Place Patient Label Here

Participant Information Sheet & Consent Form

Interventional Study - *Adult providing own consent*

AUSTIN HEALTH

Title	**A double-blind, randomised, placebo-controlled trial to examine the biological effects of oestradiol depletion and to investigate the efficacy of denosumab in preventing microstructural bone decay in women with oestrogen-receptor-positive, non-metastatic breast cancer receiving oestradiol deprivation therapy**
Short Title	**The biological effects of oestradiol depletion and prevention of microstructural bone decay in women**
Protocol Number	**1**
Coordinating Principal Investigator	**A/Prof Mathis Grossmann**
Principal Investigators	**Dr. Sabashini Ramchand, Prof Jeffrey Zajac, Prof Ego Seeman, Prof David Handelsman**
Associate Investigators	**Mr. Ali Ghasem-Zadeh, Dr. Michael Ching, Dr. Belinda Yeo, A/Prof Shane White**
Location	**Austin Health and Repatriation Campus**

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research study. This is because you are premenopausal with oestrogen-receptor positive early breast cancer and are receiving endocrine therapy (ovarian suppression and aromatase inhibition) as part of your treatment. This research project is testing a treatment called denosumab, a bone strengthening medication, to prevent bone loss.

The 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?

Breast cancer is the most common solid tumour amongst women worldwide. Reducing oestrogen levels with endocrine therapy (ovarian suppression plus aromatase inhibition) is a very effective additional treatment in premenopausal women to treat breast cancer and reduce the risk of it coming back. Ovarian suppression is a treatment (either an injection or an operation to remove both your ovaries) that prevents your ovaries from producing oestrogen and aromatase inhibition is a medication that prevents other parts of your body, other than the ovaries, from making oestrogen. Therefore, the endocrine therapy that you will receive will reduce your body's oestrogen levels to almost zero.

Research has shown that in states where our body's oestrogen levels are low, such as menopause or postmenopausal women being treated with aromatase inhibition, women may experience bone loss/weakening leading to broken bones, gain of fat, inadequate handling of sugar by the body leading to diabetes, higher cholesterol levels and possibly decreased quality of life as a result of symptoms such as hot flushes, low or no interest in sex or joint pains. It has been shown that drugs that strengthen bone, such as denosumab, may lead to a decrease in the amount of bone lost during these states of low oestrogen in the body.

However, since ovarian suppression and aromatase inhibition is a relatively new treatment in *premenopausal* women with breast cancer, there are very few studies that have looked at the effect of this treatment on bone density, body composition, sugar handling, cholesterol levels and quality of life in this group of women specifically. Additionally, the effect of this treatment on bone structure has not been studied. This is important to know because bone structure is related to bone strength and resistance to bone breaking. Furthermore, the effectiveness of denosumab at preventing bone loss/weakening in premenopausal women treated with ovarian suppression and aromatase inhibition has also not been studied.

The aim of this clinical research study is to learn about the effects of reduced oestrogen levels on bone structure and to study what effect denosumab, a bone strengthening medication, has on bone structure over a 12-month period. Denosumab is a drug that has been approved by the Australian Federal Government for use in Australia to prevent bone loss.

Secondly, we also want to look at what this endocrine therapy does to body weight, body composition (amount of muscle and fat), the way the body handles sugar, cholesterol levels and quality of life.

This research has been initiated by the study doctor, Associate Professor Mathis Grossmann. The results of this research will be used by the study doctor, Dr Sabashini Ramchand, to obtain a higher degree (PhD).

3 What does participation in this research involve?

3.1 Study Design

You will be participating in a randomised controlled trial. This is a study that allows us to compare treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. We are enrolling 114 premenopausal women with early breast cancer being treated with ovarian suppression and aromatase inhibition. We will divide these women into two groups. One group will receive denosumab and the other group will receive placebo. A placebo is a medication with no active ingredients, it looks like the real thing but is not.

To try to make sure the groups are the same, each participant is put into a group by chance (random). You will have a one in two chance of being in either the denosumab group or the placebo group.

This is a double-blind study. 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.

