**Participant Information Sheet/Consent Form - Person Responsible/Medical Treatment Decision Maker**

**Non-Interventional Study** -*Person responsible/Medical treatment decision maker   
consenting on behalf of participant*

Austin Health

|  |  |
| --- | --- |
| **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 participation involve?**

**1 Introduction**

The participant is 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 the participant is 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 the participant 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 the participant can take part, you might want to talk about it with a relative, friend or local doctor.

Participation in this research is voluntary. If you do not wish for the participant to take part, they do not have to. They will receive the best possible care whether or not they take part.

If you decide you want the participant 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 the participant taking part in the research project

• Consent to the participant having the tests and research that are described

• Consent to the use of the participant’s 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 choose for the participant to take part, they will be followed up for 12 months post LT. We will ask that a series of blood tests are taken from the participant for research purposes, which will occur when they 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 and 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.

The participant’s clinician has referred them for a LT, which is not part of this study. The participant will take part in an observational trial. This means that tests will be undertaken to monitor the participant post LT, but there will be no changes in their clinical treatment.

Initial Steps

A study coordinator will approach eligible patients to discuss the research project. In cases where patients are too unwell to provide consent, their next of kin will be approached as their person responsible/medical treatment decision maker. When participants have recovered post LT, informed consent will be obtained from the participant. If the participant withdraws their consent, all data collected for research purposes will be securely destroyed.

If you agree to the participant taking part in this study, they will be reviewed by a study coordinator prior to undergoing LT. The participant will be followed up for 12 months post LT. We will ask that

the participant has additional blood sampling, which will occur at various times when they are having standard blood tests performed for LT.

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 the participant’s immune system.
      * dscfDNA: This blood test measures free DNA from the donor (originating from the transplanted liver) in the participant’s 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.
    - The participant’s blood samples will be batched for analysis at the end of their 12-month follow up, so the test results will not be provided or available for their 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 the participant’s Austin Health UR, date of birth and medical history.
  + It may be necessary for some of the participant’s health information to be obtained from other health service providers (such as another hospital, a private pathology/radiology service, their General Practitioner or a consultant).
  + Although the information collected about the participant 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 the participant’s 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 or the participant be paid. The participant will be reimbursed for any of the following costs that they incur as a result of taking part in this research project such as parking.

Local doctor involvement

It is desirable that the participant’s local doctor be advised of your decision for them to take part in this research project. If the participant has a local doctor, we strongly recommend that you inform them of the participant’s participation in this research project. If you decide that the participant will take part in this research project, the study doctor will inform the participant’s local doctor.

**4 What does the participant have to do?**

There are no lifestyle or dietary restrictions for the participant while on this study. The participant should still take their regular prescribed medication.

To take part in this study, the participant will need to comply with standard post LT care as recommended by their treating clinicians. This will involve an initial inpatient admission post LT, follow up in the outpatient clinics and readmission to hospital if complications arise. The participant will need to have additional blood sampling when they 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 Does the participant have to take part in this research project?**

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

Your decision whether the participant can or cannot take part, or to take part and then be withdrawn, will not affect their routine treatment, their relationship with those treating them or their relationship with Austin Health.

If you do decide that the participant can 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?**

The participant does not have to take part in this research project to receive treatment at this hospital. If you do agree to the participant taking part in this study, they will receive routine follow up before and after LT as determined by their treating doctor. The participant’s study doctor will discuss these options with you before you decide whether or not they can take part in this research project. You can also discuss the options with the participant’s local doctor**.**

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

There will be no clear benefit to the participant from taking part 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 the participant becomes upset or distressed as a result of their 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 the participant’s test samples?**

You will be asked to provide additional consent for the collection of the participant’s 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 participant’s stored blood samples. This means that the blood samples 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, the participant’s study doctor will tell you about it and discuss with you whether you want the participant to continue in the research project. If you decide to withdraw the participant from the study, their study doctor will make arrangements for their regular health care to continue. If you decide the participant can continue in the research project you will be asked to sign an updated consent form.

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

**12 Can the participant have other treatments during this research project?**

Whilst the participant is taking part in this research project, they may not be able to take some or all of the medications or treatments they have been taking for their condition or for other reasons. It is important to tell the participant’s study doctor and the study staff about any treatments or medications they may be taking, including over-the-counter medications, vitamins or herbal

remedies, acupuncture or other alternative treatments. You should also tell the participant’s study doctor about any changes to these whilst the participant is taking part in the research project. The participant’s study doctor should also explain to you which treatments or medications need to be stopped for the time the participant is involved in the research project.

**13 What if the participant is withdrawn from this research project?**

If you decide to withdraw the participant from this research project, please notify a member of the research team before withdrawal. A member of the research team will inform you if there are any special requirements linked to withdrawing.

If you do withdraw consent during the research project, the study doctor and relevant study staff will not collect additional personal information from the participant, 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 up to the time the participant withdraws will form part of the research project results. If you do not want them to do this, you must tell them before the participant joins 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 the participant has the relevant follow up with their 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 the participant?**

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about the participant for the research project. Any information obtained in connection with this research project that can identify the participant will remain confidential.

The participant’s name will not be recorded in the database. We will assign a study number against their Austin UR number, and use that to re-identify their 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.

The participant’s 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 the participant may be obtained from their 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 the participant taking part in this research project.

The participant’s 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, the participant’s 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 the participant 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 participation in this research project may be recorded in the participant’s health records.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to the participant’s 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 the participant’s information.

Any information obtained for the purpose of this research project that can identify the participant 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 the participant suffers 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 the participant is eligible for Medicare, they 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 and the participant will not benefit financially from their involvement in this research project even if, for example, their 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 the participant from these discoveries.

No member of the research team will receive a personal financial benefit from the participant’s 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 the participant has any medical problems which may be related to their 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 - Person Responsible/Medical Treatment Decision Maker**

|  |  |
| --- | --- |
| **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 the participant taking part in this research project as described and understand that I am free to withdraw at any time during the project without affecting their future health care.

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

I give permission for the participant’s doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Austin Health concerning the participant’s 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 participant’s research project treatment, a request may be made for them to attend follow-up visits to allow collection of information regarding their health status. Alternatively, a member of the research team may request my permission to obtain access to the participant’s 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 the participant for use, as described in the relevant section of the Participant Information Sheet, for:

|  |  |  |  |
| --- | --- | --- | --- |
|  | | | **Initial** |
| * This specific research 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 Person Responsible/Medical treatment decision maker – for Person Responsible/Medical treatment decision maker who has read the information**

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| --- |
| Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Name of Person providing consent (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Relationship of Person providing consent to Participant \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Signature of Person providing consent \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_ |

**Declaration - for Person Responsible/Medical treatment decision maker 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 person responsible/medical treatment decision maker for the participant has understood that explanation.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
|  | 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 – Person Responsible/Medical treatment decision maker**

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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 Person Responsible/Medical treatment decision maker**

I wish to withdraw the participant from taking part in the above research project and understand that such withdrawal will not affect their routine treatment, relationship with those treating them or relationship with Austin Health*.*

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| --- |
| Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Name of Person providing consent (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Relationship of Person providing consent to Participant \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Signature of Person providing consent \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_ |

**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 person responsible/medical treatment decision maker for 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.