To be printed on hospital headed paper

Patient Information Sheet

NOSTRA-Feasibility Study

NOSTRA-Feasibility: A prospective non-randomised multi-centre feasibility study to assess if patients with residual cancer following dual-targeted neoadjuvant chemotherapy treatment for HER2-positive, ER-negative early breast cancer can be identified by multiple image-guided tumour bed core biopsies

ISRCTN Number: TBC
IRAS Project ID Number: 211232

We would like to invite you to take part in a research study called the NOSTRA-Feasibility Study. The research study is run by the Cancer Research UK Clinical Trials Unit (CRCTU) at the University of Birmingham. It is funded by Roche, endorsed by Cancer Research UK and sponsored by the University of Birmingham. Before you decide if you would like to take part, we would like you to understand why the research is being carried out and what it would involve for you. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Your study doctor will go through this information sheet with you and answer any questions you may have. This information sheet is divided into two parts:

- Part 1 tells you the purpose of this study and what will happen to you if you decide to take part.
- Part 2 gives you more detailed information about the conduct of the study.

Please tell your study doctor or research nurse if there is anything that is not clear or if you would like more information. Thank you for reading this information sheet and take your time when deciding whether or not you wish to take part in the study.

Part 1

Why is this research being carried out?

The NOSTRA-Feasibility Study will help us to find out if cancer that is still present after treatment with chemotherapy, trastuzumab and pertuzumab can be detected in biopsies taken from the site of a cancer. We are asking patients if they are willing to have ultrasound guided tumour bed core biopsies of their breast after finishing chemotherapy and before having surgery.

Many patients like you are now recommended to have drug treatment before surgery. After drug treatment we operate on the breast to remove any remaining cancer. Sometimes the drugs have killed all the cancer cells in the breast and there is no cancer in the breast tissue, we call this a pathological Complete Response (pCR). Patients with a pCR are at much lower risk of disease recurrence than those where cancer is still detected at surgery. At present, patients with early invasive breast cancer, like you, will always have surgery after chemotherapy treatment. This is partly because that is what has always been done and partly because research has not been done before to see if it is possible to tell who has a pCR and who has residual cancer and requires surgery. The information from this feasibility study will be used to help us design a large clinical

trial to find out if surgery could be avoided in patients who have achieved a pCR. Radiotherapy is currently used after surgery to treat any microscopic cancer that remains in the breast. In future it may be used in combination with chemotherapy without the need for surgery. This is an important study which may lead to change in the way breast cancer is treated, saving women from potentially unnecessary surgery.

We want to learn as much as possible about early stage invasive breast cancer and will be collecting tumour samples and blood samples as part of the NOSTRA-Feasibility Study. This will allow scientists to study the tumour sample and blood samples so that they can learn more about the natural history of early stage invasive breast cancer and try to understand how the cancer cells work and to study the effects of the drugs used in the study. With tumour samples in particular, we will try to identify 'markers' that may predict which treatments will work for which patients. The collection of blood is optional and we will use the blood samples to understand why a cancer develops and also look at how DNA in the cancer is changed. You can indicate whether you wish to participate in this part of the study by selecting 'yes' within the Informed Consent Form. In total, patients donating blood samples for research purposes will have **three** sets of 70ml blood samples taken during the course of the study. You do not need to have these extra blood samples taken and deciding not to provide these samples will not affect your participation in the main NOSTRA-Feasibility Study.

What is neoadjuvant treatment?
Neoadjuvant treatment refers to drugs that are given before surgery for the treatment of breast cancer. There are several advantages of neoadjuvant treatment including the ability to shrink cancers leading to less extensive surgery, it also means doctors can monitor if the drugs are successfully treating the cancer.

What is anti-HER2 therapy?
Some breast cancer cells have a higher than normal level (known as overexpression) of a protein called HER2 (Human Epidermal growth factor Receptor 2) on their surface, which makes them grow faster. Anti-HER2 therapy are drugs that target breast cancer cells which overexpress HER2 and are very successful at treating this sort of breast cancer. The most well-known anti-HER2 treatment is Herceptin (trastuzumab). In this study two different anti-HER2 drugs (trastuzumab and pertuzumab) are used together with chemotherapy drugs, a combination which has been shown to be very good at treating this sort of breast cancer leading to a very high chance of a pCR.

What is adjuvant treatment?
Adjuvant treatment refers to surgery followed by chemotherapy and/or radiotherapy. It is given after the primary treatment to help decrease the risk of cancer recurring (coming back).

What chemotherapy regimens are being used?
Patients participating in the NOSTRA-Feasibility Study will need to receive one of three different approved combinations of neoadjuvant chemotherapy plus anti-HER2 therapy:

Regimen 1: FEC with Pertuzumab and Trastuzumab followed by Docetaxel with Pertuzumab and Trastuzumab
Regimen 2: FEC followed by Docetaxel with Pertuzumab and Trastuzumab
Regimen 3: Docetaxel and Carboplatin with Pertuzumab and Trastuzumab

FEC is a combination of chemotherapy drugs (5-fluorouracil, epirubicin and cyclophosphamide) used as a standard treatment for breast cancer. Docetaxel and carboplatin are breast cancer chemotherapy drugs that work in different ways, have different side effects and are often combined in treating HER2 positive breast cancer. If you decide to take part in the study, you will receive one of the three approved chemotherapy and anti-HER2 treatment regimens based on your treating clinician's decision.

