[insert hospital/institution logo]

Informed Consent Form for Participation in a Research Study

Study Title:	Rivaroxaban plus Acetylsalicylic Acid Versus Standard of Care for Arterial and Venous Cardiovascular Prevention After Hip Fracture Surgery in Patients with Myocardial Injury: a Pilot Randomized Trial *(HIPSTER-Pilot)*
Study Doctor:	Dr. _____; Department of _____ (Phone: _____) *Insert name, department and telephone or page number*
Sponsor/Funder:	Canadian Venous Thromboembolism Research Network

INTRODUCTION

You are invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in this trial because you have received urgent surgery for a broken hip, and there is evidence of a strain on your heart muscle. Your treating physician has determined that you require preventive measures for possible blood clots following your surgery. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

Please take your time in making your decision. You may find it helpful to discuss it with your friends and family. The study staff will tell you about the study timelines for making your decision.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study

IS THERE A CONFLICT OF INTEREST?

Describe any conflict of interest that exists or may appear to exist as it relates to any of the investigators, study staff or member of their immediate family. A conflict of interest exists if there is a potential benefit to the investigator(s), study staff or member of their immediate family beyond the professional benefit from academic achievement or presentation of the results. Examples include, but are not limited to, speaker's fees, travel assistance, consultant fees, honoraria, gifts, and intellectual property rights such as patents. A declaration of conflict of interest should include the identity of the person with the conflict of interest, the type of incentive or inducement, and its source. See examples below.

The identify individual, e.g., study doctor, insert name, is receiving personal financial payment from Identify source of funds e.g., the study Sponsor for include reason for payment e.g., providing advice on the design of the study. You may request details about this payment.

or

There are no conflicts of interest to declare related to this study.

or

The insert recipient of funding e.g., hospital is receiving financial payment from the Sponsor/Funder to cover the cost of conducting this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Each participating site must ensure that the standard or usual treatment described in below matches the standard of care at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.

The occurrence of hip fractures is estimated to increase, largely due to an aging global population. Patients who undergo hip surgeries are at risk of experiencing blood clot complications involving their veins and/or arteries following their operations. This includes events like a blood clot in the veins (venous thromboembolism, VTE) or heart attacks.

Currently, to prevent these events from occurring, several types of preventative blood thinning medications are routinely used. We refer to this as the standard of care. However, there is not much information available comparing these medications in terms of how well they work and their side effects.

Therefore, the study investigators are conducting a research study to compare the current standard of care (usually a low dose of a blood thinner) with a new regimen (referred to as the **COMPASS regimen**) in preventing venous and arterial blood clots for patients undergoing surgery for a broken hip. The trial asks if the COMPASS regimen is a safe and effective option for preventing blood clots in patients after surgery for a broken hip. The COMPASS regimen, which is a combination of the two medications (a blood thinning pill, rivaroxaban) and acetylsalicylic acid (ASA, or aspirin), has been shown to reduce blood clots in other medical situations. Further, the COMPASS regimen may provide benefits like cost savings and improved quality of life due to the lack of need for injections (which are how some of the current blood thinning medications are given).

Health Canada, the regulatory body that oversees the use of drugs in Canada, has not approved the use of rivaroxaban and ASA in combination after surgery for hip fracture. Health Canada has allowed rivaroxaban and ASA in combination after surgery for hip fracture to be used in this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study, called a pilot study or a feasibility study, is to test the study plan and to find out whether enough participants will join a larger study and accept the study procedures. This type of study involves a small number of participants and so it is not expected to prove safety or effectiveness. The results may be used as a guide for larger studies, although there is no guarantee that they will be conducted. Participation in a pilot study does not mean that you will be eligible to participate in a future larger study.

Each prophylactic (preventative) medication has its own benefits and risks, and no one is sure which regimen is better to use than the other for certain situations. Blood thinning medications have been used alone as standard of care in the prevention of venous blood clots in people at high risk across different settings. However, arterial blood clots can also occur after hip surgery, particularly in patients with signs of heart strain. ASA in combination with a low dose blood thinner may offer benefits in preventing both arterial and venous blood clots. The dose of blood thinner is lower than what is normally used to prevent blood clots after surgery, but in this study, it is being given along with ASA.

Our team is planning to investigate how the COMPASS regimen compares to standard of care in terms of effectiveness and side effects when used to prevent blood clots for patients undergoing surgery for a broken hip.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in the study. If you do not take part in the study, you will receive the usual treatment. Participation in the study is purely voluntary, and you can withdraw from the study at any time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 100 people will take part in this study, from research sites located in Ontario, Canada and Italy.

This study should take about 12-24 months to complete, and the results should be known in about 2 years.

WHAT WILL HAPPEN DURING THIS STUDY?

Assignment to a group:

- If you decide to participate then you will be randomly assigned by a computer program, with an equal chance (like flipping a coin) of receiving either one of the two preventive strategies. After randomisation, you will be told which group you are in.

