Response to Optimal Selection of neo-adjuvant Chemotherapy in Operable breast cancer

EudraCT No. 2013-004307-39

We would like to invite you to take part in a clinical trial (research study) run by the University of Birmingham. Before you decide we would like you to understand why the research is being done and what it would involve for you. Please take the time to read the following information carefully and discuss it with friends and relatives if you wish. Your doctor will go through the information sheet with you and answer any questions you may have. This leaflet is divided into two parts.

- Part 1 tells you the purpose of this study and what will happen to you if you 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. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?

This study is designed to answer two questions about breast cancer treatment:

1) To find out if two new tests called CEP17 and TOP2A that are performed on cancer tissue will help refine the selection of chemotherapy drugs to treat breast cancers before surgery.

We are trying to find out if this test will tell us if it is best to treat your cancer with an anthracycline based treatment or a taxane based treatment. Anthracyclines and taxanes are classes of chemotherapy drugs that work in very different ways to kill cancer cells. Some patients will respond best to anthracyclines while others will respond best to taxanes. At present we usually give both an anthracycline and a taxane in sequence because we don’t know which patient will respond to which class of drug but this means everyone is experiencing the side effects of both of these types of drug. If the trial is successful we will be able to use the CEP17 and TOP2A tests to decide which chemotherapy drug to give to which patient, allowing us to successfully treat the cancer without needing to expose all patients to all of the drugs.
2) To find out if a well-established surgical procedure called sentinel lymph node biopsy is a reliable test to show that chemotherapy given before surgery (neo-adjuvant chemotherapy) has eliminated all the cancer cells under the arm.

This part of the trial is only applicable to patients who we know have cancer under the arm to start with.

**What is a CEP17 test?**

The CEP17 test is a molecular test carried out on one of the long pieces of DNA or chromosome inside cancer cells. CEP17 is a region of chromosome number 17. Normal cells and many cancer cells have just two copies of CEP17. In about one third of cancers there are extra copies of CEP17 and it is these cancers which seem, from previous research, to be particularly sensitive to anthracycline chemotherapy.

**What is a TOP2A test?**

TOP2A is short for Topoisomerase 2 alpha gene. Genes provide a template for the creation of proteins within a cell. The TOP2A gene is the template for a protein enzyme that divides and rejoins strands of DNA. The chemotherapy drug epirubicin is thought to work by interfering with how this enzyme works and results in more breaks in DNA forming which ultimately causes the cancer cells to die. The TOP2A test will tell us if the number of gene copies for TOP2A is normal or abnormal. Cancers with abnormal copies of TOP2A may be sensitive to anthracycline chemotherapy.

**What chemotherapies are being tested?**

We are testing two different types of chemotherapy treatment which contain either an anthracycline (epirubicin) or taxane (docetaxel):

1) FEC (5-fluorouracil, epirubicin and cyclophosphamide)
2) TC (docetaxel and cyclophosphamide)

Epirubicin is given with two other drugs called 5-fluorouracil and cyclophosphamide, while docetaxel is given with cyclophosphamide only. The two different combinations of chemotherapy drugs (FEC and TC) being used in this study are all used as standard treatments for breast cancer.

**What is 5-Flourouracil?**

5-Flourouracil 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 Docetaxel?**

Docetaxel is a drug that is used widely to treat several cancers. Although it has 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 if my cancer is HER2 positive?**

All patients in this study will have a HER2 test performed on their biopsy specimen. We do this to see if you will benefit from a drug called trastuzumab (Herceptin). We know that giving chemotherapy and trastuzumab together results in better cancer shrinkage and more patients with no cancer left at all at the end of chemotherapy. It is routine to give trastuzumab and taxanes together as neoadjuvant treatment.
Why have I been invited to take part?

Your breast cancer team have recommended that the best way to treat your cancer is to start with chemotherapy. This is intended to eliminate as much cancer as possible. Following chemotherapy you will undergo surgery to remove any remaining cancer in the breast. Because you will receive chemotherapy first you may be eligible to take part in the ROSCO study which is being conducted at this hospital. All suitable patients are being approached to see if they would like to take part in this trial. Nationally 1050 patients with breast cancer will be invited to take part in this trial.

Do I have to take part?

It is up to you to decide whether or not to take part in this research study. 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 a 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 ROSCO Trial Office (at the Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham).

