Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Princess Alexandra Hospital (PAH)

Title	The effect of propranolol on melanoma blood vessels: A randomized controlled trial.
Short Title	The MELPROP Trial
Project Sponsor	The University of Queensland (Diamantina Institute)
Coordinating Principal Investigator	Professor Kiarash Khosrotehrani
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. This is because you have recently been diagnosed with a melanoma and have consented to have a sentinel biopsy. The research project is testing whether a drug commonly used for *other* health problems will block the formation of blood vessels in and around the tumour and related lymph nodes and therefore prevent the spread of melanoma. This drug is propranolol.

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 aim of this research is to determine whether the drug propranolol will prevent the spread of melanoma by disrupting the growth of blood vessels in and beyond the tumour.

Background

Your surgeon will have already talked to you about melanoma and why you are having a sentinel node biopsy. Your melanoma has grown and spread along the top layer of the skin and has begun to grow deeper into the second and thickest layer, the dermis. The dermis contains all of the blood vessels of the skin (arteries, veins and capillaries). These blood vessels supply nutrients and oxygen to the skin, remove waste and transport the vitamin D produced in the skin back to the rest of the body. The dermis also contains tiny vessels or tubes which carry lymph, a fluid that contains the infection-fighting cells of the immune system. Small clumps of lymph material - lymph nodes - are found in these vessels and remove bacteria and viruses from the lymph that flows through them.

If a melanoma reaches the lymph nodes and blood vessels, cancer cells may travel to other parts of the body. The lymph nodes are the most common site of spread or 'metastasis' (e.g. if melanoma on the upper arm spreads, it is most likely to spread to lymph nodes in the armpit). The 'sentinel' lymph node is the very first lymph node to receive drainage from that area. When lymph does its job to filter the skin, and drains an area of skin that contains melanoma, the sentinel lymph node is the one most likely to contain melanoma cells (if any lymph nodes are involved).

Our research team has recently made some important discoveries in relation to melanoma. They have identified (1) specific cells in blood vessels that are responsible for the formation of new blood vessels at the melanoma site (2) genes that are essential for this process and (3) the proteins that turn these genes 'on' or 'off'. Importantly, by using substances that disturb this process, they have discovered a way of reducing the chance of cancer spreading, by blood vessels, from the skin to other parts of the body. In this trial they plan to disturb the cancer spread by using a well known drug, propranolol.

Propranolol is approved in Australia. This tablet is most commonly used to lower blood pressure, prevent heart attacks and treat irregular heart beats. It is also used for migraine, tremor (shaking) or social anxiety. Propranolol is currently not approved to prevent the spread of melanoma. Therefore it is an experimental treatment for this purpose.

This research has been initiated by the study doctor Professor Kiarash Khosrotehrani.

The study is being conducted by a team of researchers based at the University of Queensland (Diamantina Institute) in Woolloongabba, Brisbane. This research is not sponsored by any commercial entity or industry.

3 What does participation in this research involve?

A melanoma specialist has considered you eligible for this trial. This is because:

- You have recently been diagnosed with a melanoma
- You have consented to have a sentinel node biopsy
- You are currently not taking, or have had no previous reactions to, propranolol (Deralin, Inderal) or to drugs in the same group (e.g. Acebutolol (Sectral), Atenolol (Tenormin), Bisoprolol (Zebeta), Metoprolol (Lopressor, Toprol-XL), Nadolol (Corgard), Nebivolol (Bystolic))
- You are not pregnant
- You are not an asthmatic

Once you have read this Information Sheet you will be asked to sign a consent form.

You will be participating in a randomized placebo controlled trial. 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).

You will be given either propranolol capsules or placebo capsules. A placebo is a medication with no active ingredients although it looks like the real thing.

This is also a double-blind trial. This 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 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.

Drug Administration

Once you have consented to the research project you will be supplied with the study drug during your visit to the Melanoma Clinic. You must take the study drug as directed by the research doctor. This will be one capsule 2 times per day (with breakfast then at bedtime) but only for the 2-3 weeks before your sentinel node biopsy.

Procedures

After the sentinel biopsy is collected the tissue will be sent to the pathology laboratory at PAH for review. It will be checked for the presence of cancer. For purposes of this research project a small portion of the sentinel node sample will later be transferred and stored at UQDI whilst it awaits analysis. This will in no way compromise your test results.

There are no other commitments i.e. no extra clinic visits, tests, procedures or questionnaires.

Additional Information

We request your permission to access your records during the trial, collecting in particular all information about your primary tumour and the sentinel node.

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

4 What do I have to do?

- You must sign the consent form provided by the research team.
- You must take the trial drug as directed by the research doctor.
- You do not need to change your routine treatment or medications.

5 Other relevant information about the research project

- A total of 24 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

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 this trial may pave the way for large-scale clinical trials of Propranolol in melanoma patients.

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

Propranolol is one of the most frequently used medications and is usually well tolerated. Any side effects usually don't last for too long and patients rarely have to stop taking it. The most common side effects are tiredness, lack of energy, slower than normal heart rate, cold or numb extremities (e.g. toes, fingers, nose) and sleep disturbances. Rare side effects include gastrointestinal upsets (poor appetite, nausea, vomiting, diarrhoea, abdominal pain), the heart not pumping as well as it should (e.g. shortness of breath, swollen legs/ankles), dizziness, worsening of asthma or a drug rash. 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.

10 What will happen to my test samples?

A sample of your sentinel node biopsy is an essential part of the research. The sample 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 biopsy 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?

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 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. As this is a 3-year project any results will not be known for at least 3 years from now.

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 biopsy sample 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 Professor Kiarash Khosrotehrani. The project is being funded by the Australian NHMRC (National Health and Medical Research Council). No member of the research team will receive any 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 following people:

Clinical contact person

Name	Christine Shen
Position	Nurse Unit Manager, Dermatology Department, PAH
Telephone	0430 278 237
Email	xiaohua.shen@health.qld.gov.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, 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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Short Title	The MELPROP Trial
HREC Reference Number	HREC/2019/QMS/51317
Project Sponsor	The University of Queensland (Diamantina Institute)
Coordinating Principal Investigator	Professor Kiarash Khosrotehrani
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 the University of Queensland (Diamantina Institute) 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 sentinel node biopsies 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