If you were taking aspirin before you broke your hip, it will be or would have been stopped before your surgery. If you are assigned to the standard of care group (control group), it will be up to your medical team to decide when to start it again. If you are assigned to the COMPASS group, you will re-start taking your aspirin 3-5 days after your surgery.

As part of your routine hospital care, you will have laboratory (e.g., blood tests) and radiological tests (e.g., X-rays) performed. We will be collecting this information along with reviewing your doctor’s notes regarding your surgery and recovery from your medical records for the study period, including the follow-up period (up to 90 days after the randomization).

After providing consent, there will be two additional follow-up telephone calls with the study staff that will occur 30- and 90-days after the randomization. The study staff will contact you to ask whether you have had any new medical problems. This will take 10 to 30 minutes, depending on

how many problems you have had and the amount of information the study team will need to collect.

No other aspect of your care will be modified.

WHAT IS THE STUDY INTERVENTION?

If you agree to take part in this study, you will be randomized into one of the two groups:

Group 1 (usual standard of care): If you are assigned to this group, you will receive standard of care prophylaxis regimen prescribed by your doctors. You will receive the regimen for up to 30 days, based on whatever the usual duration is at your hospital. The standard of care prescribed could include, but are not limited to, any of the following regimens listed below:

- Low-molecular-weight heparin (LMWH) as a needle under the skin:
  - Enoxaparin: 40 mg given once daily or 30 mg twice daily,
  - Dalteparin: 5000 IU once daily (or alternative dosing based on institutional protocol)
  - Tinzaparin: 4500 IU once daily
- Fondaparinux: 2.5 mg once daily as a needle under the skin
- Direct oral anticoagulant (DOAC) (a pill) started after surgery or after a period of LMWH.
  - Rivaroxaban 10 mg once daily
  - Apixaban 2.5 mg twice daily

OR

Group 2 (intervention): If you are assigned to this group, you will receive the COMPASS regimen as your prophylactic treatment. The COMPASS regimen consists of two types of tablets: rivaroxaban 2.5 mg twice daily and acetylsalicylic acid (ASA or aspirin) 75-100 mg once daily, combined. You will receive this treatment for 90 days, which will be started between three and five days after your surgery. Your physician could prescribe any blood thinner for a maximum of four post-surgery days in the meantime (i.e., until you start the COMPASS regimen).

Other aspects of your medical care regarding your broken hip will not be changed.

WHAT ARE THE STUDY PROCEDURES?

Follow-up:

- All participants will be assessed at 30- and 90-days post-randomization via telephone follow-up. You will be asked about any new medical problems you have had, including heart attack stroke, or blood clots. If you haven't had any new problems, the follow-up will take approximately 10 minutes, while it may take up to 30 minutes if the study team needs to collect the details of multiple problems. Your medical records will also be reviewed by the study team to check for information that is relevant to the study.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical condition.
- Tell the study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these.
- Take the prescribed prophylactic regimen, based on the group that you were assigned to (standard of care regimen or COMPASS regimen).
- Participate in the telephone follow-up at days 30 and 90 post-randomization.
- Ask the study team or the study doctor if you have any questions or concerns.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study intervention will last for about 90 days from the day of the group assignment (i.e., randomization).

After you consent to participate, you will be assigned to one of the two groups mentioned above between 3- and 5-days post-surgery. You will be followed up by the research team at 30- and 90-days post-randomization.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff. You will have the option to stop the study drug but continue the follow-up, or to also stop the follow-up.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study. No information will be collected after you withdraw your permission.

If you withdraw, information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no information will be collected or sent to the sponsor after you withdraw your permission.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- You are unable to complete all required study procedures.
- New information shows that the study intervention is no longer in your best interest.
- The study doctor no longer feels this is the best option for you.
- The Sponsor decides to stop the study.
- The research ethics board withdraws permission for this study to continue.

If this happens, it may mean that you would not receive the study procedures for the full period described in this consent form.

If you are removed from this study, the study doctor will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor.

You are receiving blood thinners to prevent clots after your hip surgery. The main risk associated with the use of blood thinners is increased risk of bleeding, which may vary in severity from mild to severe. In the three months after the surgery, patients receiving standard of care are at 7% risk of developing major bleeding events, 1% risk of developing blood clots in the veins (venous thromboembolism, VTE), 10% risk of experiencing a heart attack, 14% risk of dying from issues related to blood clots (i.e., vascular mortality). and 30% risk of experiencing an elevation in blood markers suggesting heart strain, correlated with poor outcomes.

A previous study tested the COMPASS regimen (a combination of low-dose rivaroxaban and aspirin) in people with stable heart condition, which is different from the patient population in this study. That study lasted about two years and compared the combination to a similar dose of rivaroxaban used after surgery. It showed that patients who received the COMPASS regimen had a 16% relative risk reduction in heart attack, stroke, or cardiovascular death, with a 13% relative risk increase in major bleeding. Although the study suggested a trend towards a decrease in venous blood clots, the COMPASS regimen has never been adequately tested for prevention of venous blood clots. We are not sure if the same results will be seen in patients following surgery for a broken hip, such as yourself.

