PARTICIPANT INFORMATION SHEET AND CONSENT FORM

CLINICAL TRIAL

Effect Pentoxifylline and Vitamin E on throat strictures treated by endoscopic dilatation

Invitation

You are invited to participate in a research study investigating whether combination of Pentoxifylline and Vitamin E improve throat strictures treated by endoscopic dilatation.

The study is being conducted by:

Department of Gastroenterology & Hepatology

Dr Michal Szczesniak

Dr Peter Wu

Prof Ian Cook

Department of Radiation Oncology

A Prof Julia Maclean

A Prof Peter Graham

Before you decide whether you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. What is the purpose of this study?

Treatment for head and neck cancer with radiotherapy often results in formation of rigid scar tissue in the throat which causes narrowing and problems with swallowing. Current treatment is called a dilatation and involves stretching of the throat to break open this scar tissue. While the response rate is good (75%) it is not durable with a relapse rate of 50% at 19 months.

The purpose of this study is to gather preliminary information and determine the feasibility of a large trial testing whether a combination of a drug Pentoxifylline with Vitamin

E taken after dilatation improves the effectiveness of the dilatation treatment and makes the effects longer lasting.

2. Why have I been invited to participate in this study?

You have been invited to participate in this study because you have been treated with radiotherapy for head and neck cancer and have problem swallowing. Your doctor suspects this problem is caused by scar tissue in your throat and should be treated with dilatation.

3. What if I don't want to take part in this study, or if I want to withdraw later?

Participation in this study is voluntary. It is completely up to you whether you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

New information about the treatment being studied may become available during the course of the study. You will be kept informed of any significant new findings that may affect your willingness to continue in the study.

If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason. However, it may not be possible to withdraw your data from the study results if these have already had your identifying details removed. The data will be de-identified once all participants have completed the study, we expect this to happen no earlier than July 2020.

4. What does this study involve?

If you agree to participate in this study, you will be asked to sign the Participant Consent Form. Your involvement in this research project will be approximately 12 months and the duration of the entire research project will be 2 years.

If you agree to participate in this trial, you will then be asked to undergo the following procedures:

i) Endoscopic dilatation(s): This is recommended regardless whether you decide to participate in this study or not and will be carried out at Day Surgery/Endoscopy Unit of St George Hospital. The risks and benefits of the procedure will be explained to you by your physician and you will need to sign a separate consent form. You can speak with your doctor about any questions you may have regarding this procedure.

Depending on how severely narrowed your throat is, endoscopic dilation procedure might need to be repeated several times. Typically, patients require 3 to 4 procedures in fortnightly intervals. Your treating doctors will be able to tell you how many dilatations you are likely to need following the initial gastroscopy.

ii) Pentoxifylline and Vitamin E treatment

After your last endoscopic dilatation, you will be randomized to receive tablets containing combined Pentoxifylline and Vitamin E or inactive placebo tablets. A placebo is a treatment that looks like the genuine medicine but contains no active ingredient. The chance of receiving active drug is 50%. You will need to take these tablets as prescribed for 12 weeks.

The treatment being investigated in this study differs from the standard treatment offered in this institution because of its use of combination of two agents that have been found to have properties that may be useful in treating problematic scarring caused by radiotherapy.

The trial is ‘randomized’ meaning that sometimes doctors don’t know the best way of treating patients with a particular condition, so comparisons need to be made between different treatments. To do this, study participants are put into groups and given different treatments, and the results are compared to see whether one treatment is better. To ensure the groups are similar to start with, a computer allocates each study participant into a group randomly, like the flip of a coin. Neither the doctor nor the study participant can decide which treatment the participant receives.

