TO BE PRINTED ON
HOSPITAL HEADED PAPER

Triple Negative breast cancer Trial (TNT)

A study for women with ER, PR, and HER2 negative recurrent breast cancer

(incorporating the BRCA Trial)

PATIENT INFORMATION SHEET

We are inviting you to take part in a clinical trial called **TNT**. Part 1 of this information sheet is about this research and what taking part involves. Part 2 gives you further information about how the study is being carried out.

Before deciding whether to take part, please read it carefully and discuss it with other people if you wish. Please ask your doctor or nurse if there is anything you do not understand or if you want more information. Take your time to decide.

This study is approved by Cancer Research UK and Breakthrough Breast Cancer. Both charities are providing financial support.

breakthrough breast cancer

CANCER RESEARCH UK

Part 1: About the Triple Negative Trial

This study aims to improve treatment for patients with two different types of breast cancer by seeing if a drug called carboplatin works better than the current best standard treatment.

What are the two types of breast cancer being studied?

Not all women with breast cancer have the same type. Some breast cancers do not show evidence of markers that help doctors tell if hormone treatments such as tamoxifen or other drugs such as Herceptin will be of benefit. These are hormone receptors and the HER2 receptor. This type of breast cancer is called triple negative. Another type is caused by inherited genes that greatly increase the risk of breast cancer. This can be the BRCA1 or BRCA2 gene. Women who carry one of these genes may not necessarily have triple negative breast cancer, but because it is comparatively rare, there is no special treatment known to target this type of breast cancer.

Why am I being invited to take part?

Your cancer specialist has invited you to take part in this study either because you have had a diagnosis of triple negative breast cancer, or you are known to carry the BRCA1 or BRCA2 gene. Your breast cancer has also now returned. This is called relapsed, recurrent, secondary or metastatic breast cancer. If your breast cancer has spread beyond the breast, your hospital doctor has explained to you exactly which parts of your body the breast cancer is affecting, and recommends that chemotherapy is the best treatment option for you. Between 370 and 450 breast cancer patients with a similar diagnosis from all over the country will be invited to join this study.

What is the purpose of this research study?

Currently there is little difference between the chemotherapy treatment given to women with triple negative breast cancer, women who are known BRCA1 or BRCA2 carriers, and those with other types of breast cancer. Recent laboratory research has shown that the types of breast cancer cells in these types of breast cancer respond differently to some chemotherapy drugs and that a chemotherapy drug called carboplatin may be of benefit. This means that women with these types of breast cancer may respond better when treated with carboplatin but we do not know this yet.

We are comparing the effect of carboplatin to another chemotherapy drug called docetaxel. Docetaxel is often used to treat women with breast cancer which has relapsed. It is currently the best treatment available for slowing down the progression of breast cancer in patients who have relapsed, and is widely used to slow the progression of all types of breast cancer

What treatment is being tested?

We want to see if carboplatin can slow down breast cancer progression better than docetaxel. Carboplatin is not a new drug. It is already widely used to treat lung and ovarian cancer.

What are the side effects of treatment?

Both docetaxel and carboplatin have some side-effects which are listed below. No-one can predict whether you will have any of these. It is important that you tell your hospital doctor or research nurses about any problems you have at each hospital visit. Their telephone numbers are at the end of this information sheet.

Some side effects include:

- Nausea: some patients feel sick, or are sick, but this usually only lasts for a few hours. You will be given special anti-sickness medication to help prevent this (called anti-emetics).
- Loss of appetite, sore mouth and/or a change in how food tastes. You should speak to your hospital nurse or consultant as they can arrange a dietician or nutritionist to help you with your diet.
- Diarrhoea. This can be easily controlled with medicines that your doctor gives you but remember to drink plenty of fluids if you have diarrhoea.
- Tingling or numbness in your hands or feet (called peripheral neuropathy). Your doctor may adjust your chemotherapy dose if this is causing you problems.
- Hair loss. Only some patients have hair loss and it is less common with carboplatin. This usually starts 2-3 weeks after the first cycle and does grow back about 3-6 months after your chemotherapy.
- Rash on your skin
- Feeling tired and weak
- Docetaxel can cause aching muscles & joints and fluid retention