3.2 Details of your involvement

We would need your agreement and signature on the consent form before doing any study assessments. All study assessments will be conducted at Austin Health/Heidelberg Repatriation Hospital.

After this, the initial steps will take about 30 minutes. These are:

- Medical Interview. One of our study doctors will ask about your medical history and the medications you are taking. We can get some of this information from your Austin Health medical record.

- Physical examination: height, weight, waist circumference, hip circumference, blood pressure and heart rate

If that information confirms that you are eligible for the study, we will do the first study assessment (this will take about 3 hours):

- Blood test. These are normal blood tests involving a small needle in your arm. This will be a fasting blood test which means you will be asked not to eat or drink for 8 hours prior to the test. We are checking hormone levels, electrolytes, kidney and liver function, vitamin D, bone health, blood sugar and insulin levels, and cholesterol levels. If you have a chance of becoming pregnant, a pregnancy test (βHCG) will also be done. 20ml of blood (4 teaspoons) will be collected in addition to your standard blood tests.

- DXA scan (dual energy X-ray absorptiometry): is a safe, painless test that will be performed to assess bone density at the forearm (radius), hip and spine and will also examine total body composition and fat mass. This will be performed at Austin Health (Heidelberg Repatriation Hospital) and will take approximately one hour of your time.

- HR-pQCT scan (high-resolution peripheral quantitative computed tomography) - is a new form of low radiation CT scan that will be performed to assess bone density and bone structure at the forearm and shinbone. This will be performed at Austin Health (Heidelberg Repatriation Hospital) and will take approximately one hour of your time.

- Quality of life questionnaire (this should take approximately 15 minutes to complete)

If you remain eligible for the study on the basis of your blood test results, you will be given your allocated subcutaneous injection (either 60mg denosumab or equivalent placebo). The injection will look the same so that neither you or your study doctor will know which treatment you have received. The injection will be administered by one of the study doctors.

You will have 3 other study visits during the 12-month study period.

3-month visit (1 hour)
- Medical interview, physical examination and blood tests as described above

6-month visit (4 hours)
- Medical interview, physical examination, quality of life questionnaire, blood tests, DXA scan, and HR-pQCT scan as described above.
- Subcutaneous injection of either 60mg of denosumab or equivalent placebo will be administered by a study doctor (this will be your last injection, total 2 injections for the duration of the study)

12-month visit (4 hours)
- Medical interview, physical examination, quality of life questionnaire, blood tests, DXA scan, and HR-pQCT scan as described above.

At this point the study is over and you will stop taking the treatment and continue to see all your usual clinics. Currently, it is not known whether there is a benefit in continuing denosumab long-term in premenopausal women unless they have a low trauma fracture/broken bone. Therefore, we will not continue denosumab after the study ends unless clinically indicated. This will be discussed with you during your usual clinic visits.

3.3 Costs and reimbursement

Additional Costs

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

Reimbursement

You may be reimbursed, upon production of a receipt, for any reasonable travel, parking, meals and other expenses associated with the research project visit.

3.4 Your local doctor

If you decide to participate in this research project, the study doctor will inform your local doctor.

4 What do I have to do?

Apart from attending the study visits for the assessments and treatments outlined above, there are no lifestyle or dietary restrictions. If you are a blood donor, you will be able to continue to donate blood.

You will continue to take all your regular medications. Certain medications would exclude you from participation in the study but we will make sure that you are not taking these before enrolment (these are steroid medications like prednisolone or dexamethasone and medication to treat osteoporosis). During the duration of the study, should you require these medications to be started, please discuss this with our study doctors first, as we may need to take you out of the study. We will not prevent you from taking any medications that you need for your medical care.

5 Other relevant information about the research project

This study is being conducted only at Austin Health. Overall 114 women such as you will participate in the study. The Austin Health researchers will be collaborating with Professor David Handelsman from the ANZAC Research Institute in Sydney to enable very accurate measurement of hormone levels in the blood samples.

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 participate, you will continue to receive all your usual care from all your regular clinics at Austin Health.

8 What are the possible benefits of taking part?

There will be no benefit to you from your participation in this research.

