

**UNIVERSITY OF CALGARY**

**CONSENT TO PARTICIPATE IN RESEARCH**

**TITLE:** *Targeted Therapy with Glycogen Synthase Kinase-3 Inhibition for Arrhythmogenic Cardiomyopathy (TaRGET)*

**SPONSOR:** *Hamilton Health Sciences through its Population Health Research*

*Institute*

**FUNDER**: *Canadian Institute for Health Research (CIHR)*

INVESTIGATORS**:** *Dr. Erkan Ilhan (403-956-3686)*

# INTRODUCTION

Dr. Ilhan from the Cumming School of Medicine at the University of Calgary and associates are conducting a research study.

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something described here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form for your records.

You were identified as a possible participant in this study because you have a condition called arrhythmogenic cardiomyopathy (ACM). Your participation in this research study is voluntary.

# WHY IS THIS STUDY BEING DONE?

Arrhythmogenic cardiomyopathy (ACM) is a heart muscle problem where muscle cells die and are replaced with scar or fat cells. ACM puts you at risk for fast heart rhythms which can lead to serious complications. The typical treatment for ACM is to place a small device inside the body, which shocks the heart if a life-threatening rhythm occurs, this device is called an ICD (implantable cardioverter-defibrillator).

Tideglusib is a new type of drug that has shown promise in treating myotonic dystrophy, a disease that affects the regular muscles of the body and causes weakness. Tideglusib has recently been studied in mouse models of ACM (mice that develop ACM after their DNA has been changed to contain a mutation that causes ACM in humans). When tideglusib was given to these mice before the disease had developed, it prevented the development of disease. When the scientists waited until the mice had developed ACM, feeding the mice tideglusib stopped progression of the disease and partially reversed it. Because of these hopeful results, we're now planning to test tideglusib in a controlled study involving real people with ACM to see if it could be effective for them too.

The purpose of this study is to understand the effects that tideglusib has on your heart's electrical activity compared to a placebo.

Health Canada, the regulatory body that oversees the use of drugs in Canada, has not approved the sale or use tideglusib. However, Health Canada has allowed tideglusib to be used in this study.

# HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 120-150 people will take part in this study from 19 research sites across Canada. Five participants will take part in this study through the University of Calgary. This study should take 2 years to complete, and the results should be known in 2.5 to 3 years.

# WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

If you decide to participate, then you will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group.  Neither you, the study staff, nor the study doctors can choose what group you will be in.

This is a double-blind study, which means that neither you, the study doctors or other research staff will know which group you are in. Requests to reveal your group assignment will not be considered until this study has been completed and the results are known. However, your group assignment can be identified if medically necessary.

Before being randomized into one of the below groups, you will undergo tests to ensure your eligibility for the study:

* 7-day cardiac monitor, shipped to your home and applied by yourself
* Blood, urine, and pregnancy (if applicable) tests
* Hepatitis B and C blood tests
* Blood sample taken for storage and future testing.

The study also plans to collect blood samples to store for future research on your DNA and serum biomarkers (proteins in your blood). Further testing may be done to better understand your vulnerability to ACM and factors that affect your response to tideglusib. There is a separate but optional consent form for this portion of the study.

Once these additional tests are completed, you will be randomized into one of two groups and the study drugs will be sent to your home.

***Group 1: Experimental Intervention:*** *If assigned to this group, you will be given 1000mg of tideglusib (taken by mouth) daily.*

***Group 2 (Non-Experimental Intervention):*** *If assigned to this group, you will be given the matching drug that looks like tideglusib but does not contain any active ingredients.*

The study drug(s) assigned to you are for you alone and must not be shared with others. If someone accidentally takes your study drug, please contact your emergency medical service provider, and inform your study doctor.

Immediately following randomization, you will undergo some additional testing:

* ECG and ECHO (heart ultrasound) tests
* Exercise questionnaire.

Subsequent visits will be done every 2-4 weeks to repeat local lab testing (blood and urine) until your final visit after 6 months. The final visit will also include an ECG, echocardiogram, 7-day cardiac monitor, exercise questionnaire, and blood sample for storage. The 7-day cardiac monitor and echocardiogram are to be completed within the final 2 weeks of the treatment period.

**WHAT WILL HAPPEN WHEN I AM FINISHED WITH THE STUDY?**

You may not be able to receive tideglusib after your participation in the study is completed. Dr. Ilhan will talk to you about your options as the end of the study approaches.

# HOW LONG WILL I BE IN THIS STUDY?

Your participation in the study will last approximately 6 months.

You may be seen more often if Dr. Ilhan determines that this is necessary.