While the drugs are acting on the cancer cells in your body they also temporarily reduce the number of normal cells in your blood. This can cause:

- A decrease in the number of white blood cells (called neutropenia). This can increase the risk of getting an infection. You may be given antibiotics to take at the time your white blood cell count is most likely to drop to give you protection from infection.
- A decrease in platelets in your blood (called thrombocytopenia). You may notice that you bruise or bleed more easily.
- A decrease in the number of red blood cells (called anaemia). You may feel tired or look pale. In very rare cases, you may need a blood transfusion to increase your red blood cell levels.

Because of the side effects to the blood cells, you will have regular blood tests. Your treatment may be delayed for a short time if any of the cell counts are too low. This will allow your blood cell count to recover.

Effects on fertility and menstruation

Chemotherapy can cause menopausal symptoms such as hot flushes and vaginal dryness, and if you have not yet gone through the menopause, it can stop your periods. This can be permanent, especially if you are getting near to a natural menopause.

Pregnancy and contraception

Even if your periods stop, you must take care not be become pregnant during the chemotherapy, because of the risk of damage to the developing baby. If you are able to have children or have only recently had the menopause, your hospital doctor will arrange for you to have a pregnancy test before entering the trial. You will also have to use extra contraceptive measures during your treatment and for six months after your treatment has stopped. Please discuss this with your doctor.

It is important to remember that many of the side effects, including menopausal symptoms can be controlled or treated. If you experience a high fever, unexplained bruising or bleeding or you suddenly feel unwell for any reason, ***you should contact your doctor or research nurse straight away and not wait until your next clinic appointment.*** Their contact details are at the end of this leaflet.

What are the alternatives for treatment?

Treatment for recurrent breast cancer depends on many different individual factors. Treatment options include radiotherapy and chemotherapy. You and your doctor will have already discussed that chemotherapy is the best treatment option for you. Docetaxel is the most likely chemotherapy drug your hospital doctor would prescribe. Make sure you discuss all the available treatment options with your doctor before deciding if you want to take part in this study. Your doctor will organise any other treatment or care you may need.

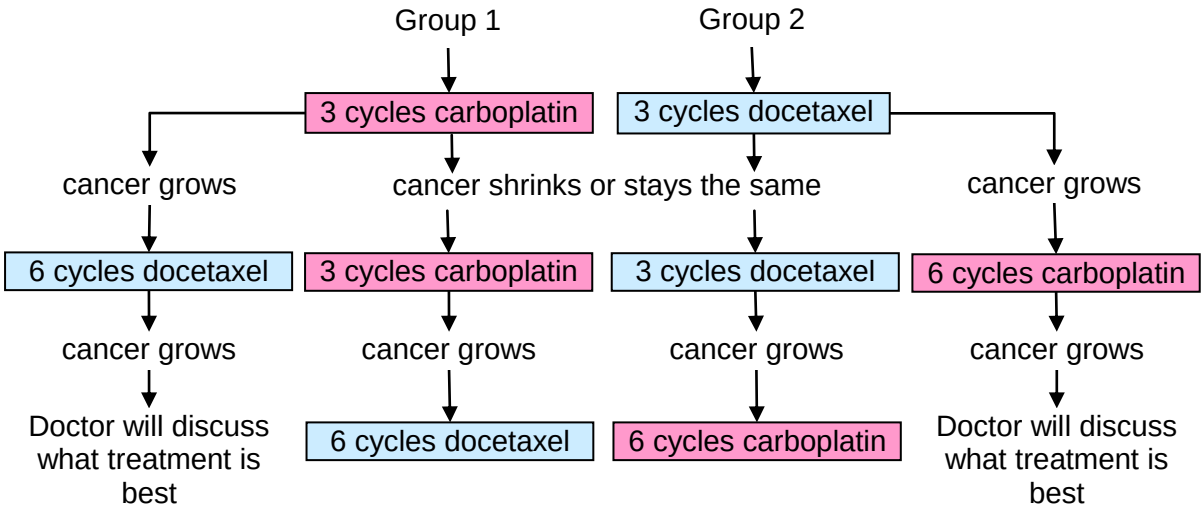
What will happen to me if I take part?

