RESEARCH CONSENT
Date Approved: May 15, 2019
Inova IRB: Joanne Muratori, IRB Coordinator
IRB File #18-3002

Informed Consent for a Research Study

Study Title:	A Pilot Study Comparing the Effectiveness of an Opioid-Sparing Analgesic Regimen and an Opioid Based Regimen on Post- Operative Pain Control in Cardiac Surgery Patients (INOVA OPIOID)
Principal Investigator:	Ramesh Singh MD
Site of Investigation:	Inova Heart and Vascular Institute (IHVI) 3300 Gallows Road Falls Church, Virginia 22042
Study Related Contact Information:	Patricia Saulino RN BSN MPA Senior Research Coordinator Cardiac Surgery and Critical Care Research IHVI patricia.saulino@inova.org 703-776-4711

Introduction
You may be eligible to take part in a research study. This research consent form gives you important information about the study. It explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, choices for participation and your rights as a research participant.

Please take your time to review this information carefully. You may also wish to talk to others (for example, your family, friends, or other doctors) about your participation. The decision to participate is yours. You may leave the study at any time without losing any benefits you would have normally received. If you decide to take part in the study, you will be asked to sign your name and the date at the end of this form. We will give you a copy of the form so that you can refer to it while you are involved in this research study. We encourage you to ask questions now and at any time in the future.

What if I am already participating in another study?
Are you already participating in any other research studies? Yes ☐ No ☐
If yes, please state which study (ies) _____

While participating in this study, you may not take part in any other research study without approval from the principal investigator.

Why is this study being done?
The purpose of this study is to avoid the use of opioid based pain medications. Opioid medications can cause serious side effects which can include but are not limited to ileus, which is a blockage most commonly in the lower intestine but can occur anywhere along the intestinal tract. Ileus is considered an emergency and can require surgery. Other side effects associated with opioids are sedation or extra sleepiness that can lead to not being able to take deep breaths

which can result in a longer time before your standard of care surgical breathing tube can be removed, or may cause post- operative pneumonia due to lack of taking deep breaths. It is well known that opioids also have the potential to cause addiction and long term use can even increase a patient's sensitivity to pain.

Two groups will participate in this study after being randomly assigned. One group will receive the opioids that are currently given to patients as the standard of care for post- operative cardiac surgery pain. The second group or the study group will receive oral (by mouth) gabapentin and intravenous (IV) acetaminophen. Gabapentin is a medication that is usually used to control seizures. Gabapentin affects certain nerves and chemicals in the body that are involved in seizures. But research has been done that has found that it is also effective in the treatment of nerve pain and it is frequently prescribed to treat nerve pain. While nerve pain is not the only reason for cardiac surgery pain it is a strong component of this type of pain.

Intravenous acetaminophen is a non-steroidal anti- inflammatory medication and also a non-opioid analgesic. Inflammation is the body's response to tissue injury and it may cause heat, redness, swelling, and pain both inside your body where it cannot be seen and outside your body at the site of the surgical incision. An analgesic is a drug known to relieve pain. Both anti-inflammatory and analgesic medications are used to treat pain. While the exact way acetaminophen reduces pain is not known, it is known that the medication acts on the central nervous system in many different ways.

If chosen for the study group you will receive gabapentin by mouth and IV acetaminophen on a regular schedule as opposed to opioids which are given based on the patient's report of their pain scores. **Opioid medication will be available for breakthrough pain in the study group if you do not feel that you are experiencing acceptable pain relief using the gabapentin and acetaminophen alone.**

This research is being done because opioids cause harmful side effects as well as addiction. With millions of people currently addicted to opioids, addiction has become a national crisis. Many hospitals, healthcare providers and even the United States government are dedicated to research and programs that are aimed at providing acceptable pain relief and avoiding opioid based medications.

How many people will take part in this study?
About 20 people are expected to take part in this study.

What other choices do I have if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- you may choose not to participate in the study and receive opioid medication as needed after your surgery
- you may choose to take part in a different study, if one is available
- or you could decide not to be treated

How long will I be in this study?
If you decide to participate, you will be in this study for 72 hours post cardiac surgery, or until 3 days after your surgery.

What will happen if I take part in this research study?
Most medications you will have are part of the usual approach for your cardiac surgery and will be given even if you do not join the study. However, the medications that are part of the study, oral (by mouth) gabapentin and IV acetaminophen are different from the opioids that are usually given as part of your surgery. You will still be given opioid medication if you decide you are not getting enough relief from the study medications.

