CENTRE DE RECHERCHE | CHUS

RESEARCH INFORMATION AND CONSENT FORM

Study Title: The OVATION-65- Impact of permissive hypotension on end-organ damage in the elderly

Study Number and Date: MP-31-2018-1789

Funding Agencies: Centre de recherche du CHUS
Université de Sherbrooke

Principal Investigator: Dr. François Lamontagne, Intensivist

Co-Investigators: Dr. Frédérick D'Aragon, Intensivist,
Dr. Charles St-Arnaud, Intensivist
Dr. Michaël Mayette, Intensivist,

FOR INFORMATION

Monday through Friday, from 8 am and 4 pm, you can reach:

Dr. François Lamontagne, Intensivist	Tel.: 819-346-1110, ext. 74974
Élaine Carbonneau, Research Coordinator	Tel.: 819-346-1110, ext. 16208
Marie-Hélène Masse, Research Coordinator	Tel.: 819-346-1110, ext. 14173
Marilène Ladouceur, Research Assistant	Tel.: 819-346-1110, ext. 14169

or dial "0" and ask the operator to call them on pager # 7125.

We are seeking your participation (or that of your family member) in a research study because you (or your family member) have been admitted to an intensive care unit and will need medication administered into your veins to raise your blood pressure. However, before you agree to participate, please take the time to read, understand and carefully consider the following information. If you agree to take part in this research study, you will be asked to sign the consent form at the end of this document and we will give you a signed copy for your own records.

This Information and Consent Form explains the goals, procedures, risks and inconveniences, and benefits of the study as well as providing the names of the people to reach if needed. This document may contain information or words that you do not understand. Please ask the study investigator or members of the study staff to answer your questions and explain any word or information you do not understand.

NATURE AND GOALS OF THE RESEARCH STUDY

This study aims to determine whether the target blood pressure used to adjust the dosage of the blood-pressure-increasing medication changes the evolution of participants treated in the Intensive Care Unit (ICU). Vasopressors are drugs that are given intravenously to increase the blood pressure of patients with diseases causing dangerous pressure drops that can be harmful to the organs of the body. When a doctor

prescribes a vasopressor, he asks that the dose be adjusted to achieve a specific blood pressure. However, although vasopressors have been used for nearly a century, we still do not know whether it is preferable to try and normalize the blood pressure of our patients (which requires high doses of vasopressors) or tolerate a lower pressure (which is not normal, but requires smaller doses of drugs). The current practice is quite variable, some doctors preferring to increase the blood pressure, others preferring to restrict doses of these powerful drugs and tolerate a lower blood pressure (hypotension).

The goal of this study is to determine if tolerating a lower mean blood pressure (permissive hypotension) vs. usual blood pressure targets in hypotensive patients over 65 years of age can reduce the risk of harm associated with more aggressive vasopressor therapy. The specific objectives are to evaluate: the effect of permissive hypotension on your health status after 6 months , the effects on markers of organ injury, including the heart, brain, kidneys, liver, intestine, and skeletal muscles as well as the effects on your immune system. We wish to recruit around 100 participants at the *CIUSSS de l'Estrie - CHUS* to be among the 200 participants needed for this study that will be carried out in several hospitals.

Your physician has determined that you are eligible to participate in our study and you have been selected as a participant because you are being (or will soon be) treated in the ICU and because you were prescribed vasopressor drugs.

RESEARCH STUDY PROCEDURES

If you agree to participate in this study, you (or your family member) will be assigned to one of the following two groups: The first group includes participants who are being given vasopressors for an average blood pressure of 60-65 mmHg (limiting the amount of vasopressors given); the second group includes participants who are receiving vasopressors following usual care. Your assignment to one of these two groups was determined randomly by a computer that will not retain information about you. The odds of being assigned to either group were 50% (1 in 2 chances or half-and-half). The treating team will be aware of which group you have been assigned to.