The trial is also ‘double blinded’ meaning that neither the doctor nor the study participant knows which treatment the participant is receiving (although, if the doctor needs to find out, he/she can do so).

iii) Monitoring of your symptoms

Following the completion of all the dilatations we will call you monthly to monitor your progress. We will ask if you have noticed any side effects, whether you were able to take trial medication as prescribed and if there have been changes to your regular other medication. We will also ask if you have any concerns and any feedback regarding participation in the study. At 3, 6, and 9 months you are welcome to attend clinic appointments and complete a swallowing questionnaire. We will continue to provide you with standard medical care and discuss ongoing treatment options with you if required. If visiting St George hospital is inconvenient we can post questionnaires to you with reply-

paid return envelopes. You will also need to either bring or post (reply-paid satchel will be provided) unused medication back to us at 3 months.

iv) Gastroscopy to measure throat size and stiffness

12 months after your last dilatation we will arrange for you to have another gastroscopy. The main purpose of this examination is to determine how narrow your throat is 12 months after dilatation and it will allow us to determine if the treatment has improved the size the stricture. This procedure will be performed in the Day Surgery/Endoscopy Unit of St George Hospital. Before the procedure you will be given a sedative drug via an injection into your vein. Once you are asleep the doctor will examine your throat with a flexible camera and measure the size and stiffness of your throat using a catheter called the EndoFLIP. This involves placement of collapsed 10-cm long balloon (2.8mm in diameter) through your mouth into your throat. The balloon is then inflated with saline solution through a syringe that is controlled by a computer. The measurement will take 3 minutes to complete and you will remain sedated for this part of the procedure. The balloon catheter will then be removed from your throat at the end of the procedure. The reason we need to do this is because

If the doctor notices that your throat has narrowed again they can dilate it again during this procedure as in step (i). It will be discussed with you whether you want to have this dilatation with your treating doctors beforehand.

v) Restrictions:

Participating in the trial will require some restrictions on your lifestyle during the study. <u>You will not be able to take any vitamin E supplements for the duration of the study. This includes multivitamins and any vitamin-enhanced food or drinks containing vitamin E.</u>

5. How is this study being paid for?

The study has been funded by Cancer Institute NSW through a translational cancer research centre program.

All of the money being paid by the funding body to run the trial will be deposited into an account managed by University of New South Wales. No money is paid directly to individual researchers.

6. Are there risks to me in taking part in this study?

All medical procedures involve some risk of injury. In addition, there may be risks associated with this study that are presently unknown or unforeseeable. Despite all reasonable precautions, you might develop medical complications from participating in this study. The known risks of this study are:

i) The following adverse effects have been reported for Pentoxifylline:

Most commonly (between 1% and 3%): upset stomach, nausea, vomiting, bloating, dizziness and headache.

Rarely (less than 1%): Anorexia, cholecystitis, constipation and a dry mouth/thirst, tremor, anxiety and confusion, chest pain, low blood pressure, shortness of breath, swelling, itchy skin, rashes and urticaria

Very rarely (isolated cases): inflammation of tissue covering brain and spinal cord, bleeding, liver dysfunction, reduced blood clotting, pancytopenia, decrease in red or white blood cells, nosebleed, flu-like symptoms, sore throat, nasal congestion, brittle fingernails, blurred vision, conjunctivitis, earache, partial loss of vision, bad taste in the mouth, excessive salivation, malaise, sore throat, swollen neck glands, weight change

There is increased risk of bleeding while taking Pentoxifylline. You should contact the investigators if you experience unexpected or prolonged bleeding. You should also tell us if you are prescribed anti-clotting medication including aspirin, or if your current anti-clotting medication is changed or dose adjusted.

It is important that women participating in this study are not pregnant and do not become pregnant during the study as the study drugs may damage an unborn baby.

The effect of the study *drugs* on an unborn baby is unknown. If you are a woman of childbearing age and there is any possibility that you are pregnant, the researchers will need to perform a urine pregnancy test before you start in the study.

If necessary, you should use reliable contraception (such as oral or implanted contraception, an IUD or have had a tubal ligation if you are female, or condoms if you are male) during the course of the study. If at any time you think you, or your sexual partner, may be pregnant it is important to let the researchers know immediately.

ii) Measurement of throat size and stiffness

This is performed during follow-up gastroscopy by using a catheter called the EndoFLIP. Previous studies have shown that EndoFLIP device can be used in various

clinical conditions (including the stricture that you have) with no reported harmful effect. It will prolong your sedation time by up to 3 minutes.