The biopsy that was taken to show you have a cancer will be sent to a NHS testing laboratory to have the CEP17 and TOP2A tests performed on the cancer cells. The tissue sample will then be sent on to a Cancer Research UK research laboratory at the University of Edinburgh where it will be stored for additional research.

The study doctor or research nurse will ask you details about your health and other illnesses. They need to know about any treatments you take, including things you take without a prescription such as herbal remedies. Please tell them if you have heart disease or any other serious medical condition.

Some additional tests may be needed if you are entering the study to confirm that it is safe and that we have all the information we need. All patients in ROSCO will have a heart ultrasound (echocardiogram) before treatment starts. This is routine in many hospitals before starting treatment with anthracyclines. By the time you are given this leaflet you will probably have already had most of the tests you need, such as mammograms and ultrasound examinations, before you can enter the trial. You may need additional tests such as CT scans or MRI scans and you will need to have a clip placed inside the centre of your cancer. If there are abnormal or suspicious lymph glands under the arm these will have been, or will be, biopsied with a thin needle or a core biopsy will be performed, just like the one used to take the breast biopsy. All of these tests and procedures are routine in patients having chemotherapy.

Once the result of your CEP17 and TOP2A tests is known your study doctor will again call the ROSCO Trial Office and you will have a treatment allocated to you (FEC or TC). This treatment will be allocated through a process called randomisation. This means the doctors and you will not select your treatment; it will be allocated at random by a computer, with an equal chance of being randomised to each treatment type.

There is a small chance that for technical reasons it will not be possible to measure the CEP17 or TOP2A in your tumour sample. If this is the case you will not be able to enter the trial. If this happens your study doctor will discuss other treatment options with you.

Taking part in the research study

Before you start treatment a blood sample will be taken for research as well as for routine tests. Some of the blood will be used to obtain DNA which will be used to look at the genes that are responsible for how the body eliminates drug. We will try and find out if some people carry altered genes that may account for the variation in effectiveness of treatment and the degree of side effects experienced whilst on chemotherapy. You can indicate whether you wish to participate in this part of the study by selecting ‘yes’ within the Consent Form. You will start chemotherapy with the allocated treatment as soon as is practical. Taking part in the study will not delay your treatment by more than a week. You will receive chemotherapy through a vein or a central venous catheter.
How often are the treatments given?

We usually describe chemotherapy treatments as being given in cycles of treatment. Before surgery you will receive one of the following depending on which treatment you are allocated:

- FEC which is given for three weeks for 4 cycles
- TC which is given for three weeks for 4 cycles

If your breast cancer is HER2 positive you will also receive intravenous (into a vein) or subcutaneous (under the skin) injections of trastuzumab during your treatment. Trastuzumab is currently given every three weeks for a whole year. It is not known if this is the correct duration of treatment and there are clinical trials addressing this question. Your study doctor may ask you to participate in one of these trials. This will not affect your ability to take part in ROSCO. Patients receiving trastuzumab will need a heart ultrasound after the second cycle of chemotherapy.

You will be monitored carefully during treatment to see if your tumour is shrinking and to monitor any side effect you may experience.

Once you have completed all of your chemotherapy a repeat ultrasound will be performed and all patients will have a repeat heart ultrasound. An additional optional blood sample will also be taken.

When will my surgery take place?

About 3-6 weeks after chemotherapy has completed you will undergo surgery. The type of operation 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 chemotherapy 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?

We will look at the tissue removed during the operation to see if there is any cancer left. This will be done by a pathologist in your local hospital but also by specialist pathologists based in Edinburgh.

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 to give 6 cycles of chemotherapy and a few doctors may recommend a further two cycles of the same chemotherapy to try and maximise the chances of killing any remaining cancer cells that have travelled out of the breast that have survived. It is not known for certain that this is always needed and your study doctor may decide after discussion with you that no further chemotherapy is required. If you are having treatment with trastuzumab, because your cancer is HER2 positive, this will continue for up to a year in total.

If there is still cancer left after surgery then the risk of the cancer returning in the future is higher and you will require more chemotherapy. Your study doctor will therefore continue your chemotherapy treatment but you will be given the opposite treatment to that which you were allocated, so if you received FEC first you will go on to receive TC and vice versa.

