertising. If you choose to communicate by email or text messaging, UVA cannot control this potential loss of privacy but we want to tell you about this possible risk.

You do not have to agree to communicate with the study team by email or text message to be in this study. If you agree to texting or emailing, the study team will collect your phone and /or email address from you that you would like them to use to contact you. Please note, if you agree to text messaging, charges may apply depending on your data/text plan with your phone provider.

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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.

If an interpreter is involved in the consent process because the potential subject does not speak English well or at all, the participant should NOT sign on the line above – leave this line blank. Instead, the participant should sign the IRB approved Short Form or full consent written in the language they can understand. A modification to add signature lines for interpreter also required.

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

Signature of 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 **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):
☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.
The follow up information will be collected by:

- Obtaining information from my medical records

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

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

Person Obtaining Consent

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

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