Everyone who agrees to take part in this research study will be allocated to one of two groups of patients. Half the patients are in each group. It is important that the two groups are as similar to each other as possible. This is because we need to be sure that if one group does better than the other group, it is because of the chemotherapy treatment, and not because the patients in the two groups are somehow different from each other. The only way to make sure that the groups are as similar as possible is to allocate them to a group *at random.* Each group of patients receives a different chemotherapy treatment:

Group 1 receive carboplatin. **Group 2** receive docetaxel.

Regardless of which group you are in, you will have chemotherapy once every 3 weeks. This is called a cycle, and a course of chemotherapy is 6 cycles. You will go to your hospital for each cycle. This will be a day visit and you will not have to stay overnight. The chemotherapy treatment will be given slowly into a vein as an infusion or ‘drip’ which will take about one hour and is not an injection. You will be checked very carefully at each cycle to make sure that the chemotherapy is helping and you are not having unacceptable side effects.

After your first 3 cycles (about two months) you will have a CT scan to see if your cancer has reduced in size, remained the same, or grown (called progression). If your cancer has got smaller or remained the same, you will have 3 more cycles of the same treatment. If your cancer has grown, you will be switched to the other treatment. If your cancer grows, or you have serious side effects before the end of your first 3 cycles, you may switch to the other treatment before you have completed 3 cycles. What will happen if your cancer grows is shown in the diagram below:



If you take part in this study you will not need to make any extra hospital visits for treatment overall. The precise number of visits you need to make will depend on how you respond to treatment.

What do I have to do?

If you are agreeable, we would like to take a blood sample from you of about 4 teaspoons (20ml). Your hospital doctor or nurse will take this blood sample at the beginning of the study and, where possible, at the same time as one of your routine blood samples. The section on 'Future Biological Studies With Tissue and Blood Samples' in section 2 of this leaflet explains why we want to do this.

We will also ask you to complete a short family history questionnaire which asks about other members of your family who may have had cancer. It will take about 10-20 minutes to complete. This information may help us improve treatment for patients with your type of breast cancer in the future. If you are concerned about a family history of breast cancer you should discuss this with your oncologist. You can also look at http://www.nice.org.uk/CG041. You can be referred to the NHS Genetics service if it is appropriate.

Before chemotherapy:

Your doctor will discuss with you what blood tests and x-ray tests you need. These are standard, routine tests that all patients undergo before starting chemotherapy. These tests help your doctor assess how well the treatment is working and include:

- *Routine blood tests*
- *CT scan (Computerised Tomography):* a special type of x-ray to allow your doctor to see a three dimensional picture of your tumour. It is painless and takes about 10-20 minutes. You may have an injection of a type of dye (called contrast medium) just before the scan which helps to make the scan clearer.
- *MRI scan (Magnetic Resonance Imaging):* you will have this if appropriate. It is like a CT scan but takes 30-90 minutes and is noisy. You will be asked to lie very still on a couch inside a metal tunnel.
- *Bone scan:* a tiny dose of radioactive material is injected into your vein. You then lie on a bed so a camera can take special pictures of your bones. The tiny dose of radioactive material is safe, and virtually disappears from your body within 24 hours.

During chemotherapy:

It is standard for all patients having chemotherapy to have routine blood tests just before each cycle of chemotherapy. You may also need routine blood tests in between the cycles.

You will be given a card which has the details of this trial and the drugs being used. Please carry it with you at all times while you are taking part in this study.

At the end of the third and sixth chemotherapy cycle you will have a routine CT scan to see if your cancer has responded to the chemotherapy treatment. Details about the scans are given above.