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

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

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

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

9.1 Possible risks associated with taking denosumab

Denosumab has been approved by the Australian Therapeutics Goods Administration (TGA) for the following indications:

1. Denosumab 60mg every 6 months for prevention of bone loss in (i) any adult (irrespective of age) who has sustained a minimal trauma fracture or (ii) women or men ≥ 70 years who have osteoporosis

2. Denosumab 120mg every 4 weeks for (i) secondary prevention of metastatic breast/prostate cancer irrespective of age or (ii) adults with inoperable giant cell tumour of the bone

Denosumab is given as a subcutaneous injection either in the arm or the abdomen; it is very similar to a 'flu shot'. Having a drug injected may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

Hypersensitivity/Anaphylaxis

With all medications there is a risk of anaphylaxis or hypersensitivity to the medication. There have been rare events of drug related hypersensitivity/anaphylaxis reported with denosumab. You will be asked to monitor closely for symptoms such as dizziness; wheezing or difficulty breathing; shortness of breath; throat tightness; swelling of your face/lips/tongue/throat/other parts of the body; itchy skin; hives; or a rash. If any of these symptoms develop, you must seek urgent medical care. If an anaphylactic or other significant allergic reaction occurs, you will receive appropriate medical treatment, denosumab/placebo will be discontinued and you will be withdrawn from the trial.

Denosumab preparation contains the inactive ingredients acetate, sodium hydroxide and sorbitol. Participants who have allergic reactions/adverse events to these substances should not participate in the study.

Other Adverse Reactions

Denosumab has been studied in over 10 500 women with postmenopausal osteoporosis in clinical trials for up to 8 years of continued treatment. In the 2 major phase III trials that assessed the safety of denosumab in 7808 women aged 60-91 and 322 women aged 43-83, the incidence of serious adverse events with denosumab was 25.3% compared to 24.3% in the placebo group (group that did not receive denosumab).

The most common adverse events reported in studies, occurring in **greater than or equal to 10%** of postmenopausal women (total number = 8,091) in either the denosumab group or the placebo group were not considered serious. These are: back pain (34.1% denosumab, 34.0% placebo), joint pain (20.4% in each group), high blood pressure (15.3% denosumab, 16.1% placebo), nasal congestion/runny nose/sore throat (14.8% denosumab, 15.6% placebo), pain in arms/legs (11.8% denosumab, 11.2% placebo) and osteoarthritis (10.9% denosumab, 11.1% placebo).

Adverse events reported in **at least 2%** of postmenopausal women (total number = 8,091) and **at least 1% more frequently in the denosumab treated women than in the placebo treated women were**: elevated cholesterol levels (7.0% denosumab, 5.9% placebo) and eczema (includes dermatitis, allergic dermatitis, atopic dermatitis and contact dermatitis) (3.1% densumab, 1.7% placebo).

Low calcium levels: 2 out 4050 patients (0.05%) had low levels of calcium after denosumab. Low calcium levels usually occur as a result of being vitamin D deficient or decreased kidney function. If you have decreased kidney function (eGFR<45ml/min/1.73m^2) or are known to have low calcium levels, you will not be able to participate in the study. All study participants will have

their vitamin D levels checked before being administered with either denosumab or placebo to ensure that they are at an adequate level.

Skin infections: Although very uncommon, skin infections needing hospital treatment were reported slightly more frequently in the denosumab group (16 of 4050, 0.4%) versus the placebo group (3 of 4041, 0.1%). These cases were mostly cellulitis.

Atypical femoral fracture – a minimal trauma fracture of the thigh bone that occurs in a different location and is of a different type of fracture compared to thigh bone fractures that occur with osteoporosis. In the largest and longest study to assess the safety of denosumab, 3004 women were treated with denosumab for a total period of 5-8 years. Out of these 3004 women, 2 women developed atypical femoral fractures. One woman developed an atypical fracture after 7 years of treatment (14 doses of denosumab) and the other woman developed an atypical femoral fracture after 3 years of treatment (6 doses).