# ARE THERE ANY POTENTIAL RISKS THAT I CAN EXPECT FROM THIS STUDY?

Side Effects:

You may experience side effects from participating in this study. While some side effects are known, you may experience other unexpected side effects. You should address unanticipated side effects with Dr. Ilhan:

* Increased liver enzymes in the blood – this effect does not cause any physical symptoms and should return to normal once treatment has stopped.
* Potential kidney dysfunction
* Tiredness
* Feeling sick or unwell
* Pain or tenderness in body
* Fever
* Rash
* Diarrhea
* Headache

The likelihood of any of these side effects are not currently known and there is a risk that a rare or previously unknown side effect may occur. If you are concerned about any of your side effects, you should contact the study team immediately.

Blood sampling:

You may experience some discomfort from blood draws, as well as bruising, swelling or infection at the needle site. Some people feel dizzy or light-headed for a few minutes after their blood is drawn.

Allergic Reactions:

Rare or unknown side effects could occur, including life-threatening reactions. As with any drug, it is possible you could experience an allergic reaction, such as itching, skin rash, facial swelling, difficulty breathing, and a sudden drop in blood pressure which may lead to shock with loss of consciousness and/or seizures, including death. For any of these symptoms, seek medical attention immediately.

It is also possible that other drugs (prescription or non-prescription), vitamins or herbals may interact with tideglusib. This could either prevent the drug from not working as expected or result in serious side effects.

Reproductive Risks:

Currently, the effects of tideglusib on an unborn baby (fetus) are unknown.

If you are able to have or father children, you must avoid becoming pregnant or fathering a child while participating in the study. The study drug could harm an unborn child or nursing infant.

If you are female, pregnant or plan to become pregnant during the study, or are breastfeeding, you **cannot** participate in the study. By signing the consent form, you confirm to the best of your knowledge that you are not pregnant now, not currently breast-feeding and do not plan to become pregnant or start breastfeeding during the study. If you are a female who can become pregnant (that is, started your periods, not surgically sterile or has not gone through menopause), you must have a negative blood pregnancy test at screening before you can enter the study.

Furthermore, if you are a female who can become pregnant or a male who has a female partner who can become pregnant, you and your partner must use an effective form of contraception from screening, during the treatment period and for at least 30 days (for female subjects) or 90 days (for male subjects) after the last dose of the study drug.

# ARE THERE ANY POTENTIAL BENEFITS IF I PARTICIPATE?

This study will help the researchers learn more about tideglusib. Hopefully this information will help in the treatment of future patients with arrhythmogenic cardiomyopathy like yours.

# WHAT OTHER CHOICES DO I HAVE IF I CHOOSE NOT TO PARTICIPATE?

You can choose to end your participation in this research at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact Dr. Ilhan or study staff.

You may be asked questions about your experience with the study intervention, and to have laboratory tests and physical examinations considered necessary to safely stop your study involvement. Even though you decide to no longer participate in the study, you may decide to allow Dr. Ilhan to contact you a few times throughout the study to find out how you are doing.

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.

If you no longer want your samples to be used in this research, you should tell the research coordinator (403-210-6414). If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

# CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?

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

* Your health changes and the study drug is no longer in your best interest.
* You are unable to tolerate the study intervention.
* 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 is stopped by your country’s regulatory authority, national and/or local ethics board, and/or the study sponsor (Population Health Research Institute) who oversees the study.
* For women: You become pregnant while on the study.

If you are female and become pregnant during the study, you must discontinue the study intervention. However, you will remain in the study and continue to be followed by Dr. Ilhan until the end of the trial.

# WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME?

During the study, the researchers could learn something about you that they didn’t expect. For example, the researchers may find out that you have another medical condition. The researchers will consult with medical experts as needed to evaluate the findings and will then share these results with you. You will be helped with arranging appropriate follow up and care.

I consent for the researchers to share findings with me:

❑ YES

❑ NO

**ARE THERE COSTS ASSOCIATED WITH PARTICIPATING IN THE STUDY?**

Tideglusib will be supplied at no charge while you take part in this study.

The costs of your medical treatment will be paid for by your provincial medical plan to the extent that such coverage is available.

You may not be able to receive the study medication after your participation in the study is completed. There are several possible reasons for this, some of which are:

* The study drug may not turn out to be effective or safe.
* The study drug may not be approved for use in Canada.
* Your caregivers may not feel it is the best option for you.
* You may decide it is too expensive and insurance coverage may not be available.
* The study drug, even if approved in Canada, may not be available free of charge.

The study doctorwill talk to you about your options as the end of the study approaches.

Taking part in this study may mean that you need to make more visits to the hospital/clinic than if you were getting the standard of care treatment. You may:

* Have more travel costs.
* Need to take more time off work.
* Have other additional personal costs.