After chemotherapy:

If your cancer has got smaller or remained the same size you will continue to have CT scans every 3 months after your treatment. This allows your doctor to monitor any changes after your treatment has finished. You may receive these follow up scans more frequently depending on your hospital's normal procedure.

Do I have to take part?

It is up to you to decide whether or not to take part. If you agree to join then change your mind you can still withdraw without giving a reason. If you withdraw from the study it will not affect the standard of care you receive. It is routine for your GP to be told if you are taking part in this research.

What are the benefits and risks of taking part?

There is no guarantee that you as an individual will benefit directly. We hope that the information we gain in the study will benefit patients who develop triple negative breast cancer in the future and that you will have helped by taking part. If you are in Group 2 and do not receive carboplatin when you first join the study, you will be offered it later on if your breast cancer progresses again.

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

What if there is a problem?

Information about what to do if you want to complain about the way you have been dealt with during the study or any possible harm you might suffer is given in Part 2.

Will my taking part in the study be kept confidential?

All information about you taking part in this study is confidential. More details about this are given in Part 2.

Your specialist is:

Contact telephone numbers:

Part 2: General information about how TNT is conducted

Future Biological Studies with Tissue and Blood Samples

We are asking your permission to store **tissue samples** and a **blood sample** for future research into ER- PR- HER2- breast cancer. The donation of a blood sample and tissue samples is entirely voluntary, and you can still take part in this study if you do not want to donate them.

When you were first diagnosed with breast cancer, small portions of the tumour were removed at the time of your biopsy and also some lymph nodes from under your arm. You may have had another biopsy when your cancer returned – or may have further biopsies in future as part of your on-going diagnosis or care. These are known as tissue samples and are normally stored in the pathology laboratory of the hospital in which you were treated. With your permission we can request these tissue samples directly from the pathology department where they are stored, and you do not need to do anything.

Finally, we may also ask your permission to perform one additional needle biopsy of your tumour recurrence before your treatment **if it is safe and accessible to do so**. You will need to come to hospital as a day case to donate this tissue. The procedure usually lasts about one hour and you will be given local anaesthetic so you do not feel any pain. **You do not have to agree to this additional biopsy to take part in this study**.

Your samples of **breast cancer tissue** and **lymph nodes** will be sent to Guy's & St Thomas' Breast Tissue and Data Bank to be analysed. There are many factors (called biological markers, including genetic material) that researchers are interested in testing for as they may help predict which tumours will respond to treatment or they may tell us something new about the behaviour of the tumour. These tissues will also be used to help scientists try to develop new treatments for this type of breast cancer in the future.

Your **blood sample** will be sent to a specialist laboratory at the Institute of Cancer Research where genetic material (DNA) will be extracted and stored. This DNA will be used to help us discover whether particular genetic variations lead to this form of breast cancer and also lead to specific drug responses.

We are asking for your permission now, to study these markers in your blood and in your tumour tissue both at the laboratories where they are stored and elsewhere in the future, so that researchers would not need to contact you again as new markers are identified. Any future research would have to be approved by a national ethics committee and the Trial Management Group. The samples will be stored indefinitely on behalf of the Trial Management Group.

Sometimes researchers find that samples can help to establish products that could be patented and licensed. Your samples would be considered a gift and you would not benefit financially.

Neither you nor your doctors will be told of the results of any additional research tests. These results are unlikely to help your doctor treat your disease any differently or directly benefit you as an individual. We hope what is learnt from these studies could benefit patients with your type of breast cancer in the future. The only exception is if you are referred to a clinical geneticist, and

following counselling you ask for results of tests for an inherited breast cancer gene to be released. If this were to happen, your clinical geneticist will be able to ask for the results and would also arrange for you to be re-tested to confirm them.

If you do not want to donate either blood or stored tissue, or have another biopsy taken, please initial the boxes on the consent form that say no to this part of the study. If you decide to take part, and later change your mind, you are free to withdraw your permission for researchers to use your tissue or blood sample at any time and your samples will be destroyed.

Whatever you decide to do your care will not be affected in any way.

