TO BE PRINTED ON HOSPITAL HEADED PAPER

Patient Information Sheet

FAST-Forward
(lymphatic radiotherapy sub-study)

Clinical trial testing a 1-week course of curative breast radiotherapy against a standard 3-week schedule in early breast cancer

We are inviting you to take part in a clinical trial called FAST-Forward. This information sheet explains why the research is important and how you would be able to help. The information is in two parts: part 1 talks about the purpose of the study and what will happen if you decide to participate, and part 2 gives more detailed information about how the study is run.

Before making up your mind, please read the information sheet carefully and talk with your family and friends. You may also want to discuss it with your GP. Please ask your specialist, nurse or radiographer if there is anything you want more information about. Take time to decide.

This study is approved by the National Institute for Health Research (NIHR) and is supported financially via the Health Technology Assessment Programme

Part 1

People who have been diagnosed with early breast cancer are usually prescribed radiotherapy as part of their curative treatment. Clinical trials in the UK and Canada suggest that the same, or even better, results can be achieved with a lower total dose of radiotherapy given in fewer, larger daily doses. We want to see whether the number of doses can safely be reduced even further without reducing the beneficial effects of radiotherapy.

What is the purpose of the study?

The FAST-Forward trial compares the UK standard of 15 treatments over 3 weeks with 5 treatments over 1 week. The purpose of the study is to test if the shorter treatment is at least as safe and effective as the standard treatment.

Why am I being invited to take part?

You have been diagnosed with breast cancer and your specialist has recommended a course of radiotherapy to your breast or chest wall (after mastectomy) and to the local gland (lymph node) area. About 4,500 breast cancer patients from all over the UK will take part.

About Radiotherapy

Radiotherapy uses high-energy waves called x-rays that have been used for many years to treat cancer patients. We know that cancer cells are sometimes still present after surgery to remove the tumour, even though the surgeon also removes an area (margin) of healthy tissue around the tumour and the pathologist sees no cancer cells at the edges of the surgical specimen under the microscope. Radiotherapy destroys cancer cells left after the operation, even though we have no evidence that any cells remain. You have also been recommended to have radiotherapy to the gland area.

What are the side effects of radiotherapy?

All treatments have potential side effects whether they are given as part of a trial or not. Your specialist will discuss any side effects that you may experience as a result of your radiotherapy. Some of these will only occur during the course of your treatment and for a few weeks after and may include reddening and soreness of the skin and tiredness. Some patients (about 1 in 3) experience mainly mild long-term side effects months and years later in the tissues that were exposed to the radiotherapy. These side-effects include a reduction in the size of the breast, hardening and tenderness in the breast and stiffness over the rib-cage, including the chest muscles, swelling of the arm and stiffness of the shoulder. Inflammation of the cartilage of the ribs can occur and more rarely there may be cracked ribs. Scarring to the lung may occur in a small area behind the breast, but this doesn't usually cause any symptoms. It is nearly always possible to protect the heart from the radiotherapy. A very rare side effect from

treatment of the gland area is damage to the nerves (brachial plexus) to the arm. Though it is very rare, it is mentioned as a side effect because the effects are permanent. In those patients that do notice one or more side-effects, the majority find that they do not interfere significantly with day-to-day living.

What are the treatments being tested?

When the FAST-Forward study was developed in 2011 the study consisted of three treatment groups. Women taking part in the study either received standard treatment (the control group) or one of two test groups as detailed below:

Control Group - this is 15 daily doses of radiotherapy, treating once a day (not weekends) for 3 weeks. This is the UK standard treatment.
Test Group 1 - this is 5 daily doses of radiotherapy, treating once a day (not weekends) for 1 week.
Test Group 2 - this is the same as the treatment programme as Test Group 1 except that the daily dose is slightly lower.

The two test groups were included to help us identify a 5-daily dose equivalent to the standard treatment of 15 daily doses. We expected that the differences in the side effects would be small but detectable. Since opening, the study has collected information from over 4000 patients who were allocated to one of these three treatment groups. This information is regularly reviewed by an independent committee of experts who are not directly involved in FAST-Forward. They report that the overall side effects are reassuringly low and that Test Group 1 is no longer needed.