Osteonecrosis of the jaw - a poorly healing, sometimes painful jaw bone disorder. This has been reported very rarely with denosumab. In one of the largest and longest studies assessing the safety of denosumab, out of 3879 postmenopausal women treated with denosumab for 8 years, 8 women developed osteonecrosis of the jaw. Good oral hygiene and regular dental care is important to reduce the risk of osteonecrosis of the jaw.

Fertility/Hormone Profile

In animal studies, female fertility and menstrual cycles were not affected by denosumab even at doses much higher than what we would normally use. Additionally, progesterone, oestradiol and luteinising hormone levels were also unaffected by denosumab. No data are available on the effect of denosumab on human fertility.

Pregnancy/Breastfeeding

The effects of denosumab on the unborn child and on the newborn baby are not known. Because of this, it is important that you are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the study if you are pregnant or trying to become pregnant, or breast-feeding. If child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project and at each study visit. If you do not take your endocrine therapy (ovarian suppression and aromatase inhibition) all the time ie you miss doses, you are strongly advised to use effective contraception during the course of the study. You should discuss methods of effective contraception with your treating doctor. If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

Please also carefully read the consumer medicine information on denosumab, which you will receive together with this Participant Information Sheet and Consent Form, and ask any questions you may have.

9.2 Other possible risks

a) Placebo injection - we do not expect any side effects from the placebo subcutaneous injection. Some minor discomfort, bruising, minor infection or bleeding is possible. If this happens, it can be easily treated.

b) Blood tests - collection of blood samples with a needle may be associated with minor discomfort at the site of blood collection, bruising, minor infection or bleeding. If this happens, it can be easily treated.

c) DXA scan (dual energy X-ray absorptiometry) - it is a safe, painless procedure that is used for monitoring bone density in patients.

d) HR-pQCT scan (high-resolution peripheral quantitative computed tomography) - this is a new form of CT scan that is used for assessing bone density and structure. It is safe and painless but requires you to lie still for 5 minutes.

This research study involves exposure to a very small amount of radiation from DXA and HR-pQCT scans. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The total effective dose from this study is about 0.042 mSv. At this dose level, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be minimal.

9.3 Risk of diagnosing a previously unknown condition

Assessments done in this study (medical interviews, physical examination, blood tests, scans) are for research purposes and not clinical care. However, there is a possible risk that we might find something unexpected that will have implications for your health. If this occurs, you will be notified of this result and, if required, medical care will be available at Austin Health.

10 What will happen to my test samples?

10.1 What will happen to my blood samples?

A mandatory part of participation in this study is the collection of blood samples.

Most of your blood samples will be analysed by Austin Health Pathology on the day that blood is collected from you and then these samples will be discarded within 14 days. The results of these tests will go into your Austin Health medical record and also be collected separately in your study file.

Each time you have a blood test for this study, 3 tubes (20ml, 4 teaspoons) will be stored in a locked freezer in the Austin Health Endocrine Department Laboratory. Your blood will be stored by a coded study number. External organisations/researchers, such as the ANZAC Research Institute, will not be able to identify you using this study number. Your study number will be linked to your hospital record number on a password-protected file on a University of Melbourne, Department of Medicine-Austin Health server. This means that your study doctors will be able to re-identify you in order to gain access to your clinical information recorded in your paper or electronic medical record during this research project. All personnel reviewing your sample results and medical records will be required to keep all the information confidential in accordance with the law.

At the end of the study, some of these frozen samples will be sent to the ANZAC Research Institute laboratory in Sydney where Professor Handelsman will supervise the hormone tests and send the results back to us. These results will be entered into your study file. Your blood will not be sold by Austin Health, however the ANZAC Research Institute will charge study doctors a fee to recover some of the costs of analysing the samples. Blood samples will be discarded by the ANZAC Research Institute within 14 days of analysis.

The rest of the frozen samples will be stored indefinitely in the locked freezer in the Endocrine Department Laboratory. This is in case any blood tests need to be repeated and in case a new research question arises which we could answer by going back to these old blood samples.

In the Consent Form below, we ask you to consider whether you will allow this indefinite storage of your blood samples for future unspecified research. Any future research would not be conducted without first being approved by the Austin Health Human Research Ethics Committee.

You may wish for your blood samples to be used for this study only, and not consent to future use of your blood samples. You have this option in the Consent Form below.

10.2 What are the possible benefits of storing my blood for future research?

It is unlikely that future research done using your blood samples will provide you or your family with a direct benefit. The results generated by research are expected to be of interest only to the researchers. They are not expected to have an effect on the outcome of your disease or response to treatment. Because your samples will be stored indefinitely and be made available for future research, they may not be used for many years, until new research approaches or techniques are developed. Therefore, any benefit might not be to you but to future generations.

10.3 What are the possible risks of storing my blood for future research?

Genetic analysis involves the study of genetic material (DNA and/or RNA), which is shared with your blood relatives. Some genetic research has the potential to identify genetic abnormalities that might have implications for family members. If a genetic abnormality (also known as a mutation) is detected that has relevance for a living participant or family member, the Austin Health Human Research Ethics Committee will be informed and guidance be will sought on how best to communicate this information to you and your family.

10.4 What if new information arises from my blood stored for future research?

Discoveries arising from research carried out using your sample are not expected to have medical importance for you and your family. The vast majority of research projects that will use your samples are unlikely to reveal anything of medical importance specifically for you or your family. However, if such a discovery is made, the researcher is required to inform the Austin Health Human Research Ethics Committee. The committee will examine the research data and decide whether or not it may be in your interests for you to be contacted.

10.5 Do I have to have my blood stored for future research and can I withdraw consent later?

Providing consent to have your blood stored for future research in our women's health databank is voluntary. If you decided to participate and later change your mind, you are free to withdraw from the project at any stage. You would need to notify a member of the research team so that any samples still remaining can be destroyed. Please contact the study team member named at the end of this document if you would like to withdraw your consent. It would not be possible to withdraw research information that has already been published.

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 decided 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?

It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins, or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

13 What if I withdraw from this research project?

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

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. 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 reasons such as:

- Unacceptable side effects
- The drug being shown not to be effective
- The drug being shown to work and not need further testing

15 What happens when the research project ends?

When the research project ends, you will be un-blinded. This means you will find out whether you were receiving the denosumab or placebo during the study. Currently, it is not known whether there is a benefit in continuing denosumab long-term in premenopausal women unless they have a low trauma fracture/broken bone. Therefore, we will not continue denosumab after the study ends unless clinically indicated.

All participants in the study will be invited to have ongoing monitoring and management of their bone health in our Adjuvant Endocrine Breast Cancer clinic where they will receive individualised assessment and management advice regarding their bone health and other potential side effects of ovarian suppression and aromatase inhibition. Any abnormal results that may be of relevance for your health will be discussed with you and, provided you consent, will be forwarded to your treating doctor.

The results of the study may be published in academic journals. You will not be identified in these publications. The research staff can let you know the results of the study when they are available.

Part 2 How is the research project being conducted?

16 What will happen to the 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 and securely stored. Only the researchers named above will have access to it and it will only be disclosed with your permission. Information on paper will be stored in a locked filing cabinet within a locked office located at Austin Health. Your information will be stored in a folder that will contain a study number only and not your name. The code to match up names with study numbers will be kept electronically. Electronic information such as this will be stored on a password protected computer system on a server at The University of Melbourne – Austin Health. Your paper and electronic data will be stored for 15 years following completion of this study. At the end of 15 years, the information that is purely for this study (i.e. that does not also form part of your Austin Health medical record) will be permanently destroyed (deleted or shredded)

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

Your health records and any information obtained during the study are subject to inspection (for the purpose of verifying the procedures and the data) by the Australian Government's Therapeutic Goods Administration (TGA), or Austin Health Human Research Ethics Committee, 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. This is because results will be published in aggregate only and include no features that could identify any individual participant.

In accordance with the Australian and/or Victorian privacy Laws and other relevant laws you have the right to access the information collected and stored by the researchers about you. 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

17.1 Complaints

If you have a complaint about any aspect of your medical care or treatment at Austin Health please raise this with your doctor directly. If this is not possible or does not resolve the complaint, then the Centre for Patient Experience will help you. You can speak to a consumer liaison officer at the Centre for Patient Experience by calling (03) 9496 3566.