The tissue samples removed during your surgery will be sent to Edinburgh to be examined by the specialist pathologists. The tissue will be kept at the University of Edinburgh for storage for later research. If at any time your hospital finds that it needs to recall any of your tumour samples, this will be performed without delay.

What happens if the first four cycles of chemotherapy does not shrink the cancer?

If the cancer has not shrunk very well, your doctor will discuss the possibility of having more chemotherapy before surgery. If this is considered potentially beneficial, you will need to have a second biopsy of the breast cancer to be sure there is still living cancer present and not just scarring. If there is still invasive cancer in the biopsy, you will have 4 more cycles of chemotherapy. Your operation will be scheduled for when your second course of chemotherapy is finished. If you need more chemotherapy you will be treated with the drugs you have not already had so if you received FEC first you will go on to receive TC and vice versa. Your biopsy sample will be reviewed by the specialist pathologist and the tissue kept in Edinburgh as described above.
What about the glands under the arm (axilla)?

If a pre-chemotherapy biopsy shows cancer

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). A recent technique called sentinel lymph node biopsy (sometimes called SLNB) is a routine procedure used to find out if there are cancer cells in the 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.

We don’t yet know if sentinel lymph node biopsy is a reliable way of telling if all the cancer has gone if there was cancer in the glands before chemotherapy. In this trial if you have a biopsy that shows cancer cells in the axilla, we would like to do a sentinel lymph node biopsy and then a complete axillary clearance operation all at once so we can find out if sentinel lymph node biopsy is a good way of finding out if the cancer has all gone or not. This will add a short amount of time to your operation. 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.

You can indicate whether you wish to participate in the end of treatment sentinel lymph node biopsy and axillary clearance component of the study by selecting ‘yes’ within the Consent Form.

If a pre-chemotherapy ultrasound or biopsy is normal

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 not form part of the ROSCO trial and will be the standard treatment offered by your doctor but may well involve a sentinel node biopsy, briefly the options are summarised below.

Sentinel node biopsy before chemotherapy

Your doctors may recommend a sentinel node biopsy before chemotherapy. If this 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 it shows cancer, then most surgeons would recommend an axillary clearance after your chemotherapy.

Sentinel node biopsy after chemotherapy

Your doctors may recommend a sentinel node biopsy after your chemotherapy. This can be done as part of your breast cancer operation. 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 doctors recommend an axillary clearance as the only procedure and this will be performed at the same time as your breast operation.

Other treatments

Once your chemotherapy and surgery are completed you may require radiotherapy, and if your cancer has oestrogen receptors (ER positive) you will be commenced on hormone therapy. These treatments are standard treatments and not part of the ROSCO trial.

Follow up

You will have regular follow up visits at the hospital to check on your progress. After 5 years we will ask all ROSCO participants to attend for a heart ultrasound so we can understand any late effects of treatment on heart performance. Your study doctor will provide us an update on your progress each year for at least 5 years. If you are discharged from hospital follow up, we will ask your doctor to
Keep in contact with you by telephone and to check your NHS records or ask your GP for an update on your progress.

**Extra research**

**Blood samples**

We want to learn as much as possible about breast cancer from the ROSCO study. In the future we hope to extend the work we do on blood samples by collecting and storing extra blood samples both during and after your chemotherapy and we may ask you to provide some additional research blood samples in the future. Where possible, these will be taken at the same time as a routine blood test. You do not need to have these extra blood samples taken and deciding not to provide these samples will not affect your participation in ROSCO.

**Quality of life**

As part of the ROSCO trial, we are very interested in how your treatments might affect your Quality of Life and well-being. We think it is very important to find out how patients taking part in the ROSCO trial feel, both emotionally and physically and to study any side effects in some detail.

To get reliable information about Quality of Life, we need about 500 patients to tell us more about their treatment experience. This information will be used to compare the possible advantages and disadvantages of each treatment combination. The results will make it a lot easier to advise future patients about what their experience of treatment might involve.

If you agree to take part in the optional Quality of Life sub-study you will be asked to complete six identical Quality of Life questionnaire booklets at the following times:

1) Prior to commencement of chemotherapy
2) Following completion of cycle 2
3) Following completion of cycle 4
4) Six weeks after completion of surgery
5) One year post-randomisation
6) Two years post-randomisation

The first questionnaire will be given to you by your research nurse and the remaining questionnaires will be sent to you in the post from the ROSCO Trial Office.
Summary

The assessments and tests are summarised in the table below:

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Expenses and payments

No expenses or payments are available for this study.