Based on this evidence, the Research Ethics Committee has approved a change to the FAST-Forward study so that women recruited into the study from now on will therefore be allocated to one of the following groups:

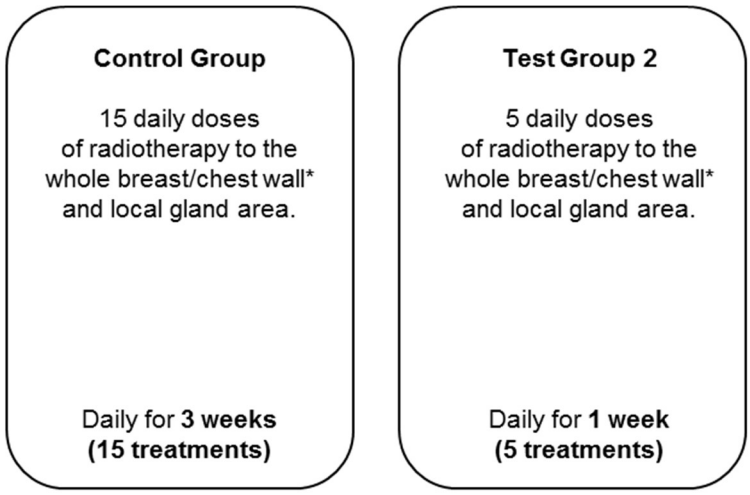
Control Group - 15 daily doses of radiotherapy, treating once a day (not weekends) for 3 weeks (UK standard treatment).
Test Group 2 - 5 daily doses of radiotherapy, treating once a day (not weekends) for 1 week.

If your specialist recommends a boost dose to the area in the breast where the lump used to be, you will need additional radiotherapy, usually 5 or 8 doses, to that area. This will add several days to the total treatment time regardless of which treatment you are allocated to.

What will happen to me if I take part?

If you agree to take part in this study you will be put into one of two groups as shown in the diagram below. Each group will have a different radiotherapy schedule, and these are described below. You will be put into one of the groups at random. If one of the groups does better than the others, we wil know that this is because of differences in the treatment and not because patients in different trial groups are different to each other in some way. You will have an equal chance of being in each of the two groups. A computer program will be used to make sure this is done properly.

The two treatments are summarised in the diagram below:



*An additional dose of radiotherapy may be needed to the area of your breast where the tumour used to be.

The treatment is usually given every weekday in the hospital radiotherapy department, with a rest at the weekend. Patients in the Control Group will need to visit the hospital for 15 treatment sessions. Patients in Test Group 2 will visit the hospital for 5 treatment sessions. If a boost dose is required this will add several days but will be the same for both treatment groups.

How is my treatment planned?

Before you begin your radiotherapy you will visit the radiotherapy department and a treatment plan will be made for you. The radiotherapy team will take accurate measurements and record exactly how your radiotherapy will be given at each visit. These measurements will require a CT (computed tomography) scan, which uses x-rays at low doses. Every patient needs an individual treatment plan because everyone has a different body shape. It is important that everyone in the study has their treatment planned to the same standard.

Will I be asked to do anything else?

Patient Reported Outcome Measures (PROMS)

All patients are being asked to complete Patient Reported Outcome Measures (PROMS) questionnaires. These provide a means of gaining insight into the way patients perceive their health and the impact of their treatment. Therefore you will be asked to complete some questionnaires to describe your own assessment of how the radiotherapy affects your general well-being and day-to-day activities up to 10 years after your surgery. In particular, we are interested in any short- and long-term changes you notice regarding arm swelling and arm movement and also to the shape and/or the feel of your treated breast. The questionnaires are contained within booklets and also include questions asking about how your treatment influences your quality of life, fatigue level and usage of healthcare services. It is important for us to understand your experience as a recipient of this treatment; this information has been very valuable in previous breast radiotherapy trials.

We will ask you to complete a questionnaire booklet before you start your treatment. This is called a baseline questionnaire, which includes a demographic form asking for your home address, GP details, level of education, marital status and occupation. The information you provide will be strictly confidential. You will be asked to complete it before you know which of the treatment groups you will be randomly allocated to, so that we know your answers are not influenced by knowing about your particular treatment. There will be further, similar questionnaires at 3 and 6 months after your treatment, and then 1, 2, 5 and 10 years after you entered the trial. On the first occasion a member of your medical research team will explain the questionnaire and answer any questions that you have. Some of the questions may seem to be a bit repetitive. There are no 'right' or 'wrong' answers. The questionnaire booklet will take about 30 minutes to complete.

You will complete the first (baseline) questionnaire at your planned visit to the clinic and after that we will send them to you at your home from our trials office the Clinical Trials and Statistics Unit (ICR-CTSU) at the Institute of Cancer Research, Sutton, Surrey. There will be a stamped addressed envelope for you to return the booklet.

