A randomised double blind study of antioxidant-rich food supplements in men prostate cancer

Information for patients and their General Practitioners

You have been invited to take part in a clinical trial by your doctor. Before agreeing to take part, you should know exactly what taking part will mean to you, and what you are required to do. This information sheet supplements the verbal explanation given to you by your doctor and research nurse. This trial has been approved by the Bedford Hospital NHS Trust Research and Development Committee and the National Research Ethics Committee.

What is the study trying to find out? This study is trying to find out if a food supplement, rich in antioxidants, reduces the rate of prostatic specific antigen (PSA) progression in patients who have been diagnosed with prostate cancer, and who are managed with active surveillance.

Why is this study important? Although there is widespread advice regarding antioxidant-rich foods and prostate cancer, there is very little clinical evidence of their benefits due to a lack of well-conducted studies. As a consequence, our knowledge is very limited and this trial is attempting to establish if antioxidant-rich foods, taken as a supplement, are beneficial to men who have been diagnosed with prostate cancer.

What if I do not agree to take part? Participation in this study is entirely voluntary. Agreeing, or not agreeing, to enter this study does not change in any way the other treatments that you will receive connected to your disease. If you withdraw from the trial at any stage, this would not in any way influence future treatment decisions.

Taking consent. Written, informed consent is required before entering this study to ensure you truly understand the implications of taking part in the study. We will also ask you if we can inform your GP that you have entered this study.

What will you have to do if you enter the study? If you agree to take part in the trial, you will be asked to have a blood test to measure your PSA, liver and kidney function, cholesterol and glucose levels. You will be randomised to receive 3 months supply of *either* the study food supplement *or* placebo, and you will be asked to take one tablet, two times a day.

Randomisation means that it is purely down to chance whether you receive the food supplement or placebo. After consent, a member of the trials team will open a sealed envelope containing a card marked with either 'tablet A' or 'tablet B', and this is the tablet that you will receive. Neither you nor the research team will know whether tablet A or tablet B is the supplement or placebo, as both the tablets and the packaging, will look the same. You will have a 66% chance of receiving the food supplement, and 34% chance of receiving the placebo (2:1 randomisation).

When the study has closed and the final patients have completed the trial, and the results analysed, you will be informed as to which tablet you had taken, and given the overall results of the study. If the trial suggests a benefit, as this is an evaluation of a food supplement and not a drug, it cannot be prescribed by your doctor. However, a dietary advice sheet will be provided by the trials unit at that stage.

The circular tablet measures 5mm in diameter and 3mm depth, and is best taken with a drink. It can be taken with or without food. If you find it difficult to swallow the tablet whole, it can be broken up and added to food, or swallowed in pieces, with a drink.

After taking the supplement or placebo for three months, you will be reviewed during an out-patients appointment in the oncology unit by your oncologist. At this point you will be asked to have a further blood test, again measuring your PSA, liver and kidney function, cholesterol and glucose levels. Provided that you have tolerated the food supplement, you wish to remain on the study and that your PSA level is acceptable to continue with active surveillance, you will then be given a further three month supply of tablets. At six months, you will have another blood test (same as above). The study will end at this point.

What is inside the tablets? The supplement and placebo have been produced by a fully licensed UK manufacturer who has fulfilled all necessary EU and UK regulations for nutritional and food products (Power Health Products Ltd). Two thirds (66%) of patients on the study will be randomised to receive tablets containing the antioxidant-rich food extracts of pomegranate, green tea, turmeric and broccoli, along with anti-caking and bulking agents necessary to keep the ingredients in a tablet form. The remaining one third (34%) of patients will receive a tablet which looks the same as the food supplement, but is actually a simple bulking agents and watercress extract, thought to have no significant antioxidant activity. This is known as a placebo. Neither you nor the research team will know which you have been randomised to.

Why are blood tests required? Firstly your doctor requires a measure of your PSA to know whether to advise continuing active surveillance. Only patients who are suitable for active surveillance can be considered for this study. Secondly, as with any intervention, even if simply dried foods, a measure of basic blood, kidney and liver functions are needed for patient safety. Your organs need to be in good order just in case there are any unexpected effects of the dried foods on your body.

How long will the trial last? If you agree to take part in the study, you will receive the food supplements for six months. You can, of course, withdraw from the study whenever you wish.

Will you have to change your diet? You are completely free to choose whatever you wish to eat and drink, but we advise avoiding other nutritional supplements.

Possible side effects. Based on information from previous studies of these ingredients, the chance of side effects is small. One study of pomegranate extract reported that, when taken at much higher quantities, there was a small incidence of diarrhoea (<2%). Any possible side effects will be recorded in trials forms during your routine visits, but if in the meantime you get a symptom which began *after* you started taking the tablets, please feel free to contact the trials unit in Bedford on 01234 795 787.

Possible interaction with other drugs. There are some potential drug inactions because, like many fruit juices, pomegranate is a weak inhibitor of cytochrome P450 (CYP2C9). There is, therefore, a small potential risk of reducing your metabolism, and thereby increasing serum levels of warfarin, and blood pressure medications such as captopril, ramipril or anti-convulsants such a carbimazole. Men on warfarin are not excluded from this study, but they will be asked to have more frequent INR tests after commencing the study, initially.

Will the information collected during the study be confidential? Yes, all the information you provide will be known only to the research team. Any trial results which are published in medical journals or at conference, will not identify you or any other individuals. If you consent to take part in this study, your records will be kept within the research unit at The Primrose Unit for 10 years. All data collected during the study will be processed and stored in accordance with the guidelines set out in the Data Protection Act of 1998 and the Good Clinical Practice (CGP) guidelines. Your GP will be informed of your participation in the study.

Who is funding this study? This study is funded from the Primrose Research & Education Fund, Bedford Hospital NHS Trust. The supplement and placebo were donated free to the trials unit for the duration of this study. The research team involved in the study are not being paid to recruit you into the study.

What if you have any further queries about this trial? Please contact Madeleine Williams, Professor Thomas' Research Manager, on 01234 795 787.

Additional concerns. If you have any additional comments or concerns about this study, you may discuss these with the investigator. If you wish to go further and complain about any aspect of the way in which you have been approached or treated during the study, you should contact PALS at Bedford Hospital.

The research team thank you for taking time to read this information sheet and for considering participating in this new research study.

Professor Robert Thomas MRCP MD FRCR
Macmillan Consultant Oncologist
September 2011

CONSENT TO PARTICIPATE IN A CLINICAL TRIAL

Title: A randomised double blind study of an antioxidant-rich food supplement versus placebo in men with prostate cancer

Name of Chief Investigator: Professor Robert Thomas

Patient trial ID number:

Please initial boxes

1. I confirm that I have read and understood the trial information sheet dated July 2011, and that I have had the opportunity to ask further questions. ☐

2. I confirm I have had sufficient time to consider whether or not I want to be included in the study. ☐

3. I understand that my participation is entirely voluntary and that I am free to withdraw at any time, without giving a reason, without my medical care or legal rights being affected. ☐

4. I understand that my medical notes may be looked at by responsible individuals from the Primrose Oncology Research Team and an independent Clinical Research Associate. I give permission for this access. ☐

5. I understand that extra blood tests will be required three times during this study. I give my consent for these additional blood tests. ☐

6. I agree to my GP being notified of my taking part in this study. ☐

7. I agree to take part in this study ☐

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Patient Name	Date	Signature

I confirm that I have explained to the patient/volunteer the nature and effect of these procedures. (Member of project team acting on behalf of Physician/Surgeon responsible for investigation)

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Name of person taking consent	Date	Signature