What is Docetaxel?
Docetaxel is a drug that is used widely to treat several cancers. Although it can have serious side effects, it is a very powerful anti-breast cancer drug. It works by interfering with structures called microtubules which help separate chromosomes and other structures during the division of cells.

What is 5-Fluorouracil?
5-fluorouracil is a drug which stops cells making new DNA needed for cell division and cancer growth. It is used to treat a wide range of cancers including breast cancer.

What is Epirubicin?
Epirubicin is a drug that causes DNA to break up into little pieces. It is used to treat several cancers including breast cancer.

What is Cyclophosphamide?
Cyclophosphamide is a drug which stops DNA being copied. It is used to treat lots of different cancers.

What is Carboplatin?
Carboplatin is a drug that causes DNA damage, resulting in cell death. It is used to treat different cancers, including lymphomas, leukaemia, myeloma, lung cancer and breast cancer.

What is Trastuzumab?
Trastuzumab is a cancer drug that stops the cells from dividing and growing by locking onto the HER2 protein and blocking the receptor. Trastuzumab is usually used to treat HER2 positive breast cancer.

What is Pertuzumab?
Pertuzumab is a drug that also targets HER2 protein and stops HER2 joining to other HER proteins so the cell doesn't receive messages telling it to grow. It is only used to treat HER2 positive breast cancer and usually given in combination with trastuzumab.

What is a tumour bed core biopsy?
Core biopsy is the procedure to sample a small amount of tissue from the breast with a "core" (meaning "hollow") needle. A 1mm x 1mm piece of tissue about 10-15 mm long would be obtained; this is smaller than the thickness of a normal pencil lead. The procedure is likely to take 10-15 minutes and is performed under local anaesthesia, meaning the breast is numbed. During the procedure, the doctor will insert a very small clip inside the breast to mark the location of the biopsy. If surgery is later required, the clip makes it easier for the surgeon to locate the biopsied area. In this study, a maximum of 8 biopsies will be taken from the area where the tumour sits, known as the tumour bed.

Why have I been invited to take part?
You are being invited to participate in this study because you have HER2-positive, oestrogen receptor (ER) negative, early stage invasive breast cancer which was confirmed by pathologists. All eligible patients are being approached to see if they would like to take part in this study. Nationally, 150 patients with early invasive breast cancer will be invited to take part.

Do I have to take part?
It is up to you to decide whether or not to take part in this research study. Your participation is entirely voluntary. If you do decide to take part you are free to withdraw at any time without having to give any reason for your decision. This will not affect the standard of care you receive.

What will happen to me if I take part?

Before starting the study
If you decide to take part in the study, you will be given a copy of this Patient Information Sheet to keep and you will be asked to sign an Informed Consent Form to show that you have agreed to participate in the study. Your study doctor will register your intent to take part in the study with the NOSTRA-Feasibility Study Office at CRCTU, University of Birmingham.

The study doctor or research nurse will ask you questions about your health (e.g. details of previous treatment or any other illness you may have) and what medicines you are taking, including things you take without a prescription such as herbal remedies. It is important to let your study doctor or research nurse know if you have high blood pressure (hypertension), heart disease or any other serious medical condition(s).

A number of assessments will be performed to confirm that it is safe for you to enter the study and that we have all the information we need. These assessments are summarised in Table 1. These are routine tests that would normally be performed for any patient having neoadjuvant chemotherapy and anti-HER2 therapy (trastuzumab and pertuzumab). The assessments will include a physical examination (measuring height and weight), diagnostic breast biopsy, mammogram and ultrasound examination, biopsy with a thin needle or a

core biopsy of lymph glands under the arm if the glands look abnormal, a heart ultrasound (Echocardiogram, ECHO) or radioisotope scan (MUGA) to check on your heart. Your doctors will need to do more tests such as CT scans or bone scans if there is any concern about cancer spread. A very small clip will be inserted inside the centre of the cancer in your breast. A number of blood tests to check your kidney and liver function (amongst others) will also be carried out. A pregnancy test will be done if appropriate. By the time you are given this information sheet you will probably have already had or be waiting for most of the tests you need before you can enter the study.

If you have consented to provide additional blood samples for research, approximately 70mls of blood (approximately 14 teaspoons) will be collected before you start treatment. Blood samples will be sent to the Institute of Cancer & Genomic Sciences at the University of Birmingham to study cancer DNA that may be present in the blood samples. Where possible we will take this blood sample at the same time as you are having other routine blood tests. You do not need to have these extra blood samples taken for research and deciding not to provide these samples will not affect your participation in the main NOSTRA-Feasibility Study.

Taking part in the research study

Treatment will commence soon after you have agreed to take part in the study. Once it has been confirmed that it is safe and that you are eligible, you will receive one of the three approved chemotherapy and anti-HER2 treatment regimens based on your treating clinician's decision. Taking part in the study will not delay your treatment.

If you have consented to provide the additional blood samples for research, approximately 70mls of blood (approximately 14 teaspoons) will be collected before you start treatment. Blood samples will be sent to the University of Birmingham to study cancer DNA that may be present in the blood samples. Where possible we will take this blood sample at the same time as you are having other routine blood tests. You do not need to have these extra blood samples taken and deciding not to provide these samples will not affect your participation in the main NOSTRA-Feasibility Study.

How often are the treatments given?

We usually describe treatments as being given in cycles of treatment. Before you start each cycle of treatment a routine blood test will be performed. You will receive chemotherapy and anti-HER2 treatment through a vein or a central venous catheter in your arm. These are standard treatments and the side effects of these drugs will be discussed later. Before surgery you will receive one of the following chemotherapy and anti-HER2 treatment regimens depending on your treating clinician's decision:

Regimen 1: FEC with Pertuzumab and Trastuzumab, three weekly for 3 cycles, followed by Docetaxel with Pertuzumab and Trastuzumab, three weekly for 3 cycles

Regimen 2: FEC, three weekly for 3 cycles, followed by Pertuzumab and Trastuzumab with Docetaxel, three weekly for 3 cycles

Regimen 3: Docetaxel and Carboplatin with Pertuzumab and Trastuzumab, three weekly for 6 cycles

You will have an ECHO or MUGA scan after cycle 3 of treatment and at end of treatment to check on your heart, these scans are part of standard care. You will be monitored carefully during treatment to see if your tumour is shrinking and to monitor any side effects you may experience. Sometimes your doctor will need to make adjustments to your treatment such as changing drug doses or giving you extra time to recover from chemotherapy.

If you have consented to provide additional blood samples for research, approximately 70mls of blood (approximately 14 teaspoons) will be collected at the end of cycle 1 of chemotherapy and anti-HER2 treatment. Blood samples will be sent to the Institute of Cancer & Genomic Sciences at the University of Birmingham for research.

When will tumour bed core biopsies take place?

You will have tumour bed core biopsies between finishing your chemotherapy and anti-HER2 treatment and having your surgery. Agreeing to have tumour bed core biopsies will not delay your surgery occurring.

When will my surgery take place?

A few weeks after your chemotherapy has been completed you will have your breast surgery. The type of surgery you need will depend on the characteristics of the cancer both before and after chemotherapy. Your surgeon will discuss the options that are suitable during your treatment. Some patients need to have a mastectomy even if the tumour has shrunk, while other patients will be able to undergo breast conserving surgery.

What will happen after surgery?

When there is no cancer left after surgery (which is called a pathological Complete Response or pCR), this is associated with a good long-term outcome and a low risk of the cancer returning in the future. However, it is conventional for all patients to receive additional trastuzumab every 3 weeks for a total of 18 cycles with or without radiotherapy as part of adjuvant treatment. This is to maximise the chances of killing any remaining cancer cells that have travelled out of the breast and have survived. Receiving trastuzumab for approximately one year is the same length of time you would receive it for if you were not taking part in the study.

The consultant pathologist at your local hospital will look at the tumour bed core biopsies and surgical excisions removed during surgery. This is to see if there is any breast cancer left in the tissue following your treatment, they will then write a report about your tumour samples. Following local pathology reporting, all the tumour samples removed during your surgery will be sent to the Human Biomaterials Resource Centre (HBRC) at the University of Birmingham for storage and will be examined by a small team of specialist pathologists. The specialist pathologists will perform a blinded review of the diagnostic biopsies, tumour bed core biopsies and surgical excision specimens to confirm whether the pathological diagnosis is consistent with the local hospital pathology reporting. If the diagnostic biopsy is urgently needed, it will be returned to the hospital pathology department immediately upon request.

Following review of tumour samples by the specialist pathologists, the sample will be sent to the Edinburgh Cancer Research Centre, University of Edinburgh for future research into breast cancer. It is difficult to be certain what this research may be. Where appropriate further ethics approvals will be sought before conducting the research but we would not normally contact you about this. If at any time your hospital finds that it needs to recall any of your tumour samples, this will be performed without delay.

If you have consented to provide additional blood samples for research, approximately 70mls of blood (approximately 14 teaspoons) will be collected alongside your routine blood tests at your first hospital appointment after having surgery. All blood samples will be sent to the Institute of Cancer & Genomic Sciences at the University of Birmingham for research.

What about lymph glands under the arm (axilla)?

<u>If a pre-chemotherapy biopsy shows cancer</u>

You will have had (or will have) an ultrasound examination to look at the lymph glands under the arm. If they appear abnormal, then biopsies will be taken to see if we can detect cancer cells in the lymph glands. If this biopsy is positive, nearly all surgeons recommend that all the lymph glands are removed at surgery (an axillary clearance). Sometimes, your surgeon may choose to instead perform a sentinel lymph node biopsy at the time of surgery (described in more detail below) but only if another biopsy is taken after treatment and shows no further cancer in the lymph gland.

