**Participant Information Sheet/Consent Form**

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

Austin Health

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| --- | --- |
| **Title** | Precision medicine in liver transplantation: a personalised approach to immunosuppression |
| **Short Title** | Precision medicine in liver transplantation |
| **Protocol Number** | LT001 |
| **Project Sponsor** | Austin Health |
| **Coordinating Principal Investigator/ Principal Investigator** | A/Prof Vijavaragavan Muralidharan |
| **Associate Investigator(s)** | Dr Tess McClure Dr Daniel Cox Dr Adam Testro A/Prof Alexander Dobrovic Dr Hongdo Do |
| **Location** | Austin Health |

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

**1 Introduction**

You are invited to take part in this research project, ‘Precision medicine in liver transplantation: a personalised approach to immunosuppression’, a prospective observational study. This is because you are potentially undergoing liver transplantation (LT). The research project is aiming to determine the utility of two novel blood tests in monitoring and managing immunosuppression post liver transplantation. One of these blood tests is called QuantiFERON-Monitor (QFM) and measures immune function. The other blood test is called donor-specific cell free DNA (dscfDNA) and measures organ injury. The research project is aiming to determine if the combination of these two tests (QFM-dscfDNA) can be used to monitor and manage immunosuppression post LT.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and research 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 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 the tests and research 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?**

LT is the only effective treatment for many patients with liver disease. Due to advances in medical care, LT has become an acceptably safe procedure and the number of LT performed each year continues to increase. Long-term, the success of LT depends on a fine balance: suppressing the immune system to avoid organ rejection, whilst maintaining it to prevent infection. Despite careful monitoring with standard blood tests, most patients will experience episodes of rejection and/or infections. Diagnosing these complications often requires expensive medical imaging and an invasive liver biopsy, prior to treatment with immunosuppression adjustment. There is a clear need for innovative tools to ‘personalise’ immunosuppression, so as to improve patient outcomes and healthcare resource utilisation.

Researchers at Austin Health have pioneered the study of two rapid and low-cost blood tests − QFM and dscfDNA − in patients post LT. This prospective observational study aims to determine the utility of combining these two tests. Specifically, this study aims to examine if the QFM-dscfDNA tests can diagnose acute rejection and infective complications post LT. The study also aims to examine if the QFM-dscfDNA tests can predict acute rejection and infective complications, monitor treatment responses and improve healthcare resource utilisation.

If you chose to participate, you will be followed up for 12 months post LT. We will ask that a series of blood tests are taken for research purposes, which will occur when you are having standard blood tests performed wherever possible.

The results of this research will be used by the study coordinators Dr Tess McClure and Dr Daniel Cox as part of their PhDs. This research has been initiated by these study doctors as well as A/Prof Vijavaragavan Muralidharan, Dr Adam Testro, A/Prof Alexander Dobrovic and Dr Hongdo Do. As a research team, they aim to contribute to research in this field to advance current knowledge and potentially lead to future studies in transplantation and liver disease.

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

No study assessments will be performed until you have read and understood the consent form, have signed and are happy to proceed.

Your clinician has referred you for a LT, which is not part of this study. You will be participating in an observational trial. This means that tests will be undertaken to monitor you post LT, but there will be no changes in your clinical treatment.

Initial Steps

A study coordinator will approach eligible patients to discuss the research project. If you agree to take part in this study you will be reviewed by a study coordinator prior to undergoing LT. You will be followed up for 12 months post LT. We will ask that you have additional blood sampling, which will occur at various times when you are having standard blood tests performed wherever possible.

Procedures

* Additional blood sampling:
  + Collection: 15-30mL of blood (equivalent to 1-2 tablespoons) will be collected at Austin Health. This will occur once before LT and 10 or more times post LT, when other blood

tests are taken for routine diagnostic purposes, as outlined in **Table 1**.