Confidentiality

Your medical notes will need to be seen by authorised members of the research team at your hospital, so that they can collect information needed for this research study, and also to check that it is correct. Your name, date of birth and NHS number will be passed to the trials office when you join the study so that they can find you again if you lose touch with your hospital in the future. 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 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.

If you agree to donate a blood sample, the tube in which the blood is sent to the laboratory will have your name and unique registration number on it. This is because all tubes of blood look exactly the same, and it is vitally important we do not get them mixed up. Once your blood sample arrives at the laboratory, it will be processed and stored using a sample code. Your name will be stored separately and securely, and would only be accessed by a researcher if they needed to pass on vital information.

We will be contacting your hospital from time to time to find out how you are getting on. Ideally we would like to do this for life, but patients sometimes 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). 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 study. Please initial the consent form to show that we have your permission to do this.

Information from your medical records, about your treatment and disease will be sent to the Clinical Trials Section at the Institute of Cancer Research. Representatives from that organisation and/or regulatory bodies 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.

What will happen to the results of the research 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.

What if something goes wrong?

It is unlikely that anything will go wrong with your treatment or care, but if you wish to complain about any aspect of the way you have been treated during the course of the study you can do so using the normal NHS complaints procedure.

If you are harmed by taking part in this research project, there are no special compensation arrangements. Healthcare professionals working on Clinical Trials are covered by NHS Indemnity and if you are harmed due to someone's negligence, you may have grounds for a legal action but you may have to pay for it.

If you do wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you. Concerns should be raised by speaking to a member of staff at your hospital or by talking to the local Patient Advice and Liaison Service (PALS) which has been established in every NHS Trust and Primary Care Trust (PCT).

Your progress will be watched closely and you will be offered whatever help is available to cope with any side effects. Occasionally some patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious. If this were to happen, full details of what has happened will be reviewed carefully by the oncologist with overall responsibility for *TNT*. These details will also be sent to the Medicines and Health Care Products Regulatory Agency (MHRA) who oversee the safety of people who take part in any research involving drugs within the UK. We are required by law to do this.

What if I don't want to carry on with the study?

If you change your mind about having the treatment in this study, we would still like to collect information about your breast cancer and general health, and use any samples of tissue you have donated. The information needed is routinely recorded in your medical records and you do not need to do anything. Collecting this information ensures that the overall quality of the research study is not impaired. You will need to tell your hospital doctor or nurse if you do not want us to collect this information about you, or if you want us to destroy tissue samples you have donated.

Who is organising and funding the research?

Cancer Research UK and Breakthrough Breast Cancer are paying for this research. It is sponsored by The Institute of Cancer Research, Surrey and King's College London and coordinated by The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU).

All treatment is provided by the National Health Service. Your doctor will not receive any personal financial payment if you take part.

The National Health Service Research and Development Executive are paying for the extra nursing and administrative costs incurred by the hospitals.

Who reviewed this study?

TNT has been approved by East London and The City Research Ethics Committee on behalf of all hospitals throughout the UK. It has also been reviewed and approved by Cancer Research UK and Breakthrough Breast Cancer.

What happens now?

Your doctor or nurse will be happy to answer any questions over the telephone or when you next go to the clinic. Once you have reached your decision let your doctor or nurse know.

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. They have published useful booklets about (1) breast cancer (2) chemotherapy, and (3) clinical trials in general. You can contact one of their specialist cancer nurses on their freephone number, 0808 808 0000. For more information about the chemotherapy drugs used in TNT, you can also look on their Internet website. To do this go to www.macmillan.org.uk, click on cancer treatment and then click on individual treatments listed under chemotherapy.

Breast Cancer Care have a message board on their Internet website where you can read or add messages about deciding to take part and your experiences of treatment. To use it, go to www.breastcancercare.org.uk, click on enter, and then click on chat.

You can learn more about clinical trials on the Cancer Research UK's patient website (www.cancerhelp.org.uk).

Thank you for interest in our research.

Your specialist is:

Contact phone numbers: