FOXFIRE – An open-label randomised phase III trial of 5-Fluorouracil, Oxaliplatin and Folinic acid +/- Interventional Radio-Embolisation as first-line treatment for patients with unresectable liver-only or liver-predominant metastatic colorectal cancer

Patient Information Sheet

You are being invited to take part in a clinical research study comparing chemotherapy with the combination of chemotherapy plus radioembolisation for colorectal cancer that has spread to the liver. Before you decide, it is important for you to understand why the research is being done and what it will involve. Your doctor and/or nurse will discuss the study with you and allow you time to ask any questions you may have. This information sheet is designed to help you understand what the study is about and you may take this sheet away with you. Please take time to read the following information carefully and discuss it with others if you wish. Please ask 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. Taking part in this study is entirely voluntary.

Why Is This Study Being Done?

When cancer of the bowel is not completely removable by surgery, or when the cancer has spread to somewhere else in your body, chemotherapy may be given with the aim of killing cancer cells. Although chemotherapy does not cure this form of bowel cancer, chemotherapy can shrink or control it for a period of time. Generally speaking, patients who receive chemotherapy live longer and have better control of their symptoms than those who do not receive chemotherapy.

Radioembolisation is a new form of treatment that has been designed to selectively deliver radiotherapy (“X-ray treatment”) to cancer within the liver, either cancer that has arisen in the liver itself or cancer that has spread to the liver from somewhere else in the body. In your case, radioembolisation would be aiming to treat the areas in your liver that contain “metastases” that have spread to there from the bowel cancer. This form of treatment has been used in a number of previous clinical trials to treat patients with your condition. The aim of this trial is to measure how well this treatment works in controlling or shrinking liver metastases when it is used in combination with chemotherapy.

Unfortunately both chemotherapy and radioembolisation can produce side effects as well as benefits, and there is no guarantee that the treatments will help every patient treated. Even when chemotherapy and radioembolisation work well, they may not control the cancer indefinitely. For these reasons, we are always trying to improve treatments and to combine effective treatments.

In the UK, the current standard treatment for patients with your condition is chemotherapy, usually given as a combination of drugs such as 5-FU (also known as ‘5-fluorouracil’) together with either irinotecan or oxaliplatin. In this study, the chemotherapy drugs that will be used are 5-FU and oxaliplatin.

In this trial, we want to see if the addition of radioembolisation to standard chemotherapy improves the results compared to when chemotherapy is given on its own. The only scientific way of finding the answer to this question is to treat half the patients with the current standard treatment (chemotherapy) and the other half of the patients with the experimental treatment (chemotherapy plus radioembolisation).
Radioembolisation uses very small radioactive particles (called SIR-Spheres microspheres, manufactured by Sirtex Medical Limited, Sydney, Australia), which have been used to treat thousands of patients worldwide. SIR-Spheres are now licensed in the UK and the rest of the European Union for use in the treatment of liver tumours, including cancers that have spread to the liver from the bowel. Radioembolisation (which is also known as Selective Internal Radiation Therapy, or SIRT) has been reviewed by the National Institute of Clinical Excellence (www.nice.org.uk), who have said that further research (such as this clinical trial) is necessary before the value for patients can be assessed. We have performed one clinical trial in the UK and Australia to tell us what doses of oxaliplatin and 5-FU chemotherapy should be used with radioembolisation. The FOXFIRE clinical trial builds on that experience to try to see how effective this combined treatment is.
In the FOXFIRE trial, we are asking the following two questions:

1. Does the combination of chemotherapy and radioembolisation improve outcomes for patients compared to chemotherapy on its own?
2. Are there any rare side effects of radioembolisation in combination with chemotherapy that we do not know about?

The FOXFIRE trial has been designed to try to answer these questions by carefully monitoring the treatment in patients with colorectal cancer that has spread to the liver.

Why have I been chosen?

You have been invited to think about entering this study because you and your doctors are considering a course of chemotherapy to treat your bowel cancer. Several hundred patients like you will take part in this trial, in at least 12 hospitals in the UK over several years. A similar trial is being conducted in Australia, New Zealand, the USA and the European Union, which will help us to answer these important research questions as efficiently as possible.

Do I have to take part?

You will be given time to consider taking part in the study. Participation in the trial is entirely voluntary. Your standard of care will not be affected if you decide not to take part in this study.

If you decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. You are free to withdraw at any time without giving a reason. This will not in any way affect any future care you will receive from your medical and nursing team. If you do withdraw your consent, your participation in FOXFIRE may mean that we have already gathered some data and blood or tissue samples. We are required to maintain access to this data and would like to use this information in the future for analysing this trial. Any tissue and blood samples collected prior to consent withdrawal belong to the sponsor and will be used anonymously according to its intended use for the trial and any future sub studies they were collected for and consented to. You are free to withdraw at any time.

What will happen to me if I take part?

In order to compare the standard treatment (treatment A) with the new combination treatment (treatment B), we need to randomise patients to receive one of the treatment options. Randomisation means that neither you nor your doctor will be able to select which treatment you will receive. The Trial Office in Oxford will use a computer to randomly allocate you to one of the two treatment groups. This will ensure that the number of patients in each of the two treatment groups is similar. The randomisation process means that you have a 50% chance of receiving treatment A and a 50% chance of receiving treatment B. The trial has been designed in this way in order that the statisticians may answer the important research questions as early as possible.

If you agree to take part in the trial, having read and understood this information sheet and once you have had any questions answered, you will be asked to sign a consent form to say that you agree to take part. You will be given a copy of the consent form to keep along with this information sheet.

We will then telephone the Trial Office who will randomise you to one of the two available treatments. This will determine which treatment you will receive.

Either  A – Standard OxMdG chemotherapy for 6 months

OR  B – Standard OxMdG chemotherapy for 6 months, with radioembolisation.

If you are randomised to Arm B of the clinical trial, although you will receive all the chemotherapy at your local hospital, your hospital may not have the facilities to do the RE treatment since it requires special equipment and expertise.

If this is the case, you may be required to travel 2-3 times to another hospital for the RE treatment, which may require 1 or 2 overnight stays. If this applies to you, exact details will be provided by the study doctor and research nurse.

Treatment A – Standard OxMdG chemotherapy

Standard chemotherapy treatment involves numerous visits to the hospital, with the chemotherapy drugs given by a drip through a needle into one of your veins through a thin rubber tube ("cannula").

The chemotherapy drugs will be given once every two weeks for 24 weeks in total, plus any additional time due to side effects such as low blood counts. On the first day of every two-week ‘cycle,’ you will come to the hospital out-patients clinic to receive a combination of the oxaliplatin and 5-FU along with a vitamin called folinic acid. The small portable pump you will be fitted with will continue to drip the 5-FU into your vein over a 48-hour period. This way of giving 5-FU is known as the ‘infusional’ or ‘de Gramont’ method, named after the doctor who developed it. However, in many hospitals, it may be possible for you to receive the treatment as an
outpatient using a small portable pump, which you can take home with you. If you opt to have pump treatment at home, you will need to be fitted with a thin tube (“line”) in the arm, shoulder or chest. This tube leads into one of the big veins in your chest and provides a place for the chemotherapy pump to be attached. Once this is fitted, you will still need to attend the hospital for a day each fortnight, but it will not be necessary to stay in hospital overnight. There are several different designs of tube and pump and your doctor will explain which is to be used and what is involved. This method is called the ‘modified de Gramont’ or ‘MdG’ chemotherapy. When combined with oxaliplatin, it is called ‘OxMdG’ chemotherapy. It is given every 14 days, unless there are problems with blood counts or other side effects.

**Treatment B – Standard OxMdG chemotherapy plus radioembolisation**

The standard OxMdG chemotherapy is given in exactly the same way as described for Treatment A, except for two factors – 1: the addition of radioembolisation which will be given once during the second ‘cycle’ of chemotherapy; 2: the dose of oxaliplatin is reduced slightly for three cycles to ensure that your white blood cell levels do not fall too low. Radioembolisation involves injecting SIR-Spheres microspheres into the blood stream of the liver. This requires two extra visits over and above the usual treatment with chemotherapy alone.

One or two weeks before the radioembolisation is scheduled to be given, you will be admitted as a day patient for a preparatory procedure which is conducted in the radiology department. Under local anaesthetic, a small incision will be made between the groin and leg, and a flexible catheter will be passed through the incision up to the liver under X-ray guidance in order to assess the blood supply to the liver tumour(s). This procedure is carried out in order to minimise the risk that the radioembolisation treatment could affect areas outside your liver (e.g. the stomach) and to ensure that it will be possible for you to receive radioembolisation. You will also be injected with a radiolabelled dye (Technetium-99 labelled Macro-Aggreated Albumin, or MAA) in order to check the amount of blood that flows from the liver to the lungs. The result needs to be within acceptable limits to ensure you can be treated safely with radioembolisation.

On the day that the radioembolisation treatment is scheduled to be given, you will be admitted as an in-patient. The radiology procedure is repeated, with the catheter guided to a position in the artery or arteries feeding the liver tumours. Once the expert radiologist is content with the position of the catheter in the blood supply of the liver, he/she will inject the radioembolisation treatment through the catheter. The SIR-Spheres used for radioembolisation treatment pass through the catheter to the liver arteries and lodge in the blood vessels of the cancer within the liver. You will be monitored for a few hours after the procedure, and you may have to stay in hospital overnight. Staying overnight will enable nursing staff to monitor whether you are experiencing any pain since you may need to take strong painkillers.

**Treatment A and B**

You will have CT scans every 2-3 months whilst you are on study. You will have a blood test once a fortnight. At this time you will also be asked about any side effects you have experienced. It is important that you tell us about any problems as it is often possible to deal with side effects with simple adjustments to the treatment (which does not compromise your treatment).

Approximately half way through the 24 weeks of chemotherapy and then again towards the end of the chemotherapy, you will have a CT scan to see how the cancer is responding. It will then be for you and your doctor to decide if any alternative treatments are likely to be helpful, such as surgery or further chemotherapy. Although you will not receive further chemotherapy in this clinical trial, you will continue to be monitored closely with clinic visits, blood tests approximately every 12 weeks and a CT scan every 8-12 weeks (this may vary slightly according to usual practice at your hospital).

If the travelling is a problem for you, support may be available to you to help with travel expenses. Please talk to your research nurse about this.

You will be asked to complete three Quality of Life (QoL) questionnaires at a maximum of five different time points – prior to starting treatment; at the start of Cycle 4 of your chemotherapy; at your 6 month assessment, annually and at progression; or 12 months after you were randomised into the trial. This will help us to assess health-related quality of life issues. You will also be asked to complete a Short Health Economics Questionnaire prior to starting treatment, 12 months after you have been randomised, and then annually. At each point, the questionnaires will take about 15 to 25 minutes to complete. If you withdraw from study treatment, you will not be required to complete any further questionnaires.

All information will be kept confidential and you will not be identified by name.

Although it is not part of the treatment being offered to you in this clinical trial, if your doctor has arranged for a licensed “biological” drug (e.g. Avastin®, Erbitux®) to be added to your standard OxMdG chemotherapy, then your participation in this clinical trial will not affect your ability to receive this additional drug. Although this does not apply to all patients, if it applies to you, the study doctor will explain this to you in more detail since the timing of the addition of the “biological” drug to standard OxMdG chemotherapy will depend on whether you are receiving OxMdG chemotherapy in Treatment Arm A or Treatment Arm B of this clinical trial.
What do I have to do?

You must tell your study doctor and/or research staff about all past and present diseases and allergies of which you are aware, and all drugs and medications which you are currently taking. While you are on the study, if you feel the need to take other medications, including over-the-counter medications or alternative therapies, please talk with your research nurse or doctor before you take them.

As with most chemotherapy treatment, if you are of childbearing age, you will need to use an adequate form of contraception to ensure that you or your partner does not become pregnant during the study.

We will give you a small card that gives details of the study and contact numbers should you need any advice. In case of an emergency, the card will inform the doctors that you are on a clinical trial and let them know what drugs you are being treated with. You will need to carry this card with you at all times and show it to any doctors treating you so that they have details of your chemotherapy and radioembolisation (if applicable).

It is important that you attend all your clinic appointments. You should also report any side effects to your study doctor, who can prescribe medicines that usually control them.

If you are having any problems with side effects, we will give you a separate sheet giving you advice about how to deal with them. We would always recommend that you get in touch with your own chemotherapy nurse. Contact details are given at the end of this Patient Information Sheet.

If you have private medical insurance, please inform your insurance company before agreeing to take part in the study.

What are the drugs or devices being tested?

**Oxaliplatin** is a liquid chemotherapy drug widely used to treat bowel cancer.

**5-FU (or 5-fluorouracil)** is a liquid chemotherapy drug widely used to treat bowel cancer.

**Folinic acid** is a vitamin which is given as a liquid to increase the effectiveness of 5-FU and is widely used in bowel cancer.

**SIR-Spheres** are the radioembolisation treatment used to treat liver tumours including those from bowel cancer.

What are the alternatives for treatment?

If you decide not to take part in this study, you will be offered the standard treatment in the UK for bowel cancer that has spread to the liver or other internal organs. This standard treatment is usually chemotherapy injections of OxMdG (oxaliplatin plus 5-FU and folinic acid) or FOLFIRI (irinotecan plus 5-FU and folinic acid).

What are the possible side effects of taking part?

**Treatment A – Standard OxMdG chemotherapy**

Common side effects include: diarrhoea, nausea, vomiting, mouth ulcers, drop in the white blood cell count – that can make you more prone to picking up germs than usual – and numbness or tingling in hands and feet, constipation, skin dryness/peeling, fatigue, anaemia and loss of appetite.

These side effects are severe in less than 1 in 10 of patients treated.

The following side effects occur rarely, in less than 1 in 10 of patients treated: allergic reaction, bleeding, dehydration, difficulty sleeping, visual disturbance, flushing, blood in the urine, blood clots in deep veins, hiccups, chest pain (more common in patients with a history of heart disease), indigestion, rash, male changes, joint aches and hair loss.

**Treatment B – Standard OxMdG chemotherapy plus radioembolisation**

OxMdG chemotherapy plus radioembolisation may cause any of the side effects listed above in ‘treatment A’. Additionally, radioembolisation may cause side effects, although it is generally well tolerated. The commonest side effect is a mild fever that begins within 24 hours of radioembolisation and usually goes away without treatment. About half of all patients develop nausea or pain in the abdomen after radioembolisation, but this usually lasts only a few hours and can be controlled with strong painkillers or anti-sickness medication. Some patients complain of feeling ‘off colour’ or rather tired for a few weeks after radioembolisation, which is due to the fact that radiation effects last for several weeks. A very small percentage of patients have developed indigestion or stomach ulcers as a result of the treatment.

Some side effects of radioembolisation (such as fever) usually go away without treatment, and most subside with time and routine medication (e.g. painkillers, anti-nausea drugs, etc). As a precaution, you will receive
some medications such as painkillers, anti-nausea and anti-ulcer drugs prior to the radioembolisation with the aim of preventing these side effects from occurring.

More serious side effects include the possibility that the SIR-Spheres microspheres used for the radioembolisation can be incorrectly delivered and do not all remain in the liver. This can be due to technical problems while inserting the catheter into the artery in the liver. If this happens, the microspheres may be inadvertently supplied to other organs in the body, including the stomach, intestine, pancreas or lungs. If this were to happen then it may cause swelling of the pancreas (pancreatitis), or stomach or duodenum issues (gastritis). If too many SIR-Spheres microspheres go to the lung, then this may cause inflammation of the lung. All of these cases would require treatment. The rate of these occurrences is low (less than 1 in 10 of all implanted patients for stomach or duodenum effects and less than 1 in 1,000 for pancreas or lung effects). Please note that the doctor giving your treatment will have been given special training to minimise these risks and to prevent serious side effects from occurring.

There is a risk that treatment with SIR-Spheres microspheres could result in a fatal complication. In this clinical trial so far, one fatal case has been reported in the first 300 patients treated.

The dose of radiation that you would receive is individually calculated for you. However, if the normal liver receives too high a dose, some patients may develop long-term damage to the normal liver. In a small number of cases (approximately 1 in 100 in other clinical trials), there has been evidence of damage to the normal healthy liver, but this risk will be minimised by careful dosing.

There is also a risk of complications from the radiology procedures. The chances of an adverse reaction occurring are less than 1 in 50. These can include allergic reactions to the contrast agent or MAA used in the radiology procedures (less than 1 in 100 chance) or damage to the liver arteries or kidney function (less than 1 in 100 chance).

You may experience some or none of these side effects, and they may be mild, moderate or severe. Many of these side effects disappear with time or can be controlled through medication. In addition there is always the risk of a very rare or previously unknown side effect occurring. You will be told about any new findings that develop which may affect your willingness to continue in the study, and given written information about the new findings. You will be asked to sign a form stating that you have been told about these problems.

It is important that you contact your doctor or chemotherapy nurse if you experience any side effects that disrupt your daily life. Your doctor might prescribe medications to ease any discomfort you may have, or your doctor might change the dose or discontinue your study medication. Rarely, side effects can become life threatening or fatal, which is why it is important to tell your doctor as soon as you experience any side effects.

If you receive radioembolisation, you may have to wait 4 weeks before having any further surgery (such as a stoma reversal).

What are the possible disadvantages and risks of taking part?

If you are female, able to have children and sexually active, or if you are male and sexually active, you must agree to use reliable birth control methods during your participation in this study and for two months after the end of the study e.g. oral contraceptive pill, diaphragm, condom. If you are pregnant, you cannot enter this study. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. If you were to become pregnant, you must notify your study doctor immediately. You would then be asked to provide information on the course of your pregnancy. You must not breastfeed during the first two weeks after treatment, and must not use any milk expressed during this period for bottle feeding of your baby. If you are male and your partner becomes pregnant, you should also inform your study doctor immediately.

The drugs that comprise OxMdG chemotherapy may affect other drugs you may take such as those used to treat epilepsy (for example, phenobarbitone, phenytoin, primidone and succinimide). If you are epileptic, this interaction may increase the risk or frequency of seizures unless the plasma concentrations of the anti-epileptic drugs are monitored and adjusted accordingly.

The drugs that comprise OxMdG chemotherapy may also be affected by other drugs, and it is very important that your study doctor should be informed about all the drugs that you take.

This study requires you to undergo a series of CT examinations to follow the progress of your treatment. You are also likely to undergo CT scans during follow-up. These are routine examinations, which you would receive whether you participated in the study or not. The total X-ray dose arising from these examinations is equivalent to more than 10 years of natural background radiation. It is unlikely that you would notice any health detriment arising from these routine CT scans.

Participants receiving ‘Treatment B’ (OxMdG chemotherapy plus radioembolisation) will receive additional radiation exposure, primarily to the areas within and immediately adjacent to the liver tumours from the
administration of SIR-Spheres (maximum dose of 2.8 gigabecquerel (GBq). You will also receive additional radiation from the preparatory radiology procedures. This is equivalent to 148 years of background radiation. You are unlikely to notice any health detriment arising from the additional radiation. The additional radiation dose is extremely small compared to the dose you will receive from the SIR-Spheres. There is a small risk of redness of the skin from the arteriogram procedures (very much like sunburn) and very occasionally redness can lead to some subtle, permanent changes in the skin of the abdomen (like a slight tan in one area of skin, less than 1 in 100 chance). The dose of SIR-Spheres radioembolisation is designed to be lethal to cancer cells in your liver. The additional risk of this radiation exposure is very small compared to the seriousness of your disease. Additional radiation exposures from the Tc-99 MAA and from the X-ray studies of the liver blood supply (liver angiography) are within the acceptable limits for diagnostic studies involving radioactive materials and are routinely used in normal medical practice.

The potential long-term risk from these radiation doses is uncertain; however, as long as the radiation is confined to your liver and lungs the side effects are usually mild to moderate. Any exposure to radiation has the potential for long-term damage such as scarring of the liver or a small risk of other malignancies developing many years later, but this risk is small and cannot be measured.