As a study participant, you will receive vasopressors to maintain your average blood pressure at the level of your assigned group. These pressure targets will remain the same throughout your treatment with this type of medication (vasopressors) until you are discharged from hospital or up to 28 days from the beginning of your participation, whichever event comes first. Also, on days 1, 3 and 7 of participation (or when you are discharged from the intensive care unit), your nurse will collect 30 ml of blood (6 teaspoons) as well as urine samples while taking the blood samples required for your medical follow-up. We will collect a little more volume than what is needed in order to compensate for unexpected losses that may arise during laboratory testing. These samples will enable us to measure certain biomarkers in your blood and in your urine that help assess the function of your heart, kidneys, muscles, brain and liver as well as your immune system. These biomarkers are already known to be useful in clinical studies and are not genetic biomarkers. During your hospital stay, we will monitor your progress to see if your organs are functioning well, if you develop other health problems and how long you will stay in the ICU and hospital. Your medical chart will be reviewed, by the investigator and the research team as long as you remain in the study. Blood test results and procedures present in your medical record will be collected for the study.

After you are discharged from the hospital, you will be contacted by phone 6 monthss after the start of your participation in the study. Your contact information will be provided to the coordinating research team.

FUTURE ANALYSES

Once the biomarker analyses have been performed as part of this study, it is possible that part of your samples may be unused. We wish to use the remainder of your samples (blood and urine) in order to answer additional questions concerning the impact of vasopressors on blood pressure targets that may arise in future. For example, we could measure a new, as yet undefined, biomarker. Only the remainder of your samples will be used and no other additional sample will be collected. At the end of the study, if some of the samples remain unused, they will be destroyed unless you agree to biobanking. A separate consent form will be presented for biobanking.

RISKS ASSOCIATED WITH PARTICIPATION IN THIS RESEARCH STUDY

Vasopressors used in this study and that you have received or may still be receiving, are approved in Canada and commonly used in the ICUs of all hospitals. The blood pressure targets we aim for in this study are also part of current medical practices.

Since your health condition required treatment with vasopressors, and continues to require treatment at this time, to our knowledge, you are exposed to the same risks, whether or not you participate in this study.

INCONVENIENCES ASSOCIATED WITH PARTICIPATION IN THE STUDY

Other than the risks described above, you (or your family member) shouldn't experience any other inconveniences.

BENEFITS ASSOCIATED WITH YOUR PARTICIPATION IN THE RESEARCH STUDY

You (or your family member) will not personally benefit from your participation in this research study. However, the findings from this study may help increase our knowledge of pressure targets, vasopressors and biomarkers. The information obtained through this study could be useful to other patients in the future.

ALTERNATIVES TO YOUR PARTICIPATION IN THIS RESEARCH STUDY

You (or to your family member) do not have to participate in this research study to be treated for your disease.

VOLUNTARY PARTICIPATION AND THE RIGHT TO WITHDRAW

Your participation in this research study is voluntary. Therefore, you may refuse to participate. You can also withdraw from the study at any time, without providing a reason, by informing the study investigator or one of his assistants.

Your decision not to participate in the study or to withdraw from it, will have no impact on the quality of care and services you (or your family member) are entitled to or on your relationship with the investigator and other stakeholders.

The study investigator, the funding agency or the Research Ethics Board may put an end your participation in the study without your consent. This may happen if new scientific developments show that participation is no longer in your interest; if the study investigator believes it is in your best interest; or if there are administrative reasons to terminate the study.

If you withdraw or are withdrawn from the study, the information and material already collected during the course of the study will be stored, analyzed or used to ensure the integrity of the study.

Any new study findings that could influence your decision to remain in the research study will be shared with you as soon as possible.

CONFIDENTIALITY

While you take part in this research study, the study investigator and study staff will collect and record information about you in a study file. Only the information needed to meet the scientific goals of the study will be collected.

This information could include data taken from your medical record concerning your past and present medical history, your lifestyle and the test results, exams and procedures you will undergo during the study.

All the information collected during the study will remain strictly confidential to the extent provided by law. To protect your identity and privacy, you will be identified by an alphanumeric code. The key linking your identity and your research file will be kept in a safe place by the study investigator.

To ensure your safety, a mention of your participation in this research project will be included in your medical file. Therefore, any person or company to whom you will give access to your medical file will have access to this information.

Your full name and your phone number will be transmitted to a qualified person of the coordinating center of the study in order to allow this person to contact you in 6 months by phone. This personal information will allow a direct identification. This information will be kept in security and confidentiality will be preserved by the qualified person and destroyed at the end of the follow-up.

Study results will be stored by the study investigator for 25 years.

Study results may be published in medical journals or discussed at scientific meetings, but it will be impossible to identify participants.