If you agree to take part in the study, you will be "randomized" into one of the study groups. Randomization means that you are put into a group by chance, like flipping a coin. Neither you, nor your doctor will choose what group you will be in. You will have a 1 in 2 chance of being in any group.

Study groups:
This study has 2 study groups.

1. Patients receiving opioids after cardiac surgery which is the current standard of care.
2. Patients not receiving opioids but receiving the pain relief alternatives of oral gabapentin and IV acetaminophen with opioid medication for breakthrough pain if necessary.

If you are randomized to the group that will receive non opioid medications, you will be given IV acetaminophen and oral gabapentin immediately after your procedure and then IV acetaminophen every six hours and oral gabapentin every 8 hours. Both medications will be scheduled and given to you regularly for 40-42 hours (unlike opiates that must be requested for every dose). You will be asked to report your pain score every 12 hours. Opioid medications will be available to you for breakthrough pain. If you should need an opioid medication, you will report your pain score to the nurse or the doctor and you will be given the opiate prescribed for the level of pain you reported. You will also report your pain score 1 hour after administration.

If you are randomized to the standard of care group, you will be given opiates that will vary based on the pain score you report to your nurse or your doctor. You will report your pain score before you receive the opioid medication and 1 hour after. For the study purposes, you will be asked to report your pain score every 12 hours.

What side effects or risks can I expect from taking part in this study?
If you choose to take part in this study, there is a risk that you may:

- The most important non-medical risk is the disclosure of your protected health information (PHI). PHI is any health information that is collected about you, including your history and new information collected during this study. You will have an opportunity to review the ways in which your PHI may be used and disclosed in the separate HIPAA Authorization for Research form.

There is also a risk that you could have side effects.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

The table below shows the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.
Risks and side effects related to **Oral Gabapentin**[1] include those which are:

Oral Gabapentin:

Side Effect	**Common**, Some may be serious In 100 people receiving Oral Gabapentin, more than 20 people may have:	**Occasional**, Some may be serious In 100 people receiving Oral Gabapentin, 4-20 people may have:	**Rare and Serious** In 100 people receiving Oral Gabapentin, 3 or fewer people may have:
	Dizziness	Weakness/fatigue	Headache
	Drowsiness	Infection	Constipation
		Extremity swelling	Nausea
		Diarrhea	Vomiting
		Dry mouth	Flatulence
			Weight gain
			High blood sugar Incoordination Pharyngitis Rash Blurred vision

Risks and side effects related to **Intravenous Acetaminophen**[2] include those which are:

IV Acetaminophen:

Side Effect	**Common**, Some may be serious In 100 people receiving IV Acetaminophen, more than 20 people may have:	**Occasional**, Some may be serious In 100 people receiving IV Acetaminophen, 4-20 people may have:	**Rare and Serious** In 100 people receiving IV Acetaminophen, 3 or fewer people may have:
	Nausea	Vomiting	Infusion site pain
		Headache	Fatigue
		Insomnia	Extremity swelling
			Liver enzyme abnormalities
			Low potassium
			Muscle spasm
			Anxiety High and low blood pressure

[1] https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020235s041,020882s028,021129s027lbl.pdf
[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022450lbl.pdf

You should talk to your study doctor about any side effects that you have while taking part in the study.

Are there reproductive risks while on this study?
You should not get pregnant, breastfeed, or father a baby while on this study because we cannot predict the effects on an unborn baby.

A pregnancy test will be performed on all women who may be pregnant before taking part in this study. This includes all women except those whose menstrual periods have not occurred for more than one year after menopause (change of life) or those who have had sterilization surgery (tubes tied) or a hysterectomy (removal of the uterus or womb). Pregnant women may not take part in this research study.

If you decide to take part in this study, you must agree to protect yourself or your partner from becoming pregnant. If you or your partner becomes pregnant when either parent is taking the drug, birth defects may occur. If you are a female and think that you might be pregnant, you must immediately tell your study doctor. It may be harmful for a child to breastfeed from a woman taking a study drug. Because of this, female participants must not breastfeed during the study and for (insert number of days/weeks) after the study ends.

If you become pregnant while taking study drug, you will agree to release your health records while pregnant. You will also agree to release your child's health records for the first year of his/her life.

Acceptable methods of contraception (birth control) while taking part in this study are:

1. Total Abstinence (no sexual intercourse), absence of menstrual periods in women for more than one year after menopause (change of life), and sterilization surgery, including tubal ligation (tubes tied) or hysterectomy (removal of the uterus or womb) in women or a vasectomy in men.
2. Oral contraceptives (birth control pills), intrauterine device (IUD), implantable or injectable contraceptives (Norplant or Depo-Provera), contraceptive patch, vaginal ring or use of condom with spermicide. These methods must be used exactly as directed.

The following methods of contraception are <u>not</u> acceptable to prevent pregnancy during study participation: diaphragm, cervical cap, vaginal sponge, and "female condom".

Are there benefits to taking part in this study?
Taking part in this study may or may not make your health better. We hope the information learned from this study will benefit others in the future.

Can I stop being in the study?
Yes. You can choose not to be in the study. You can decide to stop at any time. It is important to tell the study doctor if you are thinking about stopping or leaving the study.

Your participation can also be stopped without your approval by any of the following:

- the study doctor
- the Institutional Review Board (IRB – hospital committee that reviews and approves research),

The study doctor may decide to take you off this study for any of the following reasons:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules

What are the costs of taking part in this study?
You will not be responsible for the cost of study medications (acetaminophen and gabapentin) used as are a part of the study.

You and/or your health plan/ insurance company will need to pay for some or all of the costs of your cardiac surgery while in this study. Check with your health plan or insurance company to find out the total costs to you for treatment while on this study. You may be responsible for any co-payments and deductibles that are standard for your insurance charges

Will I be paid for taking part in this study?
You will not be paid for taking part in this study.

What if I am injured because I took part in this study?

In the event that you believe you have been injured because of taking part in this study, it is important that you call your study doctor. You can call Dr. Ramesh Singh, principal investigator, at 703- 280-5858 and he will review the matter with you. Inova Health System and the study doctor do not provide funds or free medical treatment for injuries that result from taking part in this study. Medical treatment is available to you if you are injured as a result of taking part in this study.
You and/or your health plan will be billed for the cost of this care. If your insurance does not pay for your care, or pays only a portion of the cost of such care, you may be billed for any unpaid amounts.

You should not expect anyone to pay you for pain, worry, lost income, or non-medical care costs that occur from taking part in this research study. No funds have been set aside, by Inova Health System and Inova Cardiac and Thoracic Surgery to repay you in case of injury.

You are not waiving any legal claims or rights because of your participation in this study.

Will my medical information be kept private?
We will keep your records private to the amount allowed by law. Research records are stored and kept according to legal requirements. You will not be identified in any reports or publications about this study. However, certain people and groups will have access to your research and medical records. The Inova Health System Institutional Review Board (IRB) and federal and state agencies that have authority over the study may look at your research records. Members of the study staff will also have access to your research records. Additional groups, explained in the HIPAA Authorization for Research form may also have access to these records.

You will be assigned a Patient Identification Number (PIN), e.g. 001, and this will be used to identify your study information. This PIN will be correlated with your name and medical information in a separate locked location.

What are my rights if I take part in this study?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights. A member of your research team will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

If you would like more information about your rights as a participant in a research study, contact: Inova Health System Institutional Review Board (IRB) at 571-472-3458. The Inova Health System IRB may contact you by mail or telephone to find out if you were satisfied with your study participation.

Who can answer my questions about the study?
You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor Ramesh Singh MD at703- 280-5858 or the study coordinator Patricia Saulino RN at 703-776-4711.

Where can I get more information?

A description of this clinical trial will be available on 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.

Signature

You, the undersigned have been informed about this study's purpose, procedures, possible benefits and risks, and you have read this consent and received a copy of this consent, including the separate HIPAA authorization form to use and disclose protected health information. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time. You voluntarily agree to give your consent to participate in this research study.

You are free to withdraw from the study at any time and you do not have to say why you no longer wish to participate. You will notify the Principal Investigator if you are leaving the study because of any side effects you might experience. This withdrawal will not in any way affect your future treatment or medical management. You agree to cooperate with the Principal Investigator and the research staff and to inform them immediately if you experience any unexpected or unusual symptoms.

_____	_____	_____
Signature of Subject	Printed Name of Subject	Date

_____ _____ _____

As a member of the research team, I have explained the purpose, the procedures, the benefits and risks that are involved in this research study. Any questions that have been raised have been answered to the individual's satisfaction.

_____	_____	_____
Signature of Person Obtaining Consent	Printed Name	Date

_____	_____	_____
Signature of Witness	Printed Name of Witness	Date