<u>If a pre-chemotherapy ultrasound or biopsy is normal</u>

If the ultrasound or biopsies are normal, there can still be cancer cells in the axilla because the tests are not 100% reliable. We do need to know if there are cancer cells and there are different procedures used to find out, with advantages and disadvantages to each. The type of procedure used will be the standard treatment offered by your study doctor but may well involve a sentinel node biopsy. This is a routine procedure used to find out if there are cancer cells in the lymph glands under the arm. It is frequently used in patients having surgery before chemotherapy. A radioactive tracer and some blue dye are injected into the breast the day before surgery. Then an operation is performed to find and remove the lymph gland that has absorbed the dye and tracer. Sentinel lymph node biopsy is less likely to cause long term problems than an axillary clearance. Some patients can have an allergic reaction to the blue dye injection, this is uncommon but if you have had an allergic reaction to blue dye in the past it should not be used again but the radioactive tracer can be used safely.

The options are summarised below.

Sentinel node biopsy before chemotherapy
Your study doctor may recommend a sentinel lymph node biopsy before chemotherapy. If this node is normal, it is a reliable way of knowing that the axilla is clear and no more needs to be done but it does involve an operation before your chemotherapy starts. If the lymph node biopsy shows cancer, then most surgeons would recommend an axillary clearance after your chemotherapy.

Sentinel node biopsy after chemotherapy
Your study doctor may recommend a sentinel node biopsy after your chemotherapy. This can be done as part of your breast cancer surgery. If this shows no cancer, most doctors accept this is a reliable way of telling that there will not be any cancer in the axilla. No more surgery is needed. If it shows cancer, you will need a second operation to clear the axilla. You cannot have more than one sentinel lymph node biopsy because the operation alters the flow of lymph and the technique does not work a second time round.

In some circumstances your study doctor may recommend an axillary clearance as the only procedure and this will be performed at the same time as your surgery.

Follow-up
After your treatment has finished you will have two study follow-up visits to check on your health, these will occur alongside the routine follow-up visits that your study doctor will arrange. You will be seen at the hospital (or contacted by the hospital if you have been discharged from follow-up) at 12 months and at 5 years. The purpose of the follow-up visits is to monitor for relapse of the cancer and you will also be asked about any side effects you may have experienced. Your study doctor or research nurse may contact your GP for an update on your progress if you are no longer attending clinic or cannot be contacted by other means.