Since radioembolisation involves radiation, there are a number of simple precautions that you should take for the first 24 hours post-radioembolisation, in order to minimise any possible risk to others.

a) You will be provided with information when you leave hospital. This will include a letter that you can give to a doctor or nurse should you need general medical care during the period shortly after your treatment. You will also be given a wristband to show that you have received treatment with a radioactive implant.

b) Sleep separately from your partner

c) Thoroughly wash your hands after going to the toilet

d) Clean up any spills of bodily fluids such as blood, urine or stools, and dispose of them in the toilet or household rubbish

e) It is recommended to use condoms during sexual activity during the first 24 hours after the procedure

The radioactive Yttrium-90 used in SIR-Spheres microspheres releases "beta radiation" which penetrates an average of 2.5 mm (a tenth of an inch) of human tissue, and becomes minimally active in the body within 7 days after treatment due to its normal physical decay properties. The radiation risk to others is minimal, but the simple precautions listed above are advised to help to minimise any risk, no matter how small.

In addition, there are a few precautions that you should take for the first 7 days post-radioembolisation.

f) The wristband you are given when you leave hospital should be worn at all times. This wristband will include a contact number in case you need medical attention within 7 days of your radioactive treatment.

g) Avoid close prolonged contact with pregnant women or young children.

There is a possibility that taking part in this study may affect any private medical insurance that you may have. If you are at all worried about this, please contact your insurance company before agreeing to take part in the study.

At the moment, doctors in the UK offer chemotherapy injections, requiring patients to attend the hospital clinic about 7 times every 3 months. This trial requires that patients attend clinic 7 times in 3 months for Treatment A and 9 times in 3 months for Treatment B.

What are the possible benefits of taking part?

The purpose of the trial is to find out if the addition of radioembolisation to standard chemotherapy treatment is better (more patients living longer) than the standard chemotherapy alone. Your participation in the study may help patients in the future by giving important information about whether radioembolisation works, what the side effects are and whether we might recommend it for the treatment of future patients with liver metastases from bowel cancer.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your hospital doctor will tell you about it and discuss whether you want to continue in the study. If you decide to withdraw, your doctor will make arrangements for your care to continue. If you decide to continue in the study, you may be asked to sign updated consent forms.

On receiving new information, your doctor may consider it to be in your best interests to withdraw you from the study. Your doctor will explain the reasons and arrange for your care to continue.
What happens when the research study stops?
When your treatment comes to an end after approximately 6 months, your own hospital doctors will see you regularly for follow up in their out-patients clinics, according to their usual routine.

What happens if I change my mind during the study?
We would generally recommend that you finish the course of chemotherapy. However, participation in the study is voluntary and you may leave the trial at any time without giving reasons and without affecting your future care.

What if something goes wrong?
You will receive the best medical care available during and after the trial, but because these are still relatively new treatments, unexpected side effects may occur. In the unlikely event of an injury arising from taking part in this trial, you will be provided with the necessary care.

All products used within this study are being used within their indication in Europe. All patients being treated within this study are therefore covered by standard product liability insurance for any injury sustained as a part of the clinical study. Your right at law to claim compensation for injury where you can prove negligence is not affected.

Compensation for harm arising from an accidental injury and occurring as a consequence of your participation in the study will be covered by the University of Oxford. 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 Oxford (in respect of any harm arising out of the participation in the Clinical Study) or the NHS (in respect of any harm which has resulted from the clinical procedure being undertaken). If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you can either contact the FOXFIRE Trial team on 01865 617000 or contact the University of Oxford Clinical Trials and Research Governance office on 01865 572224

Will my taking part in this study be kept confidential?
Information collected about you during the trial will be kept at the FOXFIRE Trial Office, which is part of the University of Oxford. This information is strictly confidential.

If you agree, information held by the NHS and records maintained by The NHS Information Centre may be used by the FOXFIRE Trial Office to keep in touch with you and to follow up your health status. This would include forwarding your name and NHS number to OCTO. If you choose for this not to happen, it will not prevent you from entering into the trial. This information would be retained securely and only accessed by authorised personnel.

Occasionally, at any time during or after the study, your doctor (Investigator), the FOXFIRE Trial Office staff (University of Oxford – the sponsor), Sirtex Medical Ltd (the manufacturer of SIR-Spheres) and worldwide government regulatory agencies will be allowed access to your medical records or scans (results), which identify you by name but your name will be removed before any information leaves the hospital for this particular purpose so that you cannot be recognised from it. This is so we can check the study is being carried out correctly.

