Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Princess Alexandra Hospital

Title	Feasibility and safety of topical Sirolimus in the prevention of skin cancer in solid organ transplant recipients (Protocol Name: TRANSIROTOP01)
HREC Reference Number	HREC/18/QPAH/356
Project Sponsor	The University of Queensland (Diamantina Institute)
Coordinating Principal Investigator	Associate Professor Kiarash Khosrotehrani
Principal Investigators	Associate Professor Scott Campbell Professor Adele Green Associate Professor Nicole Isbel
Location	Princess Alexandra Hospital Brisbane QLD

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project because you are an organ transplant recipient who has subsequently had multiple skin cancers such as BCC (basal cell carcinoma) or SCC (squamous cell carcinoma). The research project is testing whether Sirolimus cream applied to the skin can help in the prevention of skin cancers in organ transplant recipients.

To be eligible you must:

- be aged 18 years or older
- have received an organ transplant 12 months ago or earlier
- have had at least 5 SCCs or BCCs in the past 5 years
- currently have at least 5 keratotic lesions on the back of your forearm. These are typically scaly, sun-exposed lesions that may increase your risk of skin cancers.

However you *may not* be eligible if:

- your forearms have been treated with topical fluorouracil (e.g.Efudix), photodynamic therapy, ingenol (Picato) or imiquimod (Aldara) in the last 6 months

- you have received or are receiving Sirolimus orally
- you have a skin cancer on your forearm that requires treatment
- you have an open wound on your forearm that requires treatment
- the researchers consider you medically unstable

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 main idea of this research is to determine the safety and effectiveness of topical Sirolimus cream in solid transplant recipients at high risk of skin cancer.

Background

Keratinocyte carcinomas (e.g.BCC or SCC) are by far the most common form of cancer. People who have had a kidney or liver transplant are much more likely to get SCCs or BCCs that are caused by ultraviolet (UV) light when compared to people who have never had a transplant. Transplant patients require the long-term use of immunosuppressant drugs to prevent organ rejection however these drugs reduce the capacity of the immune system to repair or destoy UV-damaged cells, allowing these cells to develop into cancers. As a result keratinocyte cancers are a major cause of mortality, poor health, hospitalisation and cost.

Past studies have shown that Sirolimus, a new type of immunosuppressor, can reduce skin cancer rates. However it has serious side effects when taken orally. Dermatologists have in recent years used Sirolimus as a cream in some genetic skin disorders. Patients have had few side-effects and Sirolimus cream has been shown to be safe when used for long periods of time.

This study is designed to test whether topical Sirolimus (cream) will reduce skin cancer burden without having the serious side effects of systemic therapy (tablets).
This research has been initiated by the study doctor Associate Professor Kiarash Khosrotehrani. The research is being conducted by a team of researchers based at the University of Queensland (Diamantina Institute) in Woolloongabba, Brisbane and has been funded by the PA Research Foundation. This research is not sponsored by any commercial entity or industry.

3 What does participation in this research involve?

A dermatologist and transplant specialist have considered you eligible for this trial. Once you have read this Information Sheet you will be asked to sign a consent form.

Application of creams

This is a randomized placebo controlled trial. This simply means that the PAH pharmacy will randomly choose which of your forearms (right or left) will be treated with the Sirolimus cream and which forearm will be treated with the placebo (the cream which contains *no* medication). You will apply the creams to the back of your hands and wrists. You will be given tubes of cream which will be carefully labelled, describing which cream is for which forearm. You will be required to apply the creams every night at bedtime for 12 weeks.
No-one knows which tube contains the Sirolimus and it is only at the end of the study that this information will be shared with you and the research team. **It is extremely important for the success of the study that the creams are applied as directed by the dermatologist.**

Visits to the Transplant Skin Clinic at PAH
To monitor for changes in the skin on your forearms you will be required to visit the clinic on several occasions. Each visit will take approximately 30 minutes and where possible will coincide with your routine clinic visits.

- On your first visit and then 2, 4, 8, 12 and 24 weeks later the treated areas of your forearms will be photographed with a digital camera to record any changes in the surface and number of lesions. This is not painful.
- Approximately 24 weeks after the first cream application all participants will have two skin biopsies (4mm diameter), one from the treated area of each forearm. This will check for the activity of the drug and whether it may be preventing skin cancers. Local anaesthetic will be used. Researchers in the laboratory will examine and compare the biopsies to measure and compare the levels of skin thickness and signs of skin sun damage.
- At each visit you will be monitored for any possible side effects (most commonly skin dryness and irritation).

Blood tests
Approximately 2 and 12 weeks after the first cream application blood will be collected to check Sirolimus levels i.e. to check that you are not absorbing significant amounts of the medication. Electrolytes and other blood components that may indicate changes in your kidney or liver function will also be monitored as part of your routine care. The dermatologist will issue you with pathology request forms. These bloods can be done at the same time as your routine bloods. Fasting is not required.

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

Reimbursement
You may be reimbursed for any travel or parking associated with the research project visit.
You will be participating in a research project which is a 'phase 2' clinical trial. Clinical trials are research investigations in which people volunteer to test new treatments or tests to see if they prevent or manage a disease or medical condition. In a Phase 1 trial something is tested for the first time in a small group of people. If the results are promising, a larger group may be tested for effectiveness and side effects in a Phase 2 trial.

Oral Sirolimus has been shown to be effective in preventing keratinocyte cancers in previous clinical trials, as has Sirolimus cream effectively treated facial angiofibromas (non-cancerous tumours composed of blood vessels and tissue). This study is the next step in the research process and its purpose is to examine the suitability of an approach that is intended to be used in a larger scale study.

4 What do I have to do?

- You must apply the creams to the back of your hands and wrists as directed by your dermatologist.
- You are required to attend 6 sessions at the Transplant Skin Clinic at PAH within 6 months.
- You must have 2 skin biopsies, one from each forearm.
- You are requested to care for your biopsy wounds as directed by your dermatologist.
- You do not need to change your routine treatment or medications.

5 Other relevant information about the research project

- A total of 40 participants will be taking part in the project and they will be recruited over a 3-year period.
- PAH is the only site for this project.
- The project involves researchers from the Princess Alexandra Hospital and the University of Queensland (Diamantina Institute) working in collaboration
- If a skin cancer develops on your forearm/s during the study it will be treated as usual (but Sirolimus cream will not be re-applied to that area).

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 will not affect your routine treatment, your relationship with those treating you or your relationship with the Princess Alexandra 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 or any other Queensland hospital. The alternative is not to participate in this research. You will receive the same treatment and care as usual regardless of your decision.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research however:

- There may be a reduction in your risk of developing further skin cancers *in the treated forearm* (that is, the one to which Sirolimus cream was applied)
- This pilot study may pave the way for large-scale clinical trials of topical Sirolimus in organ transplant recipients.

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

- There is the possibility of an allergic or hypersensitive response to the Sirolimus cream e.g. dermatitis, asthma, allergic rhinitis (runny nose, sneezing)
- injection of the local anaesthetic for the biopsies may cause minor discomfort.
- there is a possibility that the wound may become inflamed or infected but the risk of this is reduced if wound care instructions are followed.

- There is a chance that the treatment may fail (that is, it will not result in any reduction in your skin cancer risk).
- Side-effects of Sirolimus are usually minor and include skin dryness, irritation and folliculitis (small pimples).
- Blood sampling may cause discomfort and bruising.

IMPORTANT:

In the unlikely event of a life-threatening reaction to Sirolimus cream (e.g. difficulty breathing, facial swelling) Emergency Services should be contacted by phoning 000. For all other possible side-effects and concerns please contact the Principal Investigator, Kiarash Khosrotehrani (phone numbers on page 7).

10 What will happen to my test samples?

Skin samples from the biopsies are an essential part of the research. The skin samples obtained for the purpose of this research project will be transferred to University of Queensland PC2 certified facility located at the Translational Research Institute (TRI) in Woolloongabba, Brisbane QLD. Storage within a secure laboratory can be assured as access is limited to authorised personnel only. All samples will be given a unique code (study number) and only the research team will be able to re-identify them (i.e. trace them back to you). Samples will be stored for a maximum of 7 years after the study and they will then be destroyed by incineration.

Your samples will not be used for commercial or profit-making purposes.

We are not performing any genetic testing on your skin or blood samples therefore there are no implications for you or your family.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new and important information becomes available about the treatment that is being studied. If this occurs you will be notified.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to use additional creams and laser or photodynamic therapy on the treated areas. These therapies may change the effectiveness of the cream and therefore the study results. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking.

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.

Your decision to withdraw will not affect your routine care and your relationship with your doctor.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include the treatment being shown to work and therefore not needing further testing, or publications of similar results which may seriously affect the significance of this study.

15 What happens when the research project ends?

Upon completion of the study the results will be published in a peer-reviewed journal. Information will be revealed for groups of participants: individual participants are never identified. All participants will receive a letter from the Principal Investigator.

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.

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.

Any information that can identify you (i.e. the consent form) will remain confidential and will only be used for the purpose of the research project. Consent forms will be stored in a locked compartment within the TRI facility. Your study records may be viewed for the purposes of auditing by members of the Ethics Committee.

Your skin samples will be given a study number or code (to match the code on the consent form) and only members of the research team will be able to access and re-identify them.

All information will be transferred to computer files that will be password protected and the entrance to the TRI facility will require key code access. This will ensure that only study personnel will be able to access your information. This information and documentation will be retained permanently by the university.

It is anticipated that the results of this research project will be published and/or presented in a variety of ways. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

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

In accordance with relevant Australian and QLD 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.

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 Associate Professor Kiarash Khosrotehrani. The project is being funded by the PA Research Foundation.
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 Metro South Health, Brisbane, QLD.

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 on 3443 7088 or any of the following people:

Clinical contact person

Name	Associate Professor Kiarash Khosrotehrani
Position	Principal Investigator
Telephone	(07) 3443 7088 or 0450997429
Email	k.khosrotehrani@uq.edu.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	HREC Co-ordinator
Telephone	3443 8047
Email	MSH-Ethics@health.qld.gov.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 details

Reviewing HREC name	Metro South Health
HREC Executive Officer	HREC Co-ordinator
Telephone	3443 8047
Email	MSH-Ethics@health.qld.gov.au

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Location	Princess Alexandra Hospital Brisbane QLD

Declaration by Participant

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 UQ Diamantina concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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

• **This specific research 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 study without affecting my future health care.

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

Name of Participant (please print) _____

Signature _____ Date _____

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.

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