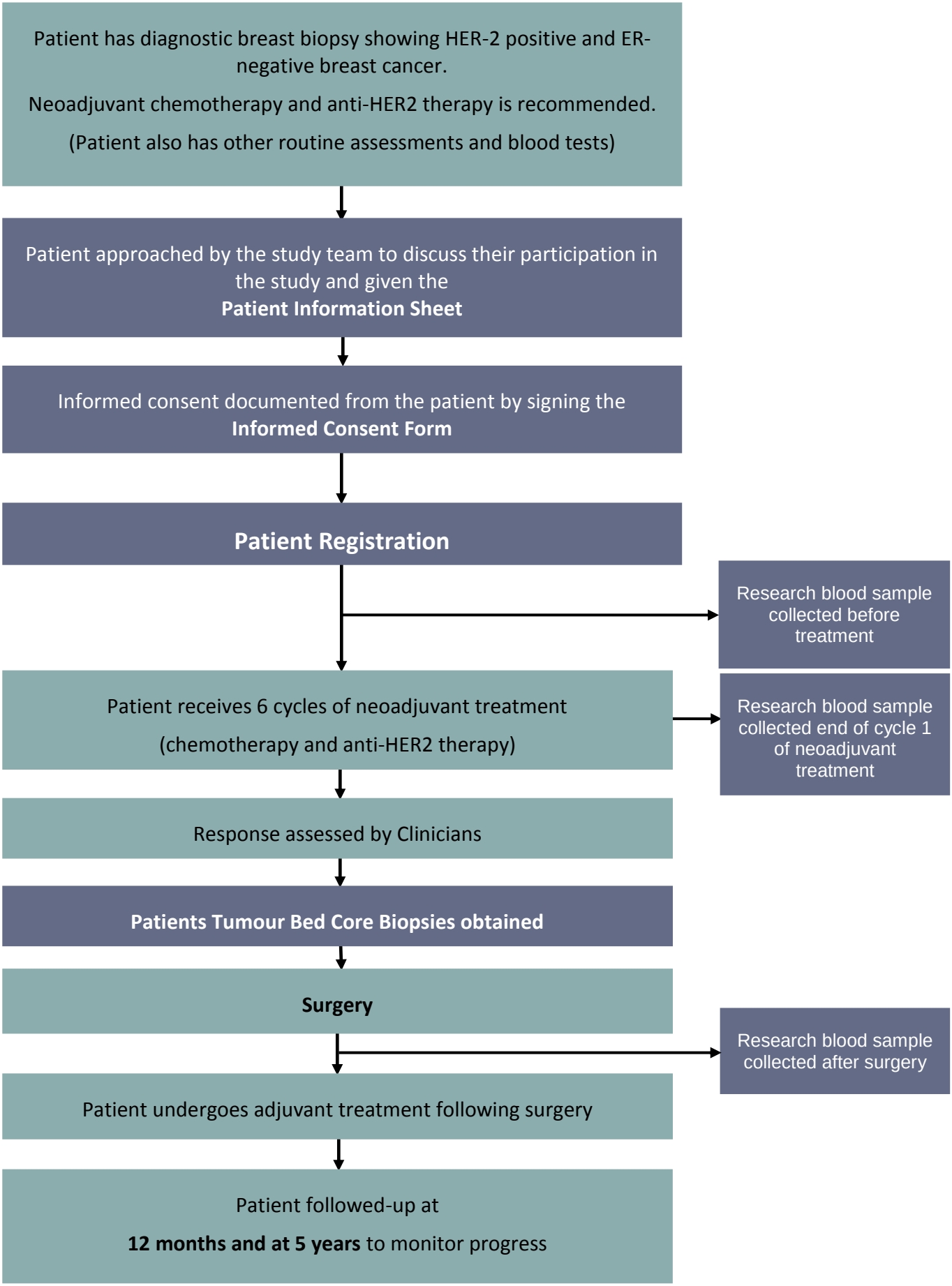
Summary

Table 1: Assessments and Tests

	Before treatment	Chemotherapy & Anti-HER2 treatment			Surgery	Additional Anti-HER2 treatment
		Before each cycle	After cycle 3	Completion of Treatment		
Biopsy	✓					Continue to complete 3-weekly cycles of trastuzumab. To complete a total of 18 cycles with or without radiotherapy.
Clip insertion	✓					
Axillary ultrasound (and biopsy if required)	✓			+/-✓		
Heart scan	✓		✓	✓		
Ultrasound	✓			✓		
Mammography	✓			✓		
Standard blood tests	✓	✓				
Blood sample collection*	✓	✓			✓**	
Physical examination	✓					
Clinical tumour measurement	✓		✓	✓		
Sentinel lymph node biopsy	+/-✓				+/-✓	
Tumour bed core biopsies					✓***	

*Blood samples (optional) taken only if consented to take part in research. In total, **three** sets of 70ml blood samples will be taken throughout the study
**Blood sample (optional) to be taken after surgery at first visit to clinic after surgery
***Tumour bed core biopsies to be collected prior to surgery

Figure 1: Patient Pathway through the NOSTRA-Feasibility Study



Expenses and payments

No expenses or payments are provided.

What will I have to do?

If you agree to take part in the study you will need to:

- Complete and sign the Informed Consent Form.
- Attend the hospital as requested for routine clinic visits and ultrasound scans. You will need to attend the hospital on an additional occasion for ultrasound tumour bed core biopsies; this will take place when you have finished your treatment and before surgery.
- Tell your study doctor or research nurse about any symptoms or side effects you experience.
- Tell your study doctor or research nurse about any medication(s) that you take at any time during the study, even if it is something that you buy without a prescription, including herbal remedies.
- Attend follow-up visits after your treatment.

What are the possible disadvantages and risks of taking part?

The associated risks or disadvantages of taking part in the study would be comparable to the risks involved with standard chemotherapy and surgery. The tests you will undergo are performed routinely; the only additional procedure that is not standard practice is the tumour bed core biopsies.

Possible side effects associated with treatment delivery and tests:

Blood sample collection: This may cause small amount of bleeding and temporary discomfort or you may feel faint. If this happens please tell the person taking the blood so that they can make sure you lie down until you are feeling better. Sometimes a bruise or redness develops at the site where the needle was inserted (but this will clear after a week or two). Please inform your study doctor or research nurse if you experience any reactions at the injection site.

Chemotherapy delivery: As chemotherapy is injected into your vein, you may feel some discomfort or pain.

Tumour bed core biopsy and surgery: You may have some pain or discomfort for a few days after the biopsy or surgery. Sometimes bruising or swelling of the breast may be experienced. It's very important to let your study doctor or research nurse know as soon as possible if you have any pain.

What are the side effects of the treatment received when taking part?

You may have side effects whilst on the study. All treatments can have side effects (known as adverse events or toxicities). You will be monitored carefully for any side effects which may be mild or very serious. Chemotherapy has numerous side effects that are well recognised and you will be given specific information on the side effects of all the drugs you are treated with. We explain the most common side effects of chemotherapy here, but we do not include all the rare ones that are unlikely to affect you.

You may get some of the side effects that are mentioned below, but you are very unlikely to get all of them. Always tell your study doctor or research nurse about the side effects you have. Your study doctor can prescribe drugs to help control some of these side effects. It is very important to take the drugs exactly as your study doctor, research nurse or pharmacist has explained. Your study doctor or research nurse will give you advice about managing your side effects. After your treatment is over, the side effects will start to improve.