What will I have to do?

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

- Attend the hospital as requested for clinic visits and ultrasound scans.
- Tell your study doctor about any symptoms or side effects you experience.
- Tell your study doctor about any medication that you take at any time during the study, even if it is something that you buy without a prescription, including herbal remedies.
- Carry your ROSCO identification card, that we will provide, that indicates you are taking part in this study. Take this card with you at all times and show it to any doctors, nurses or pharmacists treating you so that they know you are taking part in a clinical trial.

What are the alternative treatments?

Your doctors will have already discussed the standard treatment for your cancer in your hospital with you. Most centres will treat your cancer with 6-8 cycles of chemotherapy before surgery and this would most likely be a combination of anthracycline and taxane chemotherapy.

What are the possible disadvantages and risks of taking part?

Very few because you will have chemotherapy anyway. The CEP17 and TOP2A tests have been shown to identify a group of patients who benefit from the addition of anthracyclines compared to other chemotherapy treatments. It is not yet clear that these will be useful tests to help decide between taxanes and anthracyclines. The trial has been designed to allow patients to receive all the drugs because if the first 4 cycles do not shrink the cancer very well and there is still cancer in the breast, you will then receive the other type of chemotherapy treatment.

Patients that receive both anthracyclines and taxanes will receive two more cycles of treatment than normal and will therefore be required to attend more often however those who have a complete response at surgery may receive two cycles less.
Some patients get a reaction to the blue dye used in a sentinel lymph node biopsy.

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

**Possible side effects**

Chemotherapy has numerous side effects which are well recognised and you will be given specific information on the side effects of all the drugs you are treated with. A common side effect from all chemotherapy drugs is a risk of severe infections that the body cannot fight due to low white blood cells caused by chemotherapy. You will be given instructions about who to contact if you feel unwell during chemotherapy. This is especially important if you develop a high fever. Other common side effects are nausea, fatigue, sore mouth and mouth ulcers, diarrhoea, 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. Taxanes cause nerve damage experienced as numbness and tingling in feet and hands. Docetaxel can cause joint aches and muscle pains.

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.

**Exposure to radiation**

If you were not taking part in the study you might have a CT scan, a bone scan, and a mammogram. These tests are used routinely to determine the extent of the cancer and will also be performed if you take part in ROSCO. Some hospitals use a type of heart scan called a MUGA scan instead of a heart ultrasound. MUGA scans use small doses of short acting radioactive tracer which is injected into a vein. If your hospital uses this type of test and you were not participating in the study you would receive 5 of these scans. If you take part in ROSCO you may receive an additional 2 MUGA scans. If you agree to take part in the optional sentinel lymph node sub-study you may also have a radioactive tracer injected into your tumour.

These scans/tests (except ultrasound) use radiation that can contribute to causing cancer at a later date. The dose from the extra MUGA scans and the radioactive dye is equivalent to about 7 years of average natural background radiation. 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 miscarriage. It is essential that if you are sexually active and have childbearing potential, you must take adequate contraceptive measures. You cannot take part in ROSCO if you are pregnant. If you inadvertently become pregnant while on treatment, you must notify your study doctor immediately.

If you are female and become pregnant whilst on the trial, or you are male and your partner becomes pregnant, 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?**

Taking part in ROSCO has the potential to reduce the amount and type of chemotherapy you are treated with without losing benefit from chemotherapy.
What happens when the trial stops?

When all patients in ROSCO have completed treatment, the results will be analysed and published. We will follow all patients up for a minimum of 5 years to gain information on long term effects on breast cancer control and side effects. We will organise a final heart ultrasound on all patients after 5 years.

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.

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 trial, 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 Consent Form. Sometimes your study doctor might consider it to be in your best interests 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.

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 National Health Service (NHS) complaints procedure. Details can be obtained from your hospital.

Harm

If you are harmed and this is due to someone’s negligence then you may have grounds for legal action for compensation against the University of Birmingham or the NHS Trust treating you 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. The sponsor (University of Birmingham) of the trial 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 Data Protection Act 1998 and will be kept strictly confidential. All information will be securely stored at the ROSCO Trial Office on paper and electronically and will only be accessible by authorised personnel.