17.2 Treatment Available

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?

The names of the researchers are listed at the top of the first page. All of the researchers except Professor D Handelsman work at Austin Health. Associate Professor M Grossmann designed the study, and he is in charge overall. Some of the blood samples will be sent to Sydney where Professor Handelsman who works at the ANZAC Research Institute will analyse them. Dr S Ramchand is a PhD candidate at the University of Melbourne-Austin Health. This study will form part of her PhD thesis and she will be responsible for the day-to-day running of the study.

This study has been approved by Austin Health. Funding for the study comes from Associate Professor M Grossmann's research fund.

18.1 Financial benefit from this research

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.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Austin Health, 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 that may be related to your involvement in the project (for example, any side effects) you can contact:

Clinical contact person 1

Name	Dr Sabashini Ramchand
Position	Principal Investigator
Telephone	03 9496 5000 or 0478 168 578
Email	sabashini.ramchand@austin.org.au

Clinical contact person 2

Name	Associate Professor Mathis Grossmann
Position	Coordinating Principal Investigator
Telephone	03 9496 5000
Email	mathisg@unimelb.edu.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:

Complaints Contact Office

Name	Complaints contact person
Position	Office for Research
Telephone	03 9496 4090
Email	ethics@austin.org.au

If you need to contact the Human Research Ethics Committee that approved this project, then you may contact:

Reviewing HREC and Local HREC Executive Officer

Reviewing HREC name	Austin Health Human Research Ethics Committee
HREC Executive Officer	Chelsea Webster
Telephone	03 9496 3248
Email	ethics@austin.org.au

Place Patient Label Here

Consent Form - *Adult providing own consent*

Full Study Title	**A double-blind, randomised, placebo-controlled trial to examine the biological effects of oestradiol depletion an to investigate the efficacy of denosumab in preventing microstructural bone decay in women with oestrogen-receptor-positive, non-metastatic breast cancer receiving oestradiol deprivation therapy**
Protocol Number	**1.0**
Coordinating Principal Investigator	**A/Prof Mathis Grossmann**
Principal Investigators	**Dr Sabashini Ramchand, Prof Jeffrey Zajac, Prof Ego Seeman, Prof David Handelsman**
Associate Investigators	**Mr. Ali Ghasem-Zadeh, Dr. Michael Ching, Dr. Belinda Yeo, A/Prof Shane White**
Study Site:	**Austin Health and Repatriation Campus**

Declaration by Participant

I have read the Participant Information Sheet. 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 Austin Health concerning my disease 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 study treatment or withdraw from the study, the information collected from me already will be used as part of the results of the study, although no new information will be collected.

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 _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

*Witness is not to be the investigator, a member of the study team or their delegate and must be 18 years or older.

THE UNIVERSITY OF MELBOURNE

Austin Health

Place Patient Label Here

Declaration by Participant related to use of blood samples

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

	This specific research project only
	This research project and any future research EXCEPT genetic testing
	This research project and any future research INCLUDING genetic testing

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to
Participant's Signature (please print) _____

Signature _____ Date _____

*Witness is not to be the investigator, a member of the study team or their delegate and 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.

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

Full Study Title	**A double-blind, randomised, placebo-controlled trial to examine the biological effects of oestradiol depletion an to investigate the efficacy of denosumab in preventing microstructural bone decay in women with oestrogen-receptor-positive, non-metastatic breast cancer receiving oestradiol deprivation therapy**
Protocol Number	**1.0**
Coordinating Principal Investigator	**A/Prof Mathis Grossmann**
Principal Investigators	**Dr Sabashini Ramchand, Prof Jeffrey Zajac, Prof Ego Seeman, Prof David Handelsman**
Associate Investigators	**Mr. Ali Ghasem-Zadeh, Dr. Michael Ching, Dr. Belinda Yeo, A/Prof Shane White**
Study Site:	**Austin Health and Repatriation Campus**

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.

Name of Participant (please print) _____

Signature _____ Date _____

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

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.

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.