Risk of infection

Chemotherapy drugs can reduce the number of white blood cells in your blood. This will make you more likely to get an infection. You will be given instructions about who to contact if you feel unwell during chemotherapy. This is especially important if you develop a fever.

Bruising and bleeding

Chemotherapy drugs can reduce the number of platelets in your blood. Platelets are cells that help the blood to clot. Tell your doctor if you have any bruising or bleeding. This includes nosebleeds, bleeding gums, blood spots or rashes on the skin. Some people may need a drip to give them extra platelets.

Anaemia (low number of red blood cells)
Chemotherapy drugs can reduce the number of red blood cells in your blood. These cells carry oxygen around the body. If the number of red blood cells is low, you may be tired and breathless. Tell your study doctor or research nurse if you feel these symptoms. If you are very anaemic, you may need a drip to give you extra red blood cells (blood transfusion).

Diarrhoea
Diarrhoea is the most common side effects of chemotherapy. Your study doctor can prescribe drugs to control diarrhoea. Let them know if it is severe or if it doesn't get better. Make sure you drink at least two litres (three and a half pints) of fluids every day if you have diarrhoea.

Feeling sick (nausea)
This may happen in the first few days after chemotherapy. Your study doctor will prescribe anti-sickness (anti-emetic) drugs to help prevent or control sickness. Take the drugs exactly as your study doctor, research nurse or pharmacist explains to you. It's easier to prevent sickness than to treat it after it has started. If you still feel sick or are vomiting, contact the hospital as soon as possible. They can give you advice and change the anti-sickness drug to one that works better for you.

Loss of appetite
You may lose your appetite during your treatment. Try to eat small meals regularly. Don't worry if you don't eat much for a day or two. If your appetite doesn't improve after a few days, let your research nurse or dietician know. They can give you advice on getting more calories and protein in your diet. They may give you food supplements or meal replacement drinks to try. Your study doctor can prescribe some of these and you can also buy them from the pharmacy.

Heart damage
Some chemotherapy and anti-HER2 drugs affect the heart. They can cause symptoms such as shortness of breath, chest discomfort (angina) or an abnormal heart rhythm. If you experience any of these symptoms, tell your study doctor or research nurse as soon as possible.

Other common side effects are fatigue, sore mouth, mouth ulcers, constipation and dry skin. Epirubicin can cause heart damage, because of this it is not given to patients with serious heart conditions and the amount of this drug you can have in your lifetime is restricted. Cyclophosphamide and epirubicin cause a very small increase in risk of leukaemia in later life but this is rare. Docetaxel can cause nerve damage experienced as numbness and tingling in feet and hands. It can cause joint aches, muscle pains and you may experience worsening problems with your lungs.

Trastuzumab can cause temporary flu like symptoms such as shivering and a temperature after the first few administrations and can cause heart problems which can cause shortness of breath.

It's important to let your study doctor and research nurse know straight away if you feel unwell or have any severe side effects, even if they're not mentioned here.

Contact the hospital
Your research nurse will give you telephone numbers for the hospital. You can call them if you feel unwell or need advice any time of day or night.

Exposure to radiation

The tests you will undergo are used routinely except for tumour bed core biopsies, so you will not be exposed to extra radiation if you participate in this study.

Some hospitals use a type of heart scan called MUGA scan. MUGA scans use small doses of short acting radioactive tracer which is injected into a vein. You may also undergo a baseline computed tomography (CT) scan of the chest and abdomen/pelvis and this will expose you to X-ray. The radiation dose is equivalent to less than the natural background radiation in the UK that you would receive in 7 years. The Radiological Protection Division of the Health Protection Agency describes 'a few years' average natural background radiation as 'Low Risk'. The risks from these examinations would therefore be described as 'Moderate Risk' in normal healthy people. However, in your case, you are very unlikely to notice any detriment to your health

because of these examinations. The risk of developing another cancer as a result of extra scans/tests is approximately 1/1000.

Harm to the unborn child

Chemotherapy has the potential to cause birth defects and miscarriages. It is essential that if you are sexually active and have childbearing potential then you must use a highly effective method of contraception. You cannot take part in the NOSTRA-Feasibility Study if you are pregnant. If you inadvertently become pregnant while on treatment, you must notify your study doctor or research nurse immediately.

If you are female and become pregnant whilst on the study the pregnancy will need to be monitored and information about the outcome of your pregnancy will be collected from the mother's and baby's medical notes.

Breast-feeding

You should not breast feed while on chemotherapy.

What are the possible benefits of taking part?

The benefits from taking part in this study are as follows:

a) There is increasing evidence that patients who have their treatment as part of a clinical trial may have better outcomes than those who do not.

b) You would be helping doctors to know if taking biopsies from the breast after treatment is a reliable way of knowing if there is any cancer left.

c) A very special benefit from taking part in this study is that you will provide information that will help doctors change and improve the way breast cancer is treated in the future. Some women may be able to avoid unnecessary breast surgery in the future as a direct result of the knowledge gained from you taking part in this study.

d) The information we get from this study will help us to treat future patients with breast cancers better. Also the data, tumour and blood samples collected may give us a better understanding of cancer genes and DNA, and what other processes are involved in causing breast cancer and in understanding how current treatments work. This may then be used to develop a better understanding for the treatment of breast cancer in future.

What happens when the study stops?

When all patients in the NOSTRA-Feasibility Study have completed treatment, the results will be analysed and published. We will follow all patients at 5 years to gain information on long term effects on breast cancer control and side effects.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. All the information about your participation in the study will be handled in confidence. The details are included in Part 2. We ask your permission on the consent form to inform your GP that you are taking part in this research study. We will not disclose any details only the fact that you are taking part.

This completes Part 1.

If the information in Part 1 has interested you
and you are considering participation, please read the additional information in Part 2
before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss whether you should continue with the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study, you will be asked to sign an updated Informed Consent Form. Sometimes your study doctor might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, you will be told why and your continuing care will be arranged.

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

You are free to withdraw from the study at any time. You do not have to give a reason and your future treatment will not be affected. Your study doctor will discuss your treatment with you and will offer you the most suitable treatment available. However, if you choose to withdraw, we would still like to use the information we have collected up until withdrawal. If you decide to withdraw from the study it will not affect your medical care in any way. If you lose capacity to consent during the study, you would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other study related procedures performed.

What if there is a problem?

Complaints

If you have a concern about any aspect of this research study, you should contact your study doctor in the first instance who will do their best to answer your questions. You can use the contact number at the end of this sheet.

If you remain unhappy and wish to complain formally, you can do this through the Patient Advise and Liaison Services (PALS) or the National Health Service (NHS) complaints procedure. Details can be obtained from your hospital.

Harm

It is unlikely that taking part in this study will harm you. However, in the event that something does go wrong and you are harmed and this is due to someone's negligence then you may have grounds for legal action for compensation against the sponsor of the study (University of Birmingham) or the NHS Trust but you may have to pay your legal costs. NHS Trust and Non-Trust Hospitals have a duty of care to patients treated, whether or not the patient is taking part in a clinical trial and the normal NHS complaints mechanisms will still be available to you (if appropriate). The sponsor (University of Birmingham) of the study does not hold insurance against claims for compensation for injury caused by participation in this study and they cannot offer any indemnity.

Will my taking part in this study be kept confidential?

All information collected about you for this study will be subject to the EU General Data Protection Regulation and Data Protection Act 2018 for health and care research and will be kept strictly confidential. University of Birmingham is the sponsor for this study based in the UK. We will be using information obtained directly from your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. University of Birmingham and the NHS will keep identifiable information about you for at least 10 years after the study has finished.

All information including personal data collected indirectly or directly by the Sponsor will be securely stored at CRCTU at the University of Birmingham (NOSTRA-Feasibility Study Office) on paper and electronically and will only be accessible by authorised personnel. With your permission your study doctor will provide your initials, date of birth and hospital number when they enter you into the study and they will notify your GP that you intend to participate. They will also send a copy of your signed Informed Consent Form in the post to the NOSTRA-Feasibility Study Office.

The NHS will use your name and contact details to contact you about the research study and make sure that relevant information about the study is recorded for your care and to oversee the quality of the study. Individuals from University of Birmingham and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The NHS will pass these details to University of Birmingham along with the information collected from your medical records. The only people in University of Birmingham who will have access to information that identifies you will be people who need to contact you regarding the study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details. Your study doctor or research nurse may also need to send a copy of your Informed Consent Form to other healthcare professionals (e.g. your GP or NHS pathologist) to prove that you have given consent to take part in the study before they will provide information or tumour samples.

In the NOSTRA-Feasibility Study Office you will be identified by a unique trial number. In routine communication between your hospital and the NOSTRA-Feasibility Study Office you will only be identified by your trial number, initials and date of birth. We will need to record, and occasionally refer to you using your hospital and histopathology numbers when requesting tumour samples from your hospital. In addition, your trial number, hospital and histopathology numbers may be included on samples sent to University of Edinburgh and HBRC at the University of Birmingham for central review to help specialist pathologists identify the tumour samples. If you have consented to provide additional blood samples for research your trial number may be included on the blood samples sent to the Institute of Cancer and Genomic Sciences, University of Birmingham.

All information will be treated as strictly confidential and nothing that might identify you will be revealed to any third party other than those involved in the treatment or organisation of tumour and blood sample collection and transfer (e.g. staff at University of Birmingham and University of Edinburgh). It may be necessary to send information about you such as trial number and date of birth to the collaborating company Roche. This is for your and others protection to track the safety of the treatments used. They have the same duty of confidentiality to you as all other research study personnel.

By taking part in the study you will be agreeing to allow research staff at your hospital and from the NOSTRA-Feasibility Study Office to look at the study records, and this includes your medical records. It may be necessary to allow authorised personnel from the University of Birmingham and/or NHS bodies to have access to your medical and research records. This is to ensure that the study is being conducted to the highest possible standards.