Some of the results of the study may be presented outside the European Union and these areas may have fewer rules about data protection. However, you would never be identified individually during these presentations. Data sent to other groups in the UK and abroad will not include information that identifies you by name (only your trial number will be used) and agreements will ensure that the data is treated confidentially.

What will happen to the results of the research study?
Results of the trial are likely to be published in international medical journals, used for scientific presentations and may also be forwarded to health and regulatory authorities worldwide. The confidentiality of all patients will be maintained. You will not be identified in any reports or publications resulting from the study. If you would like to obtain a copy of the published results, please ask your study doctor.

The results of the study may be used by the researchers to change standard treatment for patients with colorectal cancer, which may be of commercial benefit to the manufacturers of the drugs or devices used.

Your GP and any other doctors who may treat you, but who are not involved in the study, will be notified that you are taking part in the study
Blood and tissue samples

The FOXFIRE trial gives us an opportunity to perform tests on tissue samples that have already been taken as part of your care or will be removed at the time of surgery, and to take an additional blood sample (maximum 50 ml of blood, equal to about 3 tablespoons) that may give us extra information on why some people are more sensitive to side effects of chemotherapy plus radioembolisation, why some people respond by shrinkage or disappearance of their liver tumours, and even why some people develop cancer in the first place.

Tissues

Scientific advances mean that we are constantly finding new tests that we can apply to the normal and cancer tissues from bowel, liver or bone marrow, that has been removed to make the diagnosis or from any surgery related to your condition that you may have undergone, or that may be removed in the future during routine follow-up or routine surgery. These tests might tell us which cancers are more likely to respond to chemotherapy, or what causes some cancers to spread or grow more quickly than others. It is not possible to give a complete list of the tests we will perform because, as scientists discover more about cancer, new tests will be developed. This is because we can store the cancer tissue for many years and use only tiny fragments for laboratory tests. It is likely that some of the cancer tissue removed will be used for research with drug companies in the search for new treatments, which could lead to commercial gain for the company. When you consent to let us use your tissues for research, we need to make it clear that you will not be entitled to any financial gain.

Blood

We would like to take an extra blood sample, which we will use to isolate your DNA. DNA is the chemical that makes up genes, the factors that we inherit from our parents that determine our characteristics (such as height, hair colour, appearance, etc). There is evidence that we can also inherit an increased chance of developing certain diseases, including cancer. Scientists who are experts in genetics would like to perform tests on the DNA collected from your blood – these could give us information on which genes might cause cancer, or increase the chance of responding to or having side effects from chemotherapy or radioembolisation. Genetic science is changing rapidly and, like the tissue tests, we would like permission to use new tests when they appear in the future.

We will store the tissue and blood in a central laboratory using a code (not your name) to identify the sample. We will set up a small committee of scientists and doctors to make sure that the tissue and blood (DNA) will only be made available to researchers working to the highest ethical standards. In the trial, we will be monitoring your treatment and progress, and we can use the code to link the tissue/blood samples to the information that we collect during the trial. However, all samples will be anonymous and the researchers working with your tissue/blood will never know your name.

Who is organising and funding the research?

The study is being organised by the FOXFIRE Trial Office (University of Oxford), and is funded by The Bobby Moore Fund, Cancer Research UK along with an educational grant provided by Sirtex Technology. The device manufacturer, Sirtex Medical Ltd., is providing SIR-Spheres for the study free of charge.

Who has reviewed the study?

The study has been reviewed by the Berkshire Research Ethics Committee (ref 09/H0505/1), has given its approval along with your Local Research Ethics Committee and Research & Development Department based at your hospital.

What if I have more questions or have not understood something?

Please feel free to ask any further questions of the doctors and nurses looking after you before deciding to take part in the trial or at any time during the study.

If you would like further information about clinical trials, it is available at the following website: http://www.cancerbackup.org.uk/Trials/Understandingtrials

Thank you for reading this information sheet.

Your local contact is: The Research Nurses at Stoke Mandeville Tel: 01296 315 908

Independent contact is: Patient Advice and Liaison Service at Stoke Mandeville Tel: 01296 316 042