INFORMATION SHEET FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

Title of Project

SYSTEMS-2: A Randomised Phase II trial of standard versus dose escalated radiotherapy in the treatment of pain in malignant pleural mesothelioma

Introduction

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take your time to decide whether or not you wish to take part.

What is the purpose of the study?

In this study, we are investigating whether using a higher dose of radiotherapy will be more beneficial than standard radiotherapy in treating pain caused by mesothelioma.

Pain is one of the most common symptoms experienced by patients with mesothelioma. Unfortunately, conventional painkillers are not always effective and in such cases radiotherapy is often given. Although we know that radiotherapy can be helpful in treating pain caused by mesothelioma, we don't yet know the best dose and schedule to use.

In an earlier clinical trial we found that standard doses of radiotherapy, 20 Gray delivered over 5 days, are effective in controlling pain for just under half of patients with mesothelioma. We hope that increasing the dose of radiotherapy will provide better pain control in a higher proportion of patients. New radiotherapy techniques and equipment mean that we can give higher doses without increasing the risks of serious side effects.

Why have I been invited to take part?

You have been asked to take part because you have previously been diagnosed with mesothelioma and you have been referred for radiotherapy for the treatment of pain.

Do I have to take part?

No – taking part in the study is entirely voluntary. If you do decide to take part, you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

If you decide to take part you will be asked to sign a consent form. Whether or not you choose to take part you will usually have had some blood tests and CT scans as part of normal medical care. If you choose to take part in the trial you will need to have some additional tests. These include a CT scan of the chest and abdomen to help with the radiotherapy planning process and some additional blood tests. Your doctor will review your painkillers to ensure that any pain you have is stable and as well controlled as possible before you start radiotherapy.

You will also be asked to complete some questionnaires that would not be part of routine medical care. These will take approximately 20 minutes to complete at each study visit.

What is involved in the study?

Radiotherapy dose is measured in units called 'Grays' (Gy) and is usually given as a number of separate treatments. You will be randomly allocated to receive one of the two following courses of radiotherapy:

Standard Treatment

A total radiotherapy dose of 20 Gray, given in 5 treatments of 4 Gray each. You will have one treatment per day for one week (Monday to Friday).

Dose Escalated Treatment (High Dose Radiotherapy)

A total radiotherapy dose of 36 Gray, given in 6 treatments of 6 Gray each. You will receive each dose on alternate days over 2 weeks.