From time to time we may be asked to share the study information (data) we have collected with researchers running other studies in this organisation and in other organisations so that they can perform analysis on the data to answer other important questions about breast cancer. These organisations may be universities, NHS organisations or companies involved in health research and may be in this country or abroad. Any such request is carefully considered by the study researchers and will only be granted if the necessary procedures and approvals are in place. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance. Under no circumstances will you be identified in any way in any report, presentation or publication arising from this or any other study.

All individuals who have access to your information have a duty of confidentiality to you.

If you choose to withdraw from the study treatment, we would still like to collect relevant information about your health, as this will be invaluable to our research. If you have any objection to this, please let your study doctor know.

You can withdraw your consent to our processing of your data at any time. Your rights to access change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. Under the provisions of the EU General Data Protection Regulation you have the right to know what information the NOSTRA-Feasibility Study Office has recorded about you. If you wish to view this

information or find more about how we use this information, please contact Legal Services at the address below. Please note that a small fee may be payable to retrieve this information.

Legal Services
University of Birmingham
Edgbaston
BIRMINGHAM
B15 2TT

You can find out what we do with your data in our Privacy Notice see https://www.birmingham.ac.uk/crctu

Involvement of the General Practitioner/family doctor (GP)

With your permission your GP will be informed that you are taking part in the study. Your study doctor or research nurse may contact your GP for an update on your progress if you are no longer attending clinic or cannot be contacted by other means.

What will happen to any samples I give?

Routine blood samples that have been taken during the study will be used to monitor your clinical condition and will be destroyed soon after the blood test. These samples will not be used for any other purpose. If consented, additional blood samples collected for research purposes will be sent for storage and subsequent cancer DNA analysis by the Institute of Cancer and Genomic Sciences, University of Birmingham.

Tumour samples will be sent to HBRC for storage and central review by specialist pathologists. Following central review they will be sent to the University of Edinburgh for future research into breast cancer. Tumour samples will be sent back to your hospital at any time if they are needed.

With your permission, access to your tumour samples will be available to other scientists whose projects are approved by the NOSTRA-Feasibility Study Trial Management Group. These scientists may work outside the European Union. Clearly we cannot describe what these future projects might involve. We would ensure that any such project is ethically approved but we would not seek further consent from you. Tumour samples used by these scientists will only be identified by your unique trial number. This will allow us to compare what scientists find out about the biochemical features in your tumour to the information regarding your response to treatment. Scientists may be given direct access to anonymised data about you; however it will not be possible to identify you directly from this information.

It is possible that information will arise from this research that is of commercial value. You or your family will not benefit financially from any commercial application arising from the use of your tumour and blood samples or data.

Will any genetic tests be done?

We intend to study the expression of genes within both blood and tumour samples. We will therefore be analysing DNA and RNA (gene messages) in tumour and blood samples. In the future it may be very important to use these samples for new research on tumour genes. Some of the genes studied will be inherited genes. However, currently none of the genes that we intend to study is known to be of medical significance.

What will happen to the results of the research study?

We intend to publish the results of this research in a cancer related medical journal. No patients will be identified in any presentations, reports or publications resulting from the study. Patients taking part in this study can find out about the results from their study doctor once the results have been published. The results will also be available on the CancerHelp website.

Who is organising and funding the research?

NOSTRA-Feasibility is a non-commercial feasibility study. The idea for the study came from doctors in the NHS and universities and these doctors lead this research study.

The study is sponsored by the University of Birmingham and is co-ordinated by the CRCTU at the University of Birmingham (the NOSTRA-Feasibility Study Office).

The project has been reviewed and approved by Cancer Research UK. It is funded by an educational grant from a drug company called Roche. Your study doctor will not receive any personal payments for including you in this research study.

The research study is being carried out by a network of doctors across the UK and has been approved by the National Cancer Research Institute Breast Clinical Studies Group.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the West Midlands-Solihull Research Ethics Committee.

What if I lose capacity to consent during the study?

If you have consented to participating in the study and subsequently lose the capacity to consent during the study for whatever reason, you would be withdrawn from the study. Identifiable data or tumour already collected with consent would be retained and used in the study. No further data or tumour would be collected or any other research procedures carried out on or in relation to you.

Further information and contact details

What Happens Now?

You will have some time to think about the study and make your decision. You may wish to discuss it with your family or friends. If you take part, you will receive a copy of this information sheet and a copy of the signed Consent Form to take home. If, at any time, you have any questions about the study you should contact your study doctor or research nurse using the details below.

Contact Details

Study Doctor: _____

Research Nurse: _____

☎: _____ Emergency (24 hours) ☎: _____

General information on breast cancer is available on the Breast Cancer Care website. You may also find it helpful to contact CancerHelp, an information service about cancer and cancer research studies by Cancer Research UK. Information about NOSTRA-Feasibility can also be found on the CancerHelp website.

Freephone: 0808 800 40 40 Website: www.cancerhelp.org.uk

CANCER RESEARCH UK