7. What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. You can undergo standard endoscopic dilatation without additional treatment. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8. What happens if I suffer injury or complications as a result of the study?

If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment.

You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is caused by the drugs or procedures, or by the negligence of any of the parties involved in the study. If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies.

If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.

9. Will I benefit from the study?

This study aims to further medical knowledge and may improve future treatment of throat strictures caused by radiotherapy. We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include a more sustained treatment effect. In other words, there is a chance that you might not have recurring symptoms for longer period of time and ultimately require fewer dilatations and greater symptom relief in the long term.

10. Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything nor will you be paid.

11. How will my confidentiality be protected?

Of the people treating you, only Dr Michal Szczesniak Dr Peter Wu Prof Ian Cook A Prof Julia Maclean and A/Prof Peter Graham will know whether or not you are participating in this study. Any identifiable information that is collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named above will have access to your details and results that will be held securely at St George Hospital.

12. What happens with the results?

If you give us your permission by signing the consent document, we plan to publish the results in scientific peer-reviewed journals and discuss the results at presentations at conferences or other professional forums.

In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish.

13. What happens to my treatment when the study is finished?

If you have had previous dilatations and, in this study, taking Pentoxifylline and Vitamin E after a dilatation is found to be of benefit to you Pentoxifylline and Vitamin E maybe considered in future dilatations if required. This decision will be made in consultation between you and your treating doctor about the most appropriate treatment for you at that time.

14. What should I do if I want to discuss this study further before I decide?

When you have read this information, the researcher *Dr Michal Szczesniak* will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him on 91132878.

15. Who should I contact if I have concerns about the conduct of this study?

This study has been approved by the South Eastern Sydney Local Health District Human Research Ethics Committee. Any person with concerns or complaints about the conduct of this study should contact the Research Support Office which is nominated to receive complaints from research participants. You should contact them on 02 9382 3587, or email SESLHD-RSO@health.nsw.gov.au and quote [18/145].

Thank you for taking the time to consider this study.

If you wish to take part in it, please sign the attached consent form.

This information sheet is for you to keep.

CONSENT FORM

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1. I,.....
of.....
agree to participate in the study described in the participant information statement set out above.

2. I acknowledge that I have read the participant information statement, which explains why I have been selected, the aims of the study and the nature and the possible risks of the investigation, and the statement has been explained to me to my satisfaction.

3. Before signing this consent form, I have been given the opportunity of asking any questions relating to any possible physical and mental harm I might suffer as a result of my participation and I have received satisfactory answers.

4. I understand that I can withdraw from the study at any time without prejudice to my relationship to St George Hospital or University of NSW.

5. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.

6. I understand that if I have any questions relating to my participation in this research, I may contact Dr Michal Szczesniak on telephone 9113 3878, who will be happy to answer them.

7. I acknowledge receipt of a copy of this Consent Form and the Participant Information Statement.

Complaints may be directed to the Research Ethics Secretariat, South Eastern Sydney Local Health District, Prince of Wales Hospital, Randwick NSW 2031 Australia (phone 02-9382 3587, fax 02-9382 2813, email SESLHD-RSO@health.nsw.gov.au .

Signature of participant	**Please PRINT name**	**Date**
_____	_____	_____
Signature of witness	**Please PRINT name**	**Date**
_____	_____	_____
Signature of investigator	**Please PRINT name**	**Date**
_____	_____	_____

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WITHDRAWAL OF CONSENT

I hereby wish to **WITHDRAW** my consent to participate in the study described above and understand that such withdrawal **WILL NOT** jeopardise any treatment or my relationship with St George Hospital or University of NSW.

Signature of participant	**Please PRINT name**	**Date**
_____	_____	_____

The section for Revocation of Consent should be forwarded to A/Prof Peter Graham, St George Hospital Cancer Care Centre, Kogarah, NSW, 2217