* + Use:
    - The blood samples will be used to measure:
      * QFM: This blood test looks at the function of your immune system.
      * dscfDNA: This blood test measures free DNA from the donor (originating from the transplanted liver) in your blood stream.
    - Remaining blood will be stored for future research projects that are extensions of or closely related to this study, or in the same general area of research.
  + Processing and storage:
    - Blood samples will be processed at the Olivia Newton John Cancer Institute and stored in the Liver Transplant Unit, Austin Health, both of which are located at 145 Studley Road, Heidelberg, Victoria, 3084.
    - Your blood samples will be batched for analysis at the end of your 12-month follow up, so the test results will not be provided or available for your ongoing standard care/treatment.
    - All blood samples will be stored for a period of seven years, after which they will be disposed off safely as per hospital/laboratory protocols in designated hazardous waste bins.

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| **Table 1: Schedule of additional blood sampling** | | |
| **Time** | | **Additional blood sampling** |
| Before LT | | x 1 |
| Post LT x 10 (as outlined below) | | |
| Day | 1 | x 1 |
| 3 | x 1 |
| 5 | x 1 |
| Week | 1 | x 1 |
| 2 | x 1 |
| Month | 1 | x 1 |
| 2 | x 1 |
| 4 | x 1 |
| 6 | x 1 |
| 12 | x 1 |
| If rejection or infection occurs | | x 3 (taken 1-3 days apart) |

* Access to Health Information:
  + As part of this project, it will be necessary to collect your Austin Health UR, date of birth and medical history.
  + It may be necessary for some of your health information to be obtained from other health service providers (such as another hospital, a private pathology/radiology service, your General Practitioner or a consultant).
  + Although the information collected about you will be identifiable, this will be re-identified with a code. Both forms of information will be held securely and confidential in order to protect your privacy.

Top of Form

Bottom of Form

Bias

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

Additional costs

There are no costs associated with participating in this research project, nor will you be paid. You will be reimbursed for any of the following costs that you incur as a result of participating in this

research project such as parking.

Local doctor involvement

It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research project. If you decide to participate in this research project, the study doctor will inform your local doctor.

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

There are no lifestyle or dietary restrictions while on this study. You should still take your regular prescribed medication.

To participate in this study, you need to comply with standard post LT care as recommended by your treating clinicians. This will involve an initial inpatient admission post LT, follow up in the outpatient clinics and readmission to hospital if complications arise. You will need to have additional blood sampling for when you have standard blood tests performed pre and post LT.

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

This study is aiming to recruit 210 patients who are undergoing LT from at Austin Health. This research involves only doctors and researchers from Austin Health.

**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.

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 Austin Health.

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.

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

You do not have to take part in this research project to receive treatment at this hospital. If you do not take part in this study, you will receive routine follow up before and after LT as determined by your treating doctor. 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?**

There will be no clear benefit to you from your participation in this research. This is an observational study and no treatment or change in care will be given. However, this study will improve our understanding of complications related to immunosuppression after LT, and may lead to further studies. This future research may lead to the development and use of innovative tools to monitor and manage immunosuppression post LT, so as to improve future patient outcomes and reduce healthcare costs.

**9 What are the possible risks and disadvantages of taking part?**  
  
Having a blood sample taken may cause some minor discomfort, bruising, infection or bleeding.

If this happens, it can be easily treated. Anaemia (low blood count) is not expected to occur with the volume of blood required for this study (11 x 30ml = 330ml over 12 months).

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team.  
This will be provided free of charge.  
  
**10 What will happen to my test samples?**

You will be asked to provide additional consent for the collection of your blood during the research project. This blood sampling is a mandatory component of the research.

Samples will be taken to perform the QFM-dscfDNA tests and blood will be stored for future ethically approved research. Both of these processes are for research purposes only. These samples will be stored securely in the Liver Transplant Unit, Austin Health. The samples will be destroyed seven years after the conclusion of the study.

You are providing extended consent for the use of the stored blood samples. This means that they will be used for this study, and may be used for future ethically approved research in transplantation and liver disease.

**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 this research project, please notify a member of the research team before you withdraw. A member of the research team will inform you if there are any 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. You should be aware that data collected by the

sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

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

This research project may be stopped unexpectedly for a variety of reasons. These may include unexpected results.

