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**Participant Information Sheet/Consent Form**

**Interventional Study** -*Adult providing own consent*

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| **Title** | Ivabradine use to improve exercise capacity in patients with transposition of the great arteries (TGA) post atrial switch repair |
| **Project Number** | 2019.017 |
| **Project Sponsor** | Melbourne Health |
| **Principal Investigator** | Dr William Wilson |
| **Location** | The Royal Melbourne Hospital |

**Part 1 What does my participation involve?**

**1 Introduction**

You are invited to take part in this research project. This is because you have transposition of the great arteries and have undergone an atrial switch operation (Mustard or Senning repair). Transposition of the great arteries (TGA) is a condition where the aorta and pulmonary arteries are reversed so blue blood is returned to the body instead of the lungs and vice versa. An atrial switch repair involved creation of channels within the heart to direct red blood to the right ventricle which is connected to the aorta (and blue blood to the left ventricle and lungs).

This research project is testing a new medication called Ivabradine in the treatment of TGA + atrial switch repair.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don’t wish to take part, you don’t have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read

• Consent to take part in the research project

• Consent to have the tests and treatments that are described

• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

**2 What is the purpose of this research?**

The purpose of this study is to evaluate the effectiveness of Ivabradine in adults who have undergone atrial switch repair for TGA, in particular, to evaluate if Ivabradine is an effective treatment to improve exercise capacity. Evidence suggests that the heart beats more efficiently at lower heart rates in your condition, therefore, Ivabradine (which acts to slow the heart rate down) may improve exercise capacity.

Ivabradine is approved in Australia to treat coronary artery disease (angina) and heart failure. However, it is not approved to treat exercise intolerance in TGA + atrial switch repair. Therefore, it is an experimental treatment. This means that it must be tested to see if it is an effective treatment to improve exercise capacity in TGA + atrial switch repair.

This research has been initiated by the study doctor, Dr William Wilson, and is being funded by The Royal Melbourne Hospital. The results of this research will be used by Dr William Wilson to obtain a PhD degree.

**3 What does participation in this research involve?**

If you agree to take part in this research project, you will be asked to sign this consent form before any study assessments are performed. Your study participation will last between 8 weeks which will include 3 visits to the study clinic.

You will be participating in a double-blind, randomised, controlled, cross-over research study.

Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random).

‘Double-blind’ means that neither you nor your study doctor will know which treatment you are receiving. However, in certain circumstances your study doctor can find out which treatment you are receiving.

This research project uses a placebo. A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not. A placebo in this research project is required to be able to compare it against the study drug, Ivabradine, to be able to evaluate if the study works and is safe to use in patients with your condition.

This is also a ‘cross-over’ study, therefore, the groups each have the different treatments in turn. So, if you are randomised to placebo for the first 4 weeks, then you will receive Ivabradine for the second 4 weeks and vice-versa.

This research project involves the following visits: Screening (at time of clinic), Baseline, Visit 2 and Visit 3.

At the Screening visit the following tests and procedures will be performed to make sure that this research project is suitable for you. These tests are part of normal clinical care (ie. Tests that you would have anyway).

* Demographic information such as your sex, age, race and ethnicity will be collected.
* An Electrocardiogram (ECG) will be performed. An ECG is a recording of the electrical activity of the heart to measure your hearts rhythm. You will have several sticky pads placed on your skin which are connected to a machine that monitors your heart.
* An echocardiogram will be performed if one has not been performed in the previous 6 months. An echocardiogram is an ultrasound of the heart. Gel is placed on your chest and a tool, similar to a hand-held microphone, is moved to different places on your chest. An echocardiogram helps your doctor check if there are any problems with your heart’s valves and chambers, and see how strongly your heart pumps blood.
* Blood will be collected for standard laboratory testing to check levels of red and white blood cells, and platelet counts in your blood to evaluate your general health, and also to check how well your kidneys and liver are working. A B-natriuretic peptide (BNP) test will also be conducted. This blood test measures levels of a particular protein associated with heart failure.
* You will wear a Holter monitor for 24 hours (if you have not already done this in the last 6 months). This involves carrying a small device (size of an AA battery) connected to three wires that join to three electrodes stuck to your chest. During that time, the device will record the rhythm of your heart. You will need to wear the Holter monitor continuously for 24 hours, even while you sleep. You will need to keep the Holter monitor dry so you will not be able to shower or bathe whilst wearing the monitor.

If the screening procedures confirm that that the study is suitable for you, and you choose to take part, you will attend a Baseline visit.