There is a chance that the COMPASS regimen may be less effective at preventing blood clots or more likely to cause bleeding than the standard of care.

- If you experience bleeding, a known risk of blood thinners, your treating team will manage it according to the standard of care. If necessary and possible, the blood thinners (whether part of the study regimen or the standard of care) will be stopped. If your doctors think it is safe to do so, the medication(s) might be restarted.
- You will continue to be followed up for outcomes by the study team, unless you choose to withdraw from the study entirely.

Although the study medications have been used in many people, there is a small possibility of risks that we do not know about, and which have not been recorded in medical books or seen in study participants to date. The study doctor will watch you closely to see if you have side effects. Any complications will be quickly identified and managed.

- If the study medication causes any unexpected side effects, the study team will keep track of them and follow up with you.

WHAT ARE THE REPRODUCTIVE RISKS?

The effects that COMPASS regimen (rivaroxaban 2.5 mg twice daily and acetylsalicylic acid (ASA or aspirin) 75-100 mg once daily, combined) may have on an unborn baby (fetus) are unknown. You must not become pregnant while taking the COMPASS regimen. The study doctor can discuss family planning with you to ensure that you do not become pregnant during the study, if it is relevant to you.

Please inform the study team if you have become pregnant while taking the study medication.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

There is no guarantee that you will receive any benefit to you in taking part in this study. By taking part in this study, you will contribute information about the study regimen that may benefit other patients or you in the future.

HOW WILL PARITICIPANT INFORMATION BE KEPT CONFIDENTIAL?

***Note**: If there will be disclosure of personal identifiers, i.e., disclosed on any research-related information/documents including samples or scans, or as part of the unique identifier, these disclosures must be justified in the REB application and approved. Please ensure that you are aware of institutional and REB policies with respect to the disclosure of personal identifiers.*

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document. Information that is collected about you will be kept for a period of 15 years as per Health Canada.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- The research ethics board who oversees the ethical conduct of this study in Ontario.
- Study Sponsor (Dr. Federico Germini) or one of his representatives from McMaster University
- Government regulatory authorities (e.g. Health Canada)
- This institution and affiliated sites, to oversee the conduct of research at this location.

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study. Your name, address, email, or other information that may directly identify you will not be used. The records received by these organizations may contain your initials and your study identification number.

Communication via e-mail is not absolutely secure. We do not recommend that you communicate sensitive personal information via e-mail.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be analyzed and published/presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of the study findings.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

WILL FAMILY DOCTORS/HEALTHCARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/healthcare provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on https://clinicaltrials.gov/ 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 website at any time.

WHAT IS THE COST TO PARTICIPANTS?

Participation in this study will not involve any additional costs to you or your private health care insurance. The cost of running the study will be paid by a grant provided by Canadian Venous Thromboembolism Research Network.

Standard of care medication will be covered by Ontario Drug Benefits, if you are eligible, while the intervention (i.e., the COMPASS regimen – rivaroxaban and ASA) will be supplied by the study team. If you are not eligible to be covered by Ontario Drug Benefits, standard of care medication may be covered by your private insurance, if applicable, or be paid out of pocket. Therefore, there would be no extra expense for participating in the study.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

Each participating site must ensure that the information below matches the compensation/reimbursement provided at that site. Site specific differences must be reflected in the Centre Initial Application and the site-specific consent form.

You will not be paid for taking part in this study. In case of research-related side effects or injury, medical care will be provided by your doctor or you will be referred for appropriate medical care.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. The results of this study will be available on the clinical trial registry (see the “Will information about this study be available online” section for more details).

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form, you do not give up any of your legal rights against the study doctor or involved institutions for compensation, nor does this form relieve the study doctor or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to the research coordinator at this institution. That person is:

_____	_____
Research Coordinator	Telephone

Insert local RC name and contact information.

If you have any questions about your rights as a participant or about ethical issues related to this study, you can talk to someone who is not involved in the study at all. Please contact the Office of the chair of the Hamilton Integrated Research Ethics Board at 905-521-2100 ext. 42013.

SIGNATURES

- All of my questions have been answered,
- I understand the information within this informed consent form,
- I allow access to medical records and related personal health information as explained in this consent form,
- I do not give up any legal rights by signing this consent form,
- I agree to take part in this study.

Signature of Participant	PRINTED NAME	Date
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:

If the participant is assisted during the consent process, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

PRINT NAME of Interpreter	Signature	Date

Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to the participant, and any questions have been answered.

[insert hospital/institution logo]

_____	_____	_____
PRINT NAME of witness	Signature	Date

_____
Relationship to Participant

Please note: More information regarding the assistance provided during the consent process should be noted in the medical record for the participant if applicable, noting the role or relationship of the impartial witness.

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