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

When the research project ends, the study doctor will ensure you have the relevant follow up with your treating doctor. This study is expected to last for 4 years. Participants will be asked at the last study visit if they would like to be provided with a summary of the results. If they would like a summary of the results, this will be sent out when the research project is completed.

**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 name will not be recorded in the database. We will assign a study number against your Austin UR number, and use that to re-identify your data if required. This will all be stored in an electronic database, protected by a password, accessible only by the study investigators. Data will be stored for a period of 10 years after study completion, in a secure password-protected form.

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.

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) by the institution relevant to this Participant Information Sheet, Austin Health, 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. We will present results describing changes observed in all patients participating in this study as a whole. Individual data will not be discussed.

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

In accordance with relevant Australian 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 that 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 project is being conducted by A/Prof Vijavaragavan Muralidharan, Dr Tess McClure, Dr Daniel Cox, Dr Adam Testro, A/Prof Alexander Dobrovic and Dr Hongdo Do.

Funding of the research is pending. An application for a grant from the National Health and Medical Research Council has been submitted. Alternate funding will be sourced from the Austin Health Medical Research Fund, Liver Transplant Unit and Department of Surgery if required.

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 to Austin Health / The University of Melbourne.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Austin Health/ The University of Melbourne, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

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 HREC of Austin Health.

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 A/Prof Vijavaragavan Muralidharan on (03) 9496 5050 or any of the following people:

* Dr Tess McClure – (03) 9496 5353
* Dr Daniel Cox – (03) 9496 5000
* Dr Adam Testro – (03) 9496 5353
* A/Prof Alexander Dobrovic – (03) 9496 5000
* Dr Hongdo Do – (03) 9496 5000

**Clinical contact person**

|  |  |
| --- | --- |
| Name | Dr Tess McClure |
| Position | Liver Fellow, Study Coordinator | |
| Telephone | (03) 9496 5353 or (03) 9496 5000 | |
| Email | tess.mcclure@austin.org.au | |

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**

|  |  |
| --- | --- |
| Position | Complaints Officer |
| Telephone | (03) 9496 4090 or (03) 9496 3248 |
| Email | ethics@austin.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:

**Local HREC Office contact (Single Site - Research Governance Officer)**

|  |  |
| --- | --- |
| Reviewing HREC name | Austin Health Human Research Ethics Committee |
| HREC Executive Officer | Ethics and Research Governance Manager |
| Telephone | (03) 9496 4090 |
| Email | ethics@austin.org.au |

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

|  |  |
| --- | --- |
| **Title** | Precision medicine in liver transplantation: a personalised approach to immunosuppression |
| **Short Title** | Precision medicine in liver transplantation |
| **Protocol Number** | LT001 |
| **Project Sponsor** | Austin Health |
| **Coordinating Principal Investigator/ Principal Investigator** | A/Prof Vijavaragavan Muralidharan |
| **Associate Investigator(s)** | Dr Tess McClure Dr Daniel Cox Dr Adam Testro A/Prof Alexander Dobrovic Dr Hongdo Do |
| **Location** | Austin Health |

**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 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 project without affecting my future health care.

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

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

I understand that, if I decide to discontinue the research project treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

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| --- | --- | --- | --- |
|  | | | **Initial** |
| * This specific project | YES | NO |  |
| * Other ethically approved research that is closely related to this research project | YES | NO |  |
| * Any future ethically approved research. | YES | NO |  |

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

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

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

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| 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.

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

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

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| --- | --- |
| **Title** | Precision medicine in liver transplantation: a personalised approach to immunosuppression |
| **Short Title** | Precision medicine in liver transplantation |
| **Protocol Number** | LT001 |
| **Project Sponsor** | Austin Health |
| **Coordinating Principal Investigator/ Principal Investigator** | A/Prof Vijavaragavan Muralidharan |
| **Associate Investigator(s)** | Dr Tess McClure Dr Daniel Cox Dr Adam Testro A/Prof Alexander Dobrovic Dr Hongdo Do |
| **Location** | Austin Health |

**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 Austin Health.

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