The baseline visit will take place within 3 months of the Screening visit. At the Baseline visit the following tests will be performed:

* An ECG will be performed.
* Short quality of life questionnaire.
* Cardiopulmonary exercise stress. This test will measure the response of the heart and lungs to exercise on a stationary bicycle.
* 24 hour Holter monitor.

You will then be randomised to receive either:

* Ivabradine 7.5mg, taken orally twice daily OR
* Placebo

You will take the study treatment you have been randomised to for 4 weeks; at two weeks, we will organise a heart rate check and potentially increase the dose to 7.5mg twice a day. A treatment crossover will occur at 4 weeks. So, if you were randomised to receive placebo for the first 4 weeks, you will then receive Ivabradine for the second 4 weeks and vice-versa.

You will attend Visit 2, four weeks after commencing study treatment, and then Visit 3, four weeks after crossover.

At Visit 2 and Visit 3 the tests and procedures performed at the Baseline visit will be repeated.

**4 What do I have to do?**

If you agree to participate in this research project, you are required to:

* Attend all of the study appointments. If you miss an appointment you must reschedule with the study doctor or staff.
* Take the study medication as instructed and return any unused medication.
* Notify the study doctor and/or study staff of any side effects you may experience.
* You must tell the study doctor about any medicines you are currently taking or may take during the course of the research project (e.g. prescription, vitamins, over the counter, herbal supplements etc.). Some of these may need to be stopped/reduced. You should avoid taking other medications that slow your heart rate during the study (eg. beta blockers or digoxin).
* You can still donate blood whilst participating in this study.

**5 Other relevant information about the research project**

Approximately 44 participants will be enrolled into the research project here at The Royal Melbourne Hospital.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

You will not receive payment for participating in this research project.

You may be reimbursed for any reasonable travel expenses upon presentation of a receipt and approval from the study staff. Please discuss this with the study team.

**6 Do I have to take part in this research project?**

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with The Royal Melbourne Hospital.

**7 What are the alternatives to participation?**

You do not have to take part in this research project to receive treatment at this hospital. Other options are available. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

**8 What are the possible benefits of taking part?**

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include improved exercise capacity (ie. ability to exercise for longer with less shortness of breath etc.).

**9 What are the possible risks and disadvantages of taking part?**

Medical treatments can cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

**Side effects associated with Ivabradine**

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| --- | --- | --- | --- |
| **Side Effect** | **How often is it likely to occur?** | **How severe might it be?** | **How long might it last?** |
| Dizziness, slow heart rate | Occasionally (occurs in 5-10% of people) | Usually mild | Stops with medication cessation |
| High blood pressure | Occasional (occurs in 5-10% of people) | Mild | Stops with medication cessation |
| Visual disturbance (mild – halos (bright circles that appear to surround a source of light) or visual brightness) | Rare (occurs in 2% of people) | Not harmful | Stops with medication cessation |
| Irregular heart rate (AF) | Rare (occurs in 2% of people) | Mild | Stops with medication cessation |
| Rash, itch | Rare (occurs in 2% of people) | Mild | Stops with medication cessation |

**Possible risks associated with procedures performed during this research project**

Blood collection

You will have your blood collected during the study. The risks of collecting blood may include tenderness, pain, bruising, bleeding, and/or infection where the needle goes into the skin and blood vein. Having your blood collected may also cause you to feel nauseated and/or lightheaded.

Performing an electrocardiogram (ECG)

The sticky pads attached to the skin may cause irritation, redness, or burning of the skin when removed.

Cardiopulmonary stress test

These are generally very safe but they are a test of maximum effort so some people do find them quite tiring to undertake. A nurse will be present throughout the testing to monitor your health and any concerns you might have.

Possible risks associated with pregnancy

The effects of Ivabradine on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least 1 month after the last dose of study medication.

Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of 1 month after completion of the research project. You should discuss methods of effective contraception with your study doctor.

*[For female participants]* If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

*[For male participants]* You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

**10 What will happen to my test samples?**

As part of this research project, you will have blood collected and tested to monitor your condition and any potential side effects.

Your blood samples will be processed and analysed by staff at The Royal Melbourne Hospital. After the tests are completed blood samples will be destroyed in accordance with local processes. The results of these tests will become part of your hospital medical record. Your study doctor will inform you of the results.

**11 What if new information arises during this research project?**

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

**12 Can I have other treatments during this research project?**

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

**13 What if I withdraw from this research project?**

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. Your data will be excluded from the primary analysis, but your data will be kept so that characteristics of those who complete the study and those who withdraw can be defined.