If you decide to participate in this study, parking at the Foothills Hospital will be reimbursed. You will need to provide your license plate and vehicle make information to the study team in advance of your appointments for your parking to be reimbursed.

# WILL MY RECORDS BE KEPT PRIVATE?

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

The researchers will do their best to make sure that your private information is kept confidential, unless required by law. Information about you will be handled as confidentially as possible, but there is always the potential for an unintended breach of privacy. The research team will handle data according to the Data Management Plan as outlined below:

* All identifiable information about you will be replaced with a code. A master list linking the code and your identifiable information will be kept separate from the research data.
* All research data and records will be maintained in a secure location at the University of Calgary. Only authorized individuals will have access to it.
* Some research data and records will be stored electronically on a server with password protection.

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:

* + Population Health Research Institute, Hamilton Health Sciences, the Sponsor of this study
* The Conjoint Health Research Ethics Board, which oversees the study at this site.
* Health Canada (because they oversee the use of drugs in Canada)

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. 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 participant ID, initials, sex, and date of birth.

Some of your health information, such as your response to the study questionnaires, results from study visits/procedures, and medicines you took, will be kept by the study sponsor in a central research database. However, information that is entered in the study database will contain only coded information.

This study requires access to your full name, address (street, city, province and postal code) and telephone number to ship the 7-day monitor and study drug directly to your home.

This study requires the transfer of personal information to third-party service providers (SP). The first SP is Icentia Inc., which is being used to ship the 7-day monitor directly to you and analyze the recordings. The following personal information will be securely transferred to Icentia Inc.: Full name (first and last name), Full address (street address, City, Province, Postal Code). The recordings sent to Icentia will be de-identified, which means the recordings will not have information that can directly identify you.

The second SP is Sentrex Health Solutions, which is being used to ship the study drug directly to you. The following personal information will be securely transferred to Sentrex Health Solutions: Full name (first and last name), Full address (street address, City, Province, Postal Code).

Both Icentia Inc. and Sentrex Health Solutions will only collect your information for the purpose of the study. There is a risk that information collected for this study could accidentally be accessed by an unauthorized party, which can lead to unwanted marketing communications or scams. All efforts are made to prevent any unauthorized access to your Information and security measures are in place to securely store and keep your information confidential. A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

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 published or presented at scientific meetings. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of the study intervention.

Future research

In addition to storing data in the study database, data from studies that are publicly funded may also be shared for future use in public databases with protections for your privacy. The goal of this data sharing is to make more research possible which may improve people’s health. Your study records may be stored and shared for future use in public databases.

Some types of future research may include looking at your information and information from other participants to see who had side effects across many studies or comparing new study data with previously collected study data. Currently, we don’t know what future research may be done using your information. This means that:

1. You will not be asked if you agree to take part in the specific future research studies using your health information.
2. You and Dr. Ilhan will not be told when or what type of research will be done.
3. You will not get reports or other information about any research that is done using your information.

Your samples provided for biobanking may be shared so that researchers from around the world can use them to study many conditions. The samples and data will be sent with only your code number attached, not your name.

# HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?

The researchers intend to keep the research *records* for approximately **15** years. Your *DNA and serum samples* will be stored at the Clinical Research Laboratory and Biobank-Genetic and Molecular Epidemiology Laboratory (CRLB-GMEL) at the Hamilton General Hospital. We plan to keep your deidentified *DNA and serum samples* indefinitely. Any future use of this research data is required to undergo review by a Research Ethics Board.

**SIGNATURES**

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a participant. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care*.*

* I have read and understood this information.
* It has been written in a language that I can read and understand.
* This study has been explained to me.
* All my questions about the study, the study drug, and possible risks and side effects have been answered to my satisfaction.
* I give permission for my doctors, other health professionals, hospitals, or laboratories to release information to the study site and study doctor about my disease and treatment for the purposes of this study. I understand this information will remain confidential.
* I have been informed that the study team will inform my other doctors about my participation in this study, and I agree to this.
* I freely agree to participate in this research study as described and understand that I am free to withdraw at any time during the study.
* I consent to the processing and transfer of my personal data as described in this consent form.
* I understand that I will be given a signed and dated copy of this document to keep.

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Participants PRINTED name Participant’s Signature Date

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Witness PRINTED name Witness Signature Date

To the best of my knowledge, the subject signing this Consent Form has had the Study fully and carefully explained by me and the subject has been given the opportunity to ask questions about the Study, the information contained in this Consent Form, and his/her participating in the Study.

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Investigator PRINTED name Investigator Signature Date

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.