For monitoring and control purposes, your study file and medical records may be examined by a representative of the Research Ethics Board or of the institution or by a person mandated by a regulatory authority. All of these individuals and organizations adhere to confidentiality policies.

You have the right to consult your study file at any time in order to verify the information gathered and to have it corrected, if necessary, for as long as this information is available to the study investigator or the institution. However, some of this information may be made available to you only once the study has ended, in order to protect the scientific integrity of the study.

COMPENSATION

You (or your family member) will not receive any compensation for expenses and inconveniences incurred due to your participation in this research study.

SHOULD YOU SUFFER ANY HARM

Should you suffer any harm due to your participation in this research study, you will be provided with all the necessary care and services, at no cost to you.

By agreeing to take part in this study, you are not waiving any of your legal rights nor discharging the study investigators, the sponsor or the institution where this research study is being conducted of their civil liability and professional responsibilities.

FUNDING OF THE RESEARCH STUDY

The study investigator has received funding from the grant agency to carry out this study.

CONTACT PERSONS

If you have any questions regarding your participation in this research study, please refer to the box on page 1.

If you have any questions regarding your rights as a participant in this study, if you have any comments or you wish to file a complaint, you may contact the *Bureau des plaintes et de la qualité des services of the CIUSSS de l'Estrie-CHUS* at the following number: 1-866-917-7903.

MONITORING OF ETHICAL ASPECTS OF THE STUDY

The *Comité d'éthique de la recherche du CIUSSS de l'Estrie - CHUS* has approved this study and is responsible for monitoring it at all participating institutions throughout Québec's health and social service network.

If you wish to reach a member of the Research Ethics Board (REB), please contact the *Service de soutien à l'éthique de la recherche du CIUSSS de l'Estrie - CHUS* at the following number: 819-346-1110, ext. 12856.

CONSENT

I declare that I have read this Information and Consent Form. I declare that the research study has been explained to me, that my questions were answered to my satisfaction and that I was given sufficient time for consideration and to make a decision. Upon reflection, I agree to participate in this research study under the conditions stated therein.

I agree that the remainder of the samples may be used for additional analyses that may arise during the study (future analyses). ☐ YES ☐ NO

Name of participant *(please print)*	Signature of participant	Date

I have explained the research study and this Information and Consent Form and I have answered all of his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

CONSENT FROM LEGAL REPRESENTATIVE (SUDDEN INCAPACITY)

Because Mr./Mrs. _____ has suddenly become incapable of giving consent for the hereinafter mentioned reason, the Civil Code of Québec allows you to give consent for him/her as his/her _____ (indicate your relationship with the participant).

As soon as Mr./Mrs. _____has sufficiently recovered, he/she will be asked to sign his/her own consent form to indicate whether he/she wants to continue taking part in this study.

REASON FOR THE PARTICIPANT NOT BEING ABLE TO GIVE CONSENT

By signing this page, I confirm that I have read the information in this Consent Form. I acknowledge that the study has been explained to me, that all of my questions have been answered and that I was given enough time to make a decision. I voluntarily give my consent so that Mr./Mrs. _____ can participate in this study.

I also agree that the remainder of the samples may be used for additional analyses that may arise during the study (future analyses). ☐ YES ☐ NO

Name of legal representative *(please print)*	Signature of legal representative	Date

I have explained the research study and this Consent Form to the participant's legal representative. I have answered all of his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

CONSENT FROM THE LEGAL REPRESENTATIVE OR CAREGIVER SUPPORTING THE PARTICIPATION OF THE PERMANENTLY INCAPABLE PARTICIPANT (PERMANENT INCAPACITY)

I declare that I have read this Information and Consent Form. I declare that the research study has been explained to me, that my questions were answered to my satisfaction and that I was given sufficient time for consideration and to make a decision.

I agree that _____ can participate in this research study under the conditions stated therein. I will receive a signed and dated copy of this Information and Consent Form.

I also agree that the remainder of the samples may be used for additional analyses that may arise during the study (future analyses). ☐ YES ☐ NO

If the incapacitated participant is represented:

Name and signature of the legal representative (representative, curator or mandatary)	Date

If the incapacitated participant is not represented by a legal representative:

Name and signature of the spouse, failing which, name of next-of-kin or name of a significant person	Date

I have explained the research study and this Consent Form to the participant's legal representative. I have answered all his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

PHONE CONSENT
(For the participant who is suddenly or permanently incapacitated)

Because Mr./Mrs. _____ is incapable of giving consent for the hereinafter mentioned reason,

REASON FOR THE PARTICIPANT NOT BEING ABLE TO GIVE CONSENT

_____

I have explained the research study and this Consent Form to the participant's legal representative. I have answered all his/her questions.