**14 Could this research project be stopped unexpectedly?**

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

• Unacceptable side effects

• The study drug being shown not to be effective

The study doctor may remove you from this research project for any justified reason according to the protocol. Examples why you may have to stop some or all study related activities, including study treatment are:

• Staying in the study would be harmful

• You need treatment not allowed in this study

• You fail to follow instructions

• You become pregnant

**15 What happens when the research project ends?**

Once the research project ends, Ivabradine will no longer be made available to you. However, the study doctor will arrange for your medical care to continue.

The results will be provided to you by the study doctor once available, and upon request.

A summary of the results may also be published at conferences or in journals. If the results of the study are presented to the public, you will not be named.

**Part 2 How is the research project being conducted?**

**16 What will happen to information about me?**

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Information captured via the activity tracking app will be sent to a secure web-based database created by the Melbourne e-Research Group. The Melbourne eResearch Group have developed numerous similar apps that are now used in clinical/biomedical research projects. All information sent from the activity tracking app to the database will be encrypted in transit.

Your health records and any information obtained during the research project are subject to inspection for the purpose of verifying the procedures and the data. This review may be done by the relevant authorities and authorised representatives of the Melbourne Health Human Research Ethics Committee, the institution relevant to this Participant Information Sheet, The Royal Melbourne Hospital, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Study identifying codes are kept separate from identifying details in a locked database accessible only to study personnel. This database is kept for 15 years after the study is completed and then securely destroyed. Data collected in the process of this study is analysed only as group data with individual identifying information removed.

Information about your participation in this research project may be recorded in your health records.

Your personal medical practitioner, if applicable, will be informed of your participation in the study.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

**17 Complaints and compensation**

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

**18 Who is organising and funding the research?**

This research has been initiated by Dr William Wilson and has been funded by The Royal Melbourne Hospital.

You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

**19 Who has reviewed the research project?**

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Melbourne Health HREC.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

**20 Further information and who to contact**

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor, Dr William Wilson on 0488 711 976 or any of the following people:

**Clinical contact person**

|  |  |
| --- | --- |
| Name | William Wilson |
| Position | Cardiologist |
| Telephone | 0488 711 976 |
| Email | wmclwilson@gmail.com |

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

**Complaints contact person**

|  |  |
| --- | --- |
| Name | Director Research Governance and Ethics |
| Position | Complaints Manager |
| Telephone | 03 9342 8530 |
| Email | Research@mh.org.au |

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

**Reviewing HREC approving this research and HREC Executive Officer detail**

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| --- | --- |
| Reviewing HREC name | Melbourne Health |
| HREC Executive Officer | Manager HREC |
| Telephone | 03 9342 8530 |
| Email | Research@mh.org,au |

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**Consent Form -** *Adult providing own consent*

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| --- | --- |
| **Title** | Ivabradine use to improve exercise capacity in patients with transposition of the great arteries (TGA) post atrial switch repair |
| **Project Number** | 2019.017 |
| **Project Sponsor** | Melbourne Health |
| **Principal Investigator** | Dr William Wilson |
| **Location** | The Royal Melbourne Hospital |

**Consent Agreement**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Royal Melbourne Hospitalconcerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

**Declaration by Participant – for participants who have read the information**

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| Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

**Declaration - for participants unable to read the information and consent form**

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| See Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 Section 4.8.9, witness \* required  Witness to the informed consent process  Name (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  \* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older. |

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

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|  | | | | | | |
|  | Name of Study Doctor/  Senior Researcher† (please print) | |  | | |  |
|  | | | | | |  |
|  | Signature |  | | Date |  |  |
|  | | | | | | |

† A senior member of the research team must provide the explanation of, and information concerning, the research project.



**Form for Withdrawal of Participation -** *Adult providing own consent*

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| --- | --- |
| **Title** | Ivabradine use to improve exercise capacity in patients with transposition of the great arteries (TGA) post atrial switch repair |
| **Project Number** | 2019.017 |
| **Project Sponsor** | Melbourne Health |
| **Principal Investigator** | Dr William Wilson |
| **Location** | The Royal Melbourne Hospital |

**Declaration by Participant**

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with The Royal Melbourne Hospital.

|  |  |  |  |  |  |  |
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|  | | | | | | |
|  | Name of Participant (please print) | |  |  |  |  |
|  | | | | | | |
|  | Signature |  | | Date |  |  |
|  | | | | | | |

*In the event that the participant’s decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.*

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**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

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|  | | | | | | |
|  | Name of Study Doctor/  Senior Researcher† (please print) | |  | | |  |
|  | | | | | |  |
|  | Signature |  | | Date |  |  |
|  | | | | | | |

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.