MonashHealth

PARTICIPANT INFORMATION AND CONSENT FORM (PICF)

Title	*Assessing the Risk Factors of Atypical Femoral Fracture*
Co-ordinating Principal Investigator	*Professor Peter Ebeling*
Co- Investigator	*A/Prof Carola Zillikens* *Prof Richard Sinnott* *Dr Fran Milat* *Dr Hanh Nguyen* *Dr Rick Dell*

Version 1 Dated 5 October 2015

1. Introduction

You are invited to take part in this research project to assess the risk of Atypical Femoral Fractures. This is because you have a history of Atypical Femoral Fractures that may have occurred in association with the use of medication used to treat osteoporosis, such as bisphosphonate or denosumab therapy. We are inviting you to participate in the genetic research on Atypical Femoral Fractures.

This Participant Information and Consent Form (PICF) tells you about the research project. It explains the tests 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 you take part or not.

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 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 genetic research?

Genes are made of DNA – the chemical structure carrying your genetic information that determines many human characteristics such as the colour of your eyes or hair. Genetic research is the study of human DNA to find out what genes contribute to diseases, such as Atypical Femoral Fractures associated with bisphosphonates. Understanding how genes relate to diseases may also explain why some people respond differently to a treatment or

medication, and why some people experience a side effect and others do not. Genetic research may discover a gene test that may allow better detection, treatment and hopefully prevention of diseases.

3. What is the purpose of this research?

With this genetic research we hope to discover whether variation in genes between people can explain why some individuals treated with bisphosphonate medication experience Atypical Femoral Fractures.

Bisphosphonates are potent and widely used osteoporosis medication and are effective at preventing fractures due to osteoporosis. Over the last 7 years, studies have raised concern that these medications may very rarely cause Atypical Femoral Fractures. These are stress fractures along the thigh-bone that occur with minimal or no trauma. Although this is a rare complication, they can result in long-term immobilization, be associated with delayed healing, or occur in the opposite thigh-bone as well.

The mechanisms leading to Atypical Femoral Fractures are not well understood, but it has been established that bisphosphonate therapy play a role. A few genes have been linked with the development of Atypical Femoral Fractures and other rare bone disorders. This is the focus of this research project and we will look at a range of genes to see if they contribute to the risk of these fractures.

This will be the first study to investigate whether variation in genes can cause Atypical Femoral Fractures in individuals treated with bisphosphonate medications. The results from this study may lead to the discovery of a gene test that could identify patients at risk of AFF. This could potentially guide patients and their clinicians on the appropriate medication to treat osteoporosis.

4. What does participation in this research involve?

Your participation in this research involves:

- Being provided with adequate information to decide whether or not you would like to participate in this study. If you agree to take part in this study, provide your consent to participate and sign the Participant Information and Consent Form;
- Completing a brief Patient Questionnaire Form regarding your health and history of osteoporosis;
- Allowing us to review your medical records, laboratory results and radiology investigations;
- Attending Monash Medical Centre to have a blood sample collected for genetic testing. We will require 20mL, or 4 teaspoons, to be collected. This blood sample will be used in genetic testing and a portion will be stored at Monash Medical Centre. The genetic analysis will involve looking at a large number of genes for variation;
- Completing a Dual-energy X-ray Absorptiometry (DXA) scan to measure your bone density if you have not had measurements within the last two years with your doctor. This is a routine test for monitoring osteoporosis;
- Completing a High Resolution Peripheral Quantitative Computed Tomography (HRpQCT) scan to measure your bone quality;

- Storing your blood sample and health information for future related research studies. Further information can be found in this document's section 11 on 'Banking' and is an optional component of this study.

If you live a substantial distance away from the study centre, but would still like to participate in this genetic research, we can arrange for an investigator to contact you via telephone to discuss your participation in the study and obtain your consent to participate over the telephone. This will involve you and the investigator signing separate copies of the consent form at the same time on the telephone. We will ask you to return your signed original to us and will collate this with the investigators signed original. We will send you a copy of the final document for your records along with a 'Pathology Request Form' for you to take to your local pathology provider, who will collect the blood sample and return it to us.

You will not incur any costs to complete the tests in this study, nor will you be paid for your participation in this research.

You are not required to make any changes in your lifestyle to participate in this research. No follow-up appointments are required.

5. What will happen to my samples?

When you consent to participate in this research you will be allocated a study participant number that will be used to label your test samples and study documentation. This ensures that personal information will not be recorded on your blood samples, and that the samples will be coded, which ensures that your privacy and confidentiality are protected. Researchers will only have coded information and will not have access to your identity.

These blood samples will be processed and a sample sent for genetic testing to the Human Genomics Facility in Erasmus Medical Centre in the Netherlands. From the blood collected, we will extract DNA (genetic material) to gain understanding on how variation in genes between people can cause Atypical Femoral Fractures. A range of genes will be tested and the results will be securely entered into a database for analysis.

We would like to store your blood sample securely at Monash Medical Centre for use in any future approved research studies that may or may not be related to the original research project. Further information can be found in this document's section 12 on 'Banking'.

6. Do I have to take part in this research?

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.

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.

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 your treating hospital.

7. What are the possible benefits of taking part?

There will not be any direct benefits to you in participating in this research. However, the study findings may provide valuable information to improve the diagnosis, treatment, prevention or care of people who have Atypical Femoral Fractures in the future.

8. What are the possible risks or disadvantages?

Blood sampling

Having a blood sample collected may cause some discomfort or bruising. Rarely, there could be a minor infection or bleeding. If this happens, it can be easily treated.

Genetic Testing

Genetic testing may raise important issues and it is important for you to carefully consider these before agreeing to participate.

Genetic testing in this research study will look at variation in many genes. Generally, the results from this study will not result in useful information about your future health risk or the health of your family members or offspring. As such we will not generally tell you the results of the studies on your samples.

Rarely, we may incidentally uncover a gene variation that may raise the possibility that you are at risk of other conditions in the future that is not related to this study. A panel of doctors, geneticists and scientists will review all incidental gene changes to see if they may be significant to your health. As the genetic test conducted in this study is for research purposes only, any incidental gene variation will need to be confirmed with an approved genetic service.

If we learn something that may have significance to the health of yourself or your family, you can have the choice to be notified of this information. The coded data can then be re-linked to your identity and contact details and you can be referred to genetic services outside this research project. The genetic services we refer you to will contact you to discuss the possible medical findings, arrange confirmatory testing, provide genetic counselling, and discuss the implications for you and your family. This may influence your decision to have children or you may be faced with the decision to make the family aware of the existence of genetic information. Family members may or may not wish to know this information.

You do not have to have this information returned to you if you do not want to. If you decide you would like to be notified about this information we will ask you to sign this section at the end of the form. In case we are unable to contact you, you can nominate your general practitioner or other medical professional to be contacted if any significant results arise in this study.

Statutory or contractual duties may require you to disclose results of genetic tests or analysis to third parties (for example, insurance companies, employers, financial and educational institutions), particularly where results provide information about health prospects. If the results are not available or you choose not to have results given to you, then your future requests for insurance will not be affected by participating in this research. If you do obtain results to your genetic tests you may then be obliged to disclose this on any future application for insurance or employment should it be requested.

DXA scan

You may be asked to undergo a DXA scan to measure your bone density. This is a routine scan to diagnose osteoporosis and you may have had this scan before.

HRpQCT

You may be asked to travel to Austin Health or Monash Health to do a further scan to measure the quality of your bones. This will be booked on a separate day and will take approximately 15 minutes to complete.

If you are having your scan done at Monash Health the following wording applies:

This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisievert (mSv) each year. The effective dose from this study is about 0.005 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.

If you are having your scan done at Austin Health the following wording applies:

This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisievert (mSv) each year. The effective dose from this study is about 0.120mSv. 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. What is the potential impact on my family if I take part?

Any information you give us will be kept confidential and we will not contact your relatives without your permission. As explained in section 8 of this document, if genetic testing in this study uncovers a genetic change significant to your health and you have requested results be returned to you, you may be faced with the decision to tell your family member. You will be provided with support from genetic services if this arises.

10. Will I be given the results of the research project?

You will not generally be given your individual genetic test results because the research on Atypical Femoral Fractures is still in an exploratory phase and the reliability of the results is unknown. However, as outlined in section 8 of this document, if we uncover a genetic change unrelated to our study on Atypical Femoral Fracture which might affect your health or the health of your family members, we would only inform you of this genetic change if you have requested this at the time of consent.

Otherwise, your results from any radiology scans completed for this research project will be forwarded to yourself and/or preferred physician.

We will not routinely give participants the final research project findings. You are welcome to contact the principle researcher to request information on study outcomes.

11. Banking (Long term storage of samples and health information)

In addition to participating in this study, we would like to seek your permission to "bank" your health information and blood sample for future research. "Banking" is storing health information and/or blood or tissue for future research studies. A "bank" is the place where the health information and/or blood or tissue is stored. The purpose of storing your blood sample in a bank is to answer questions in the future, particularly when new technology or genetic testing techniques are available.

The study doctor will store your leftover blood sample at Monash Medical Centre along with samples for many other people. Your blood sample will be stored for 15 years after the research project is over. Your blood sample and health information will be stored as individually re-identifiable specimens. This means that your sample will be coded and personal information removed so that the bank will not know your identity unless the sample is un-coded. You can decide to have it removed, destroyed or returned to you anytime by contacting the study doctor, Professor Peter Ebeling, in writing at the Department of Medicine, Monash Medical Centre, 246 Clayton Road Clayton Victoria 3168.

In the future, other doctors and scientists at this and other medical and research centres may use your coded health information, scan results and/or blood sample in future research projects that are an extension or closely related to this original project. We will not use your personal health information for a different research project without the permission of a Human Research Ethics Committee. Once all personal identification is removed, the coded information might be used or released for other purposes without asking you. Results of the research project may be presented in public talks or written articles but information will not be presented that identifies you.

The process of banking is part of the main research project. There is no direct benefit to you from banking your information, nor is there any extra physical risk to you.

If you agree to 'bank' your health information and blood sample, we will ask that you sign this section at the end of the document.

12. 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 inform you if there are any special requirements linked to withdrawing.

If you decide to leave the project, the researchers would like to keep information collected from you regarding your health information and your results from the genetic test. This is to help them make sure that the results of the research can be measured properly. If you do not want them to do this, you must tell them before you join the research project.

13. What else do I need to know?

- **What will happen to information about me?**

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law. Information about you may be obtained from your health records held at this, and other, health services for the purposes of this research.

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 relevant authorities and authorised representatives of the University of Melbourne, the Melbourne Health HREC**,** this organisation (Monash Health) or as required by law. By signing the consent section, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

Information collected from you during the study will be recorded in a re-identifiable coded form. This data will be stored for a period of 15 years after the research project is over. Only researchers involved in this research project will have access to this coded data. At the end of the storage period all data will be destroyed according to the institutions disposal of confidential data.

- **How can I access my information?**

In accordance with relevant Australian and/or Victorian privacy 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 one of the researchers named at the end of this document if you would like to access your information.

- **What happens if I am injured as a result of participating in this research project?**

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.

- **Is this research project approved?**

The ethical aspects of this research project have been approved by the Melbourne Health Human Research and Ethics Committee.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

14. Who can I contact?

For further information or appointments:

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, you can contact the Co-ordinating Principal Researcher Prof. Peter Ebeling on (03) 8572 2570.

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 the Ms. Deborah Dell, Manager, Human Research Ethics Committee, Monash Health, by telephone (03) 9594 4605.

Thank you for considering taking part in this study.

Full Project Title: Assessing the Risk Factors of Atypical Femoral Fracture
Principal Researcher: Prof. Peter Ebeling

Declaration by participant

I have read, or have had read to me in a language that I understand, this document and I understand the purposes, procedures and risks of this research project as described within it.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Monash Health concerning my disease and treatment that is needed for this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

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

Receiving information in relation to my genetic materials

If research with my DNA and/or tissue reveals some other medical condition that is significant to my health or the health of my family or future offspring:	***Yes***	***No***
a) I wish to be informed	□	□
b) If I cannot be contacted, I request that my nominated medical professional be informed of this information	□	□

Name:…….....

Contact number:…….....Contact address:……..

Consent to Banking

I consent to the storage and use of health information, DNA, and blood samples taken from me for use in:	***Yes***	***No***
a) this project and other research projects that are closely related to this research project.	□	□
b) additional undetermined Human Research Ethics Committee approved future research as described in sections 11 of this document.	□	□

Participant's name (printed) ……

Signature…….Date……..…..

Name of witness to participant's signature (printed) ……..…

Signature……..Date……

Declaration by 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.

Researcher's name (printed) ……..…

Signature……..Date……

** A senior member of the research team must provide the explanation and provision of information concerning the research project.*

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

MonashHealth

Revocation of Consent Form

Full Project Title: Assessing the Risk Factors of Atypical Femoral Fracture

Principal Researcher: Prof. Peter Ebeling

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I hereby wish to WITHDRAW my consent to participate in the research proposal named above and understand that such withdrawal WILL NOT jeopardise any treatment or my relationship with Monash Health.

I request that my genetic sample collected be destroyed.

Participant's Name (printed)……..

Signature Date

Name of Witness (printed) ……

Signature Date