The representative, Mr./Mrs._____
Name of the legal representative (representative, curator or mandatary)
Name of the spouse or next-of-kin or
Name of the significant person

has given consent by phone on _____ at _____
Date Hour

The representative also agrees that the remainder of the samples may be used for additional analyses that may arise during the study (future analyses).☐ YES ☐ NO

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

APPENDIX 1: GENETIC PHASE

(PLEASE NOTE: This part of the consent should not appear in the patient's medical file)

We invite you to participate in the genetic component of this study. This phase is optional. You may refuse this proposal and still participate in the main phase of the project.

Please note that all sections of the main consent form apply to this appendix as well.

Genetics focuses on cells in the human body that contain a type of molecule called deoxyribonucleic acid commonly referred to as "DNA". Your DNA is contained in the inherited genes that control your entire body's growth, development and functions. For instance, some genes determine the colour of your eyes or hair. DNA presents a wide array of differences or variations from one person to another. These variations may affect the risk of contracting a disease (or not) or the way individuals respond differently to a drug. The OVATION-65 project also includes a genetic sub-study focusing on the analysis of certain genes (genetics) and certain phenomena present in your environment that modify your DNA (epigenetics). These tests can be performed on the cells in your blood.

The markers of the heart, brain, kidneys, liver, intestine and skeletal muscles that we are interested in measuring as part of the OVATION-65 study as well as the molecules (receptors) that enable the vasopressors to act (beta-adrenergic receptors) on the cells of different organs are determined in part by genes. Thus, in order to better understand how to reduce organ damage related to medication (vasopressors) received during intensive care unit admissions, we propose to study the DNA as well as the variations around this DNA (called epigenetic variations) of patients included in OVATION-65. Our goal is to demonstrate that modifications in the DNA of studied markers are associated with the levels of these same blood or urine markers, which inform us on the function/involvement of the targeted organ.

If you agree to participate, we will use a portion of the samples already collected as part of the main project and an additional sample (approximately 2 teaspoons) to conduct our genetic analyses.

FUTURE ANALYSIS

Once the genetic analyses have been conducted, it is possible that a portion of the samples will remain unused. We would like to use the remainder of your samples to answer additional research questions that might arise during the course of the study. Only the remainder of your samples will be used and no other additional samples will be taken. At the end of the study, if some samples remain unused, they will be destroyed unless you agree to biobanking. Another consent form will be presented for biobanking.

SOCIO-ECONOMIC RISKS ASSOCIATED WITH PARTICIPATION IN THIS PHASE OF THE STUDY

One of the risks associated with genetic analyses is related to the disclosure of results or of your participation to third parties. Protection against genetic discrimination is not currently well defined in Canadian and Québec legislation. Thus, we cannot fully guarantee that your participation in a genetics research project will not have an impact on your chances of getting certain jobs, or of getting insurance coverage (life insurance, disability or health) for you or for members of your family.

However, as researchers, we are committed not to disclose information related to genetic results to any third party. Your results will not be made available to third parties such as an employer, a government agency, an insurer or an educational institution. This also applies to your spouse, other members of your family and your doctor. Furthermore, rest assured that no data related to any genetic results will be included in your hospital record.

VOLUNTARY PARTICIPATION AND THE RIGHT TO WITHDRAW FROM THE GENETIC PHASE OF THE PROJECT

Your participation in the genetic phase of the project is voluntary. Therefore, you may refuse to participate. You may also withdraw your consent from the genetic phase of this research project at any time. Just call the ICU research team at 346-1110 ext. 14171.

Your decision to refuse to participate in this sub-study of the project will have no impact on the quality of the care that will be provided to you or on your relationship with the healthcare team.

If you decide to terminate your participation in the genetic sub-study after providing a sample, you must notify the research team that will then destroy your sample. If your sample has already been tested and the results are already included in an analysis or publication, it will not be possible to remove this information. However, the rest of your sample will be destroyed and no further analysis will be done on your sample.

CONFIDENTIALITY

Identification:

In order to protect your identity, your samples will be identified by a unique code. Your name and your file number will not appear on the samples. The study investigator will keep a list of patients with the code numbers to identify them. This list is kept under lock and key in the research nurse's office and will not be disclosed under any circumstances.

Storage and destruction of samples:

Your samples will be kept in the principal investigator's freezers until the end of the study, unless you agree to biobanking. Another consent form will be presented to this end. The principal investigator is responsible for the destruction of samples.

COMMUNICATION OF RESULTS

Your participation and the results of the genetic analysis conducted on your samples will not be disclosed to you or to your doctor.

MARKETING POSSIBILITIES / WAIVER

Your participation in the genetic phase of this project could lead to the creation of commercial or other products that could potentially be protected by patents or other intellectual property rights. However, you will not receive any financial benefits.

CONSENT (GENETIC SUB-STUDY)

I declare that I have read this Appendix (genetic sub-study). I acknowledge that this sub-study of the project was explained to me, that all my questions were answered and that I was given the necessary time to make a decision.

I freely and willingly consent to participate in the **genetic sub-study** of this project:

I also accept that the remainder of my samples may be used for **additional genetic analyses** that may arise during the course of this study (future analysis):
☐ YES ☐ NO

Name of participant name (please print)	Signature of participant	Date

I have explained the genetic sub-study and this Consent Form to the participant, and I answered all his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

CONSENT (GENETIC SUB-STUDY)
FROM THE LEGAL REPRESENTATIVE (SUDDEN INCAPACITY)

Because Mr./Mrs. _____ has suddenly become incapable of giving consent for the hereinafter mentioned reason, the Civil Code of Québec allows you to give consent for him/her as his/her _____ (indicate your relationship with the participant) to participate in the **genetic sub-study** of the project.

As soon as Mr./Mrs. _____has sufficiently recovered, he/she will be asked to sign his/her own consent form to indicate whether he/she wants to continue taking part in this sub-study of the study.

REASON FOR THE PARTICIPANT NOT BEING ABLE TO GIVE CONSENT

By signing this page, I confirm that I have read the information in this Consent Form. I acknowledge that the **genetic sub-study** of the project has been explained to me, that all of my questions have been answered and that I was given enough time to make a decision.

I voluntarily give my consent so that Mr./Mrs. _____ can participate in the genetic sub study.

I also agree that the remainder of the samples may be used for **additional genetic analyses** that may arise during the study (future analyses). ☐ YES ☐ NO

Name of legal representative *(please print)*	Signature of legal representative	Date

I have explained all relevant aspects of the genetic sub-study of this project to the participant's legal representative and I have answered all his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

CONSENT (GENETIC SUB-STUDY)
FROM LEGAL REPRESENTATIVE OR CAREGIVER (PERMANENT INCAPACITY)

I confirm that I have read the information in this Consent Form. I acknowledge that the genetic sub-study of the project has been explained to me, that all of my questions have been answered and that I was given enough time to make a decision.

I agree that _____ can participate in this **genetic sub study** under the conditions stated therein. I will receive a signed and dated copy of this Information and Consent Form.

I also agree that the remainder of the samples may be used for **additional genetic analyses** that may arise during the study (future analyses). ☐ YES ☐ NO

If the participant is represented:

_____

Name and signature of the legal representative (representative, curator or mandatary) Date

If the incapacitated participant is not represented by a legal representative:

_____

Name and signature of the spouse, failing which, name of the next-of-kin or name of the significant person Date

I have explained the research study and this Consent Form to the participant's legal representative. I have answered all his/her questions.

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date

PHONE CONSENT (GENETIC SUB-STUDY)
(For the participant who is suddenly or permanently incapacitated)

Because Mr./Mrs. _____ is incapable of giving consent for the hereinafter mentioned reason.

REASON FOR THE PARTICIPANT NOT BEING ABLE TO GIVE CONSENT

_____

I have explained the genetic sub study and this Consent Form to the legal representative using the phone script and I have answered all his/her questions.

The representative, Mr./Mrs._____
Name of the legal representative (representative, curator or mandatary)
Name of the spouse or of the next-of-kin or
Name of the significant person

has given consent by phone on_____ at_____
Date Time

The representative also agrees that the remainder of the samples may be used for **additional genetic analyses** that might arise during the study (future analyses). ☐ **YES** ☐ **NO**

Name of person obtaining consent *(please print)*	Signature of person obtaining consent	Date and time