VUMC Institutional Review Board
Informed Consent Document for Research

Study Title:	Preemptive Pharmacogenetic-guided Metoprolol Management for Postoperative Atrial Fibrillation in Cardiac Surgery: the PREEMPTIVE-Pilot Trial
Version Date:	March 25, 2019
PI:	Miklos Kertai, MD, PhD

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

What is the purpose of this study?
You are being asked to take part in this research study because you are having heart bypass (CABG) or valve repair/replacement surgery.

Cardiac surgery patients are often given drugs called beta blockers to reduce their risk of problems, such as atrial fibrillation [A-Fib (irregular heartbeat that can lead to blood clots, stroke, heart failure, and other heart related complications)] during and after surgery. One of these beta blockers is called metoprolol. Metoprolol is has varying side effects and effectiveness in some patients. Each person responds differently to medicines. Genes play a role in how patients will respond to medicines.

Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment. Doctors believe that using genetic- guided dosing of metoprolol may reduce the risk of A-Fib and make cardiac surgery safer for patients.

After you have signed this consent, the study team will draw about a teaspoon of blood for the institutionally available PREDICT (a test to determine the gene associated with how your body metabolizes metoprolol) to be run in the VUMC lab. You will not be billed for this test. The blood draw will take only a few minutes of your time. Your genetic results will allow doctors to adjust your recommended dose of metoprolol. You will not need to attend any follow- up meetings. Test results will become part of your permanent medical record and can be used by your doctors in the future. Your PREDICT test results will also be available in "My Health at Vanderbilt" or you may contact your doctor for your test results or more information.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will

contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
Blood Draw Risks: The risks of drawing blood include pain, bruising, lightheadedness, and fainting. Rare: infection at the site of the needle stick.

Metoprolol dosing: as a result of the genetic testing your metoprolol dose could be increased or decreased before and after your heart surgery. When metoprolol dose is increased it could potentially lead to a higher frequency of side effects including low heart rate, low blood pressure, changes in blood sugar levels, dizziness and weakness requiring lowering the dose or stopping the medication. If metoprolol dose is decreased based on the results of your genetic testing this could potentially increase your risk for higher heart rate, increased blood pressure and higher risk for atrial fibrillation potentially requiring an increase in metoprolol dose or a use of additional medications to control your heart rate, blood pressure, and atrial fibrillation.

Confidentiality Risk: There is a risk of breach of confidentiality; however, we take steps to decrease this risk. Your research records will be stored in locked areas within VUMC. Research databases will only be accessible by members of the study team.

Genetic Testing: The risks of learning genetic test results may include emotional upset or insurance or job discrimination. The PREDICT test used in the current research is for drug metabolism only. This minimizes the risk of discrimination.

Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that comes from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Your sample will be used to make DNA that will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study: You may or may not benefit from participation in this study. The study doctors will learn about metoprolol dosing using genetic test results. This may benefit future surgery patients.

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Procedures to be followed:
After you have signed this consent, the study team will draw about a teaspoon of blood for the PREDICT test to be run in the VUMC lab. The PREDICT test results will tell the study team how the cells in your body react to drugs such as metoprolol. Your metoprolol dosing will be based on these test results.

Your PREDICT test results will become part of your permanent medical record at VUMC and can be used as part of your regular medical care.

Payments for your time spent taking part in this study or expenses:
You will not be paid to take part in this study; however, the PREDICT panel testing will be provided at no cost to you.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

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Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Miklos Kertai at (615) 322-4650.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:

- The study doctor does not feel it is good for you to continue
- You are allergic to or cannot take metoprolol
- You withdraw consent
- The study stops

If you are taken out of the study, you will be told the reason.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
Research records will be stored in locked offices within VUMC or in password protected databases available only to the study team.

This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

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Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
There are no plans to provide you with study results.

Authorization to Use/Disclose Protected Health Information

What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

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Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title