We would also like you to take part in three other studies which are described in the sections below. All these studies are optional and you can choose to participate in any or all of them but you do not have to take part in these additional studies just because you are going to take part in the FAST-Forward trial:

1. Blood sample study and family history questionnaire

As part of the FAST-Forward trial, we want to find out why some people are more sensitive to the side effects of radiotherapy than others. Advances in a branch of science called molecular biology enable researchers to look for inherited (genetic) differences between patients just by

analysing a blood sample. If we can use these differences to identify people who are likely to have more side effects from radiotherapy, it may allow us to adjust the dose for each individual patient in the future.

We will also ask you to complete a family history questionnaire. If you agree, please give as much information as you can about your immediate (blood) relatives, including whether or not they have had cancer. With this information we may be able to see if there is a connection between how individuals react to radiotherapy and a history of cancer in their family. This may help us to improve radiotherapy for breast cancer in the future.

We will ask you to donate a blood sample for this and future research. Further details about how the sample will be collected and stored are in part 2.

2. Tissue sample study

We want to learn more about why breast cancer grows back again in a small number of people. When you had your surgery the breast cancer was removed and some further tests were done on this tissue to help decide on the best treatment for you. Any of the cancer tissue left over is then stored in your hospital's pathology laboratory. We would like you to donate some of this stored tissue for future research into breast cancer. It is very unlikely that you will get another breast tumour, but if this does happen we would also like you to donate a small part of any new tumour, from either breast. By comparing the characteristics of the two samples we will get valuable information as to why breast cancer sometimes returns and this will help to further improve treatment in the future.

3. Photographic assessment study

Comparing photographs of patients' breasts before and at different times after treatment has been shown in previous breast radiotherapy trials to be a very accurate way of recording changes to the breast as a result of radiotherapy. We will ask to take photographs of your breasts before starting radiotherapy and again at 2, 5 and 10 years after finishing your radiotherapy. The photographs do not show your face. They help us to assess any changes in the appearance of your treated breast over the years following your radiotherapy.

You can still take part in FAST- Forward without taking part in these 3 extra studies. However if you do take part, it will help us to understand more about breast cancer and radiotherapy and may be of benefit to people undergoing radiotherapy for breast cancer in the future.

Do I have to take part in FAST Forward?

It is up to you to decide whether or not you wish to take part in the FAST-Forward trial. If you agree to join and then change your mind you can still withdraw without giving a reason. If you decide to withdraw it will not affect the standard of care you receive.

What are the alternatives for treatment?

If you decide not to take part in the trial you will get the standard radiotherapy treatment used in your hospital. Your specialist will explain what this involves.

Pregnancy and treatment

Radiotherapy can be harmful to a developing baby. If you are of childbearing age and think you may be pregnant, please tell the radiographers or your specialist. For the same reason you must guard against becoming pregnant whilst you are having treatment.

Are there any possible advantages to taking part?

Patients in the test group will have to visit the hospital less often as they will have 5 treatments instead of the usual 15. All patients are likely to benefit from a low risk of cancer recurrence in the breast after radiotherapy.

We expect that the risks of side effects and cancer recurrence in the breast will be similar for all patients in the study but we cannot be certain about this before doing the research. It is possible that the risks of side effects and cancer recurrence are lower after 5 treatments than after the standard 15. We won't know about this until after we have completed the research.

We cannot be certain the study will help you, but any information gained from this study will help improve the treatment of future patients.

Are there any possible disadvantages to taking part?

We expect that the risks of side effects and cancer recurrence in the breast will be similar for all patients in the study but we cannot be certain about this before doing the research. There is a small chance that some patients in the test group will not do quite as well as some patients in the control group. From previous work we think that the risk of worse outcomes in the test group compared with the control group is likely to be less than 1 in 20 of more women experiencing side effects, and no more than 1 in 100 extra women experiencing a recurrence of cancer in the breast within 5 years.

What do I have to do if I take part?

We will ask you to sign a consent form to say that you agree to take part. We will ask your permission to inform your GP that you are taking part in the FAST-Forward trial.

You will be randomly allocated to one of the treatments we have described and your specialist team will let you know when your treatment starts.

You will be asked to complete a baseline PROMS questionnaire before you are allocated to a treatment group. You will also be asked to complete booklets at 3 and 6 months after you have completed your radiotherapy and again at 1, 2, 5 and 10 years. These will be sent to your home address and you will be asked to send each one back to the Trials Office in the stamped-addressed envelope provided.