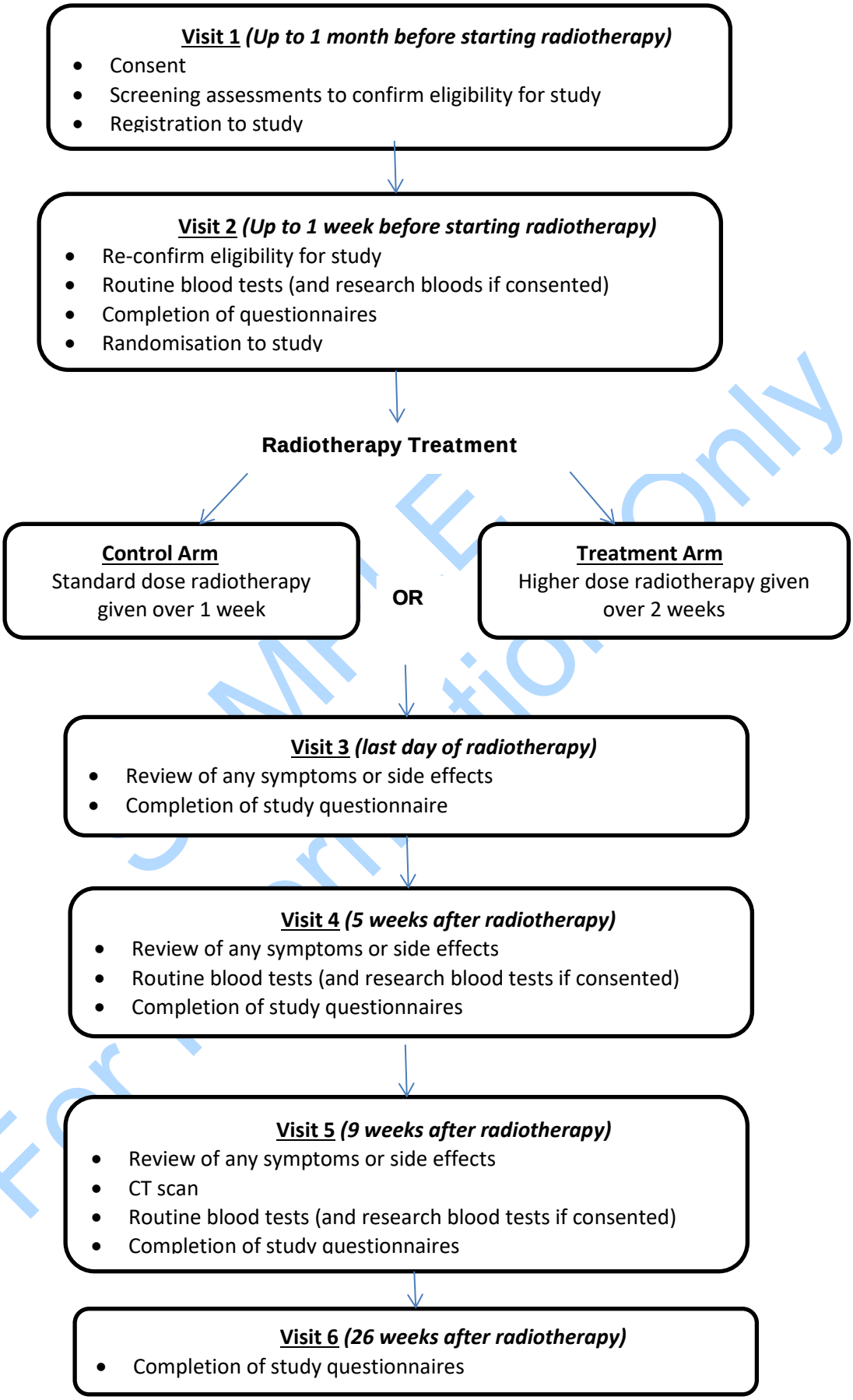
In some cases, your doctor may think you would benefit from receiving the higher dose radiotherapy at a slightly lower total dose. This might be necessary if your tumour is close to your spinal cord, or there is a large area to be treated. In this case you will receive 30 Gray given in 5 treatments of 6 Gray each, on alternate days.

During your course of radiotherapy you will see the treatment radiographers each time you attend. If you are experiencing any problems or new symptoms the radiographers will arrange for you to be seen by a nurse or doctor if necessary.

Clinic Attendance

You will be asked to attend the clinic to see your doctor 5 weeks after the start of your radiotherapy and again 9 weeks after the start of your radiotherapy. These visits are to make sure that you are well, that any side effects have settled and to see whether your pain has improved. The doctor will monitor your progress and check for any side effects, you will be asked to complete some questionnaires and you may have some blood tests. 26 weeks after the start of your radiotherapy there will be a final visit where we will ask you to complete some study questionnaires only. The schedule of appointments is shown on the next page.

Schedule of Appointments



Blood Samples for Research

You will have some blood tests as part of your routine care. We are also requesting your consent to take 3 additional blood samples to be used for research. Agreeing to the additional blood tests is completely optional and if you decide not to consent to this, it will not affect your participation in the trial or any aspect of your overall care. The aim of this research is to see if these blood tests can help to predict which patients are more likely to respond to radiotherapy. We are asking for one blood sample before your radiotherapy treatment begins and two samples after your treatment has finished (at weeks 5 and 9). These samples would be up to 25 millilitres (five teaspoonfuls) each and will initially be collected and stored in the Glasgow Biorepository before being sent to one or more research laboratories where they will be analysed. Part of the samples may also be sent overseas where they will be analysed in other laboratories researching mesothelioma. Your blood samples would be used only for ethically approved and relevant investigations that may include analysis of genetic material (DNA), by qualified researchers in academic or commercial organisations to develop new ways of detecting or monitoring mesothelioma. The tubes containing your blood samples will be anonymous (identified only by your initials and a unique study number). This is an optional part of the study and if you decide not to give consent for these blood samples to be taken you will still be able to take part in the main SYSTEMS-2 trial.

Tissue Samples for Research

We will also ask you to consider giving consent for the research team to collect any surplus tumour tissue that was removed at the time of your original operation or biopsy and was not needed to make your diagnosis or decide upon your treatment. If you agree, the tissue sample will initially be collected and stored at the Glasgow Biorepository before being sent to laboratories in Glasgow for analysis and possibly to other academic research laboratories in the UK or in other countries. Samples will not contain any information that would identify you. Tissue samples would be used only for ethically approved and relevant investigations that may include analysis of genetic material (DNA), by qualified researchers.

How long will my samples be kept?

The samples collected will be stored in the Glasgow Biorepository until they are all used or until you withdraw your consent for their use. Unused material may be stored indefinitely in case further investigations are developed in the future, which may help us understand more about the response of mesothelioma to therapy. The samples may also be used for other studies in the future relating to mesothelioma. Any such studies will

have to be approved by the SYSTEMS-2 Trial Management Group and external ethics committees. We cannot describe here all the potential tests which may be done on any samples stored and if you feel uncomfortable about this please do not consent to participate in this aspect of the study.

What happens if I change my mind about this additional research?

You are free to withdraw your consent to research being performed on these blood and tissue samples and their continued storage at any time, however, if you change your mind after giving the sample it may be that some of the material will have already been used for research. If you wish to withdraw your consent please contact (***local clinician contact details to be entered)*** and they will advise the appropriate personnel involved with the study of your decision. At this point any remaining material being stored will be disposed of and any information associated with it will be deleted.

Pregnancy

If your doctor thinks that there is a potential for you to be pregnant or become pregnant during the radiotherapy, you will need to have a pregnancy test prior to entering the trial. If you are heterosexual and sexually active, you will be advised about using contraception. Because of possible effects of radiotherapy on pregnancy, you will need to use effective contraception throughout your treatment and for 30 days afterwards. Your doctor will explain this in more detail but you should ensure that you use two of the following:

1) Oral, injected or implanted hormonal contraception (discuss with your study doctor whether this is suitable)
2) An intrauterine device (IUD) or system (IUS)
3) A barrier i.e. condom or occlusive cap with spermicidal foam/gel/film/cream/suppository;
4) Intercourse with a vasectomised male partner. Alternatively, you must exercise true abstinence for the duration of your radiotherapy and for at least 30 days after. Your study doctor will advise you regarding this.

Any woman who finds that she has become pregnant while taking part in the study should immediately tell her study doctor.

What are the possible benefits of taking part?

There may or may not be direct medical benefits to you from taking part in this trial. With the close follow up that you will receive on the study, you may find that your pain and other symptoms are well managed. The treatment you receive will not be adversely affected by participation in the trial in any way.

A potential benefit of participants receiving higher dose radiotherapy is that they may experience better pain relief.

What will be the side effects of any treatment I receive in this trial?

As well as possible benefits, trial treatments can also produce side effects. Not all side effects are known; if you suffer from something that you think may be related to your treatment within this trial please contact your trial doctor or research nurse. Potential side effects of the treatment being used in the trial are summarised below:

Radiotherapy:

- Alopecia (hair loss) in the treated area
- Tiredness
- Nausea and vomiting
- Skin soreness and redness (in the treated area)
- Pain on swallowing
- Increased breathlessness
- Cough
- Temporary increase in any of the symptoms you had when your tumour was diagnosed
- Damage to the spinal cord causing weakness or numbness (this is extremely unlikely as any dose delivered to the spinal cord will be closely monitored to ensure it is kept at a safe level)

These side effects may occur whether you receive the higher dose radiotherapy or the standard radiotherapy, however if you receive higher dose radiotherapy you may be more likely to experience them and they may be more severe. During treatment, your condition will be monitored closely for any potential side effects. You will have regular visits with the radiographer, trial doctor and research nurse. You will also have a telephone number to contact the research staff if you are concerned about possible side effects.

If you do experience side effects, additional treatments may be given to you to make them less serious or uncomfortable. If your side effects are particularly troublesome, we may advise that you miss one or more doses of radiotherapy. If they are unusually severe, we may advise that the radiotherapy is stopped earlier than planned. Many side effects go away after the trial treatment is reduced or stopped but in some cases side effects can be serious, long lasting or permanent.

If you receive high-dose radiotherapy, and your doctor advises you should withdraw from the study early because of side effects, you would not normally be offered any further radiotherapy at the lower, standard dose. If you did wish additional radiotherapy treatment you can discuss this with your doctor, who will advise if this would be appropriate for you.

What are the possible disadvantages and risks of taking part?

There are side effects associated with the radiotherapy, which are discussed above. If you are randomised to receive the higher dose radiotherapy these side effects may be more likely to occur or may be more severe. You can stop the trial treatment at any time if you or your doctor feels that the side effects are a problem for you.

Information on side effects and the treatment of these side effects will be closely monitored by doctors involved in the trial. In addition, the trial will be carefully monitored by an independent group of specialists who will regularly advise all the investigators about the safety of the trial.

If you do participate in the trial you will need to attend the hospital for extra visits, as well as having blood tests which you may not have had if you were not participating in the trial.

As part of this trial, you will be exposed to radiation from computed tomography (CT) scans and from your radiotherapy treatment. Your radiotherapy treatment uses strong (high energy) X-rays to treat your cancer, whereas CT scans use lower energy X-rays to form pictures of your body which provide detailed information about your cancer. The dose of radiation you receive from a CT scan is much less than the dose of radiation you will receive from your radiotherapy. There is a theoretical risk of developing other cancers in the future from

exposure to x-ray radiation however this risk is considered as extremely unlikely or negligible for patients with your underlying clinical condition.

In addition to these risks, some people are allergic to the contrast which is injected at the time of the CT scans. Sometimes contrast can cause damage to the kidneys. If you have previously had a reaction like this, please let your doctor know.

What is the usual treatment for my type of cancer?

The usual treatment for your type of cancer is standard dose radiotherapy.

What are the alternative treatments?

If you would prefer not to take part in the trial, your doctor will explain other options, which may include not receiving radiotherapy at all.

What happens when the study stops?

The need for further treatment depends on your response to the trial treatment. Your doctor will discuss with you whether further treatment is required and what the treatment alternatives are.

What if 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 research doctor will tell you about it and discuss with you whether you want to continue in the trial. If you decide to withdraw, your research doctor will make arrangements for your care to continue. If you decide to continue you may be asked to sign an updated consent form.

Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the trial. He/she will explain the reasons and arrange for your care to continue.

What if something goes wrong?

If you have a concern about any aspect of this trial, you should ask to speak with the research doctor/nurse who will do their best to answer your questions.

If taking part in this trial harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this trial, the normal National Health Service complaints mechanism should be available to you.

If you have private medical insurance, you may wish to check with your company before agreeing to take part in this trial to ensure that participation in the trial will not affect your insurance cover.

Will my taking part in the trial be kept confidential?

NHS Greater Glasgow & Clyde/University of Glasgow is the Co-sponsor for this study, based in the United Kingdom. We will be using information from you and 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. NHS Greater Glasgow & Clyde /University of Glasgow will keep identifiable information about you for 15 years after the study has finished.

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.

You can find out more about how we use your information at http://www.crukctuglasgow.org/eng.php.

[INSERT LOCAL SITE NAME] will collect information from [you and/or your medical records] for this research study in accordance with our instructions.

[*INSERT LOCAL SITE NAME*] will keep your name and contact details confidential and will not pass this information to NHS Greater Glasgow & Clyde/University of Glasgow. [*INSERT LOCAL SITE NAME*] will use this information as needed, 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. Certain individuals from NHS Greater Glasgow & Clyde/University of Glasgow and regulatory organisations may look at your medical and research records to check the accuracy of the research study. NHS Greater Glasgow & Clyde/University of Glasgow will only receive information without any identifying information. 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.

[*INSERT LOCAL SITE NAME*] will keep identifiable information about you from this study for 15 years after the study has finished.

You can be assured that any data collected during the course of this trial and any of the results published will not identify you personally. Your medical records will only be available to the research doctors, your hospital consultant, responsible individuals from the Cancer Research UK Clinical Trials Unit (Glasgow), trial sponsors, and regulatory authorities. For clarification, patient medical notes include Community Health Index (CHI) or NHS number.

With your permission, we will inform your general practitioner (GP) of your participation in this trial.

With your permission, the Cancer Research UK Clinical Trials Unit (Glasgow) who are co-ordinating the trial will collect your name or initials, date of birth and NHS number or Community Health Index (CHI) number. This information will be stored securely and will be kept strictly confidential, with access provided only to authorised personnel.

Your consent for participation in this trial also includes your consent to allow the use of the data in your medical/clinical record to be used for the purposes of Cancer Research. Your consent also includes allowing these data to be linked to data coming from other sources such as cancer registries and medical clinical records. All data (personal, clinical, economic and data coming from research on biological material) collected on your behalf will be treated in compliance with the European and UK applicable laws to ensure your confidentiality is maintained.

Occasionally, at any time during or after the study your doctor (Investigator), the Clinical Trials Unit staff and study sponsor, may have access to your medical records which identify you by name. This is so that we can check that the study is being carried out correctly. Any information that leaves the hospital will have your name and address removed so that you cannot be recognised from it.

What will happen if the findings may affect you personally?

If during the study, we discover information that could be relevant to your interests or health we will let you know. If you do not wish to know any information about the study as it is running, please let your doctor know.

What will happen to the results of the research study?

We plan to publish the results of the study so that the information that we have found will be available to all. This is likely to be one or two years after the study has completed. You will not be mentioned personally in any report or publication. We will provide you with the details of how and when you or your family can access the results of the study, should you wish to.

Who is organising and funding the research?

The study is being coordinated by the Cancer Research UK Clinical Trials Unit, based at the Beatson West of Scotland Cancer Centre in Glasgow, and is funded by the June Hancock Mesothelioma Research Fund and Beatson Cancer Charity.

None of the doctors or other staff conducting the research is being paid for recruiting patients into the study.

Withdrawal from the project

Your participation in the study is entirely voluntary. You are free to decline to enter or to withdraw from the study any time without having to give a reason. If you choose not to enter the study, or to withdraw once entered, this will in no way affect your future medical care. However, we would appreciate being able to continue to receive information on your progress. If you decide that we may have no further information from you for the trial, we will need to use the data collected up to the time of your withdrawal.

Who has reviewed the study?

This study was reviewed by a number of medical specialists during its development. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee. South East Scotland Research Ethics Committee 01 has reviewed and approved this study to confirm that this study considered the 'rights and protection of patients' health. In addition, the study has been reviewed by the Research and Development Department of NHS Greater Glasgow and Clyde.

Contact for further information

If you have further questions about your illness or about clinical studies, please discuss them with your doctor.

If you would like independent advice of further information you may also find it useful to contact Macmillan Cancer Support, an independent patient advisory group (freephone 0808 808 0000; website http://www.macmilan.org.uk, Head Office Address: Macmillan Cancer Support, 89 Albert Embankment, London, SE1 7UQ or the Cancer Research UK website (http://www.cancerresearchuk.org)

We have created a website for the SYSTEMS-2 study, which contains background information about mesothelioma and further information about the study which may be useful to yourself and your family. The website also contains some clinical study information which you may find helpful, although we understand that not everybody will want to read this information. Some of