With your permission your study doctor will provide your full name, address (if you agree to participate in the Quality of Life study), and NHS Number (or in Scotland the Community Health Index (CHI)) over the phone 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 Consent Form in the post to the ROSCO Trial Office.

Your study doctor or research nurse may also need to send a copy of your 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 tissue samples.

In the Trial Office you will be identified by a unique trial number (TNO). Your study doctor will provide medical data about you to the Trial Office on paper, via telephone or electronically. In routine communication between your hospital and the Trial Office you will only be identified by your TNO, initials, and date of birth. We will need to record, and occasionally refer to you using your hospital and histopathology numbers when requesting tissue samples from your hospital. In addition, your initials,
date of birth, hospital and histopathology numbers may be included on samples sent in the post to our CEP17/TOP2A testing laboratory and to the specialist pathologists in Edinburgh to help them identify the tissue samples. These identifiers will be removed prior to storage at the University of Edinburgh. Your TNO, initials and date of birth will be included on blood samples sent to the University of Cambridge. If you are taking part in the optional Quality of Life study the Trial Office will write to you at your home address.

We would also like to obtain information about your progress from your GP and the national health registries (such as the Cancer Registries or the Health and Social Care Information Centre, Data Linkage Service). In order to do this, we may need to provide your full name, address and/or NHS (CHI) number.

By taking part in the study you will be agreeing to allow research staff from the ROSCO Trial Office to look at your study records, this includes your medical records. It may also be necessary to allow authorised personnel from government regulatory agencies (e.g. the Medicines and Healthcare products Regulatory Agency (MHRA)), the University of Birmingham and/or NHS bodies to have access to information about you. 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 trial information (data) we have collected with researchers from other organisations so that they can perform analysis on the data to answer other important questions about breast cancer. Any such request is carefully considered by the trial researchers and will only be granted if the necessary procedures and approvals are in place. Trial data sent to an external organisation will be completely anonymised and it will not be possible to identify you from this information.

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. Under the provisions of the Data Protection Act 1998 you have the right to know what information the Trial Office have recorded about you. If you wish to view 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

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 and they may send them a copy of your Consent Form.

What will happen to any samples I give?

If you agree to take part in the trial samples of your tumour will be sent to an NHS testing laboratory to measure CEP17/TOP2A. To ensure the quality of the tests performed by these laboratories your samples may also be sent to another laboratory for retesting, just to make sure the results are accurate and consistent between laboratories. The ROSCO Principal Scientist (Professor Bartlett) is a leading expert in CEP17 and TOP2A biomarker research. The quality checks performed on your samples may be undertaken in Professor Bartlett's laboratory in Canada or another suitable laboratory.

Tumour samples will also be sent to Edinburgh for review by specialist pathologists. They will then be sent to the University of Edinburgh for central storage. Tumour samples will be sent back to your hospital at any time if they are needed. Blood samples will be collected and sent for centrally storage and subsequent analysis to the University of Cambridge and potentially in the future the University of Edinburgh and other research organisations.
With your permission access to your tissue samples will be available to other scientists whose projects are approved by the ROSCO 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. Tissue and blood samples used by these scientists will only be identified by your unique TNO. This will allow us to compare what scientists find out about the biochemical features in your tumour and blood to the information about 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 samples or data.

**Will any genetic tests be done?**

We intend to study the expression of genes within both blood and tissue samples. We will therefore be analysing DNA and RNA (gene messages) in tissue 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. We expect the first results to be available in approximately 5 years.

**Who is organising and funding the research?**

ROSCO is a non-commercial clinical trial. The idea for the trial 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 Cancer Research UK Clinical Trials Unit (CRCTU) at the University of Birmingham (the Trial Office).

The project has been reviewed, approved and part funded by Cancer Research UK and by an educational grant from a drug company called Celgene. At present there are no drugs in ROSCO made by Celgene but we hope to introduce some additional elements to the study in the future and for some patients this may involve being treated with a drug called Abraxane instead of docetaxel, Abraxane is made by Celgene.

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 “National Research Ethics Service Committee West Midlands – Edgbaston” Research Ethics Committee.
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) ☏: __________________________

You may also find it helpful to contact CancerHelp, an information service about cancer and cancer research studies by Cancer Research UK. Information about ROSCO can also be found on the CancerHelp website. Freephone: 0808 800 40 40 Website: www.cancerhelp.org.uk