If you are taking part in the photographic sub-study you will have photographs taken of your breasts before radiotherapy and again at 2, 5 and 10 years after you entered the trial.

If you are taking part in the blood sub-study you will be asked to donate a single blood sample and complete the family history questionnaire.

You will attend the clinic for a follow up assessment visit annually for 10 years and this will include a physical examination. This will help us to find out how radiotherapy affects the breast and surrounding tissue including the local gland area and improve treatment in the future. This examination is an essential part of the trial.

You will be followed up on a long-term basis using your medical notes, via your GP and national registers. This is because we want to know the long-term effects of radiotherapy to the breast.

Part 2

What will happen to the results of the study?

Independent experts will review the progress of the research, and the results will be published in a respected medical journal once we are sure they are reliable. No information that could identify you will be included and you will not be identified in any report or publication. The results will help us to decide the best way to give radiotherapy to patients with breast cancer in the future.

We will also write-up the results in non-medical terms once they are available. These will be sent to your hospital. Your specialist will inform you that they are available and ask if you would like a copy.

What will happen to the Patient Reported Outcome Measures (PROMS) questionnaires?

The information from the Patient Reported Outcome Measures (PROMS) forms is confidential and only the PROMS study coordinator will know who you are. You are invited to write independent comments in the PROMS booklets. These comments may be used in future publications and presentations but no information that could identify you will be included.

What will happen to the Blood and Tissue samples?

Blood: We will ask you to donate a small amount (approximately 4 teaspoons) of blood on one occasion during the trial. Your blood sample will be sent to a research laboratory and will be identified by your trial number and date of birth only. It will then be given a unique identification number and will be stored in accordance with national guidelines. Your blood may be used in future years for analyses that could include genetic analysis. The results will be used to try to discover why some people have a more severe reaction to radiotherapy than others. It will not be possible to release the results of these blood tests to you or your specialist and they will not form part of your medical records.

Tissue: Your hospital will send your stored tumour tissue block to a facility where a small amount will be taken and stored in accordance with national guidelines. Your tissue sample will be identified by your trial number, date of birth and your hospital's own unique pathology number when it is sent to this facility. The rest of your tissue sample will then be returned to your hospital's pathology laboratory where it will be kept according to local practice. The piece of tissue that we keep will be given a unique identification number and will be used in future years for analyses which will include removing DNA to look for genetic changes in the tumour. If you have agreed to donate a blood sample we would also like to compare the DNA removed from your blood with the DNA removed from your tumour. This will help us to understand the changes that happen when a cancer is formed. As with the blood tests, it will not be possible

to release the results of these tests to you or your specialist and they will not form part of your medical records.

We would also like to use your blood and tissue samples for future unspecified research into breast cancer and also the biological effects of radiotherapy. It is possible that the future research will be carried out outside of the UK but within the European Union. These studies will have separate ethical approval before your samples are used. No personal identifying information will be released to a third party.

What will happen to the photographs of my breasts?

The photographs will be stored securely as digital images and will include your unique identifying number but not your name. The images will be sent to the Institute of Cancer Research Clinical Trials and Statistics Unit, Sutton, Surrey where they will be assessed for changes over the years.

How will confidentiality be maintained?

Your medical notes will be seen by authorised members of the research team at your hospital, so that they can collect information needed for the FAST-Forward study, and also to check that it is correct. When you join the study, your name, date of birth, postcode, hospital number and NHS number will be passed to the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being co-ordinated. You will be given a unique registration number, which will be used together with your initials and date of birth on forms that the research staff will send to the trials office. All information about you will be treated as strictly confidential and nothing that might identify you will be revealed to any third party.

ICR-CTSU staff, and those conducting the study with them, may need to examine your medical records to ensure the study is being run properly and that the information collected on the forms is correct, but your confidentiality will be protected at all times.

We will contact your hospital over the years to find out how you are getting on however patients often change address and/or GP or lose touch with their hospital. If this happens we would like to use national records which are kept on everyone's health status to find out how you are. One of these is held at the General Register Office (GRO) and we will need to give them enough information to identify you. This is usually your name, date of birth and NHS number (or Community Health Index and/or hospital number in Scotland). Any details we receive from any source are confidential and will only be used for the purposes of the FAST-Forward study. Please initial the consent form to show that we have your permission to do this.

A copy of the treatment plan made for you before your radiotherapy starts will be sent to the FAST-Forward Quality Assurance team at Mount Vernon Hospital, Northwood, Middlesex. This

includes copies of your CT and treatment images associated with this plan. These will be monitored and stored by the Quality Assurance team.

Information from your medical records about your treatment and disease will be sent to ICR-CTSU. Representatives from that organisation may wish to see your hospital or clinic records to make sure the information sent was correct. All information will be kept confidential and your name and address will be removed.

We will treat all information that we have about you as strictly confidential. Nothing that might identify you will be released to any third party.

Data Sharing

The Sponsors of this study would like to be able to combine information we collect about patients in this study with information collected for other studies, if in the future it is a useful way of advancing our knowledge of the treatment of cancer. If this happens, information about you may be passed to other researchers, but they would not be able to identify you from the information provided.

We would also like to be able to make your tissue samples and information available to other researchers for future research. Any other additional research using your tissue must be approved by an independent ethics committee before it is allowed to go ahead. Any samples and information transferred to third parties will not contain your personal information, so they will not be able to identify you from the information provided.

What if relevant information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your specialist will tell you and discuss whether you should continue in the study. If you decide not to carry on, your specialist will make arrangements for your care to continue.

Will I be paid for taking part in this study?

No. Neither you nor your specialist will be paid for taking part.

What happens if something goes wrong?

If taking part in this trial were to harm you in any way, there are no special compensation arrangements. However your hospital would be liable for any harm caused by negligence on the part of the hospital staff.

We will monitor your progress very carefully both during and after your treatment and we will offer you any available treatment to help with any side effects that you may experience.

If you have a concern about any aspect of this trial you can ask to speak to one of the researchers who will do their best to answer your questions. If you are still unhappy and want

to make a formal complaint you can do this through the NHS complaints procedure. Your hospital will give you details of how to do this.

Your legal rights will not be affected by your agreeing to take part in this trial.

Regarding private insurance

If you have private medical insurance please check with the company that your medical insurance policy will not be affected before agreeing to take part.

What if I agree and then change my mind?

If you change your mind about taking part in the trial you are free to withdraw at any time. You do not have to give a reason. We would however like to ask your permission for your hospital to send information about your progress to the Institute of Cancer Research Clinical Trials and Statistics Unit. This is information that is routinely taken and you will not need to do anything extra. This will ensure that the quality of the research study is not impaired. If you do not want us to collect this information or if you want us to destroy any samples that we may have collected from you please tell your specialist or nurse.

If you withdraw from the trial your specialist will advise you about your treatment.

What happens if I am unable to continue with the trial?

If during the course of the trial you were to become incapacitated in any way we will withdraw you for your own protection. If you are still receiving radiotherapy your specialist will decide how best to complete your treatment. We will not collect any further details about your treatment or follow-up for the trial and we will not collect any further blood or tissue samples. We would however, like to ask your permission to retain any blood and tissue samples that you have already provided if you consented to their use when you joined FAST-Forward. These will be used for future research in the same way as if you had continued on the trial.

Who is organising and funding the research?

The research is being co-ordinated by the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU), Sutton, Surrey. Many hospitals throughout the United Kingdom are joining in. The trial is sponsored by The Institute of Cancer Research and funded by the National Institute for Health Research - Health Technology Assessment programme (NIHR - HTA).

Who has reviewed the design of this trial?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC). This is to protect your safety, rights, well-being and dignity. This trial

has been reviewed by experts in the field and approved by South East Coast – Brighton and Sussex REC (formerly South East Coast - Kent REC). The amended trial design has been approved by the REC and also the National Institute for Health Research – Health Technology Assessment programme which has funded the research. It has also been approved by the Research and Development Department at your hospital.

What happens now?

Your specialist, nurse or radiographer will be happy to answer any questions that you may have. You can ask when you next visit the hospital or you can telephone. Once you have reached your decision let your specialist, nurse or radiographer know. You will be asked to sign a consent form and will be given a copy to keep together with this information sheet. Please keep this information sheet and copies of the signed consent form. If, at any time, you have any questions about the study you should contact your consultant.

Further Information

Macmillan Cancer Support is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. You can contact one of their Cancer Information nurse specialists on the Macmillan Support Line: Freephone 0808 808 00 00 Monday to Friday, 9.00am to 8.00pm. In addition to their nurses, the Macmillan Support Line also has other specialist teams that can provide advice and information relating to welfare benefits, financial issues and everyday practical concerns.

You can also learn more about clinical trials on the Cancer Research UK's patient website http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial.

Thank you for your interest in our research

Your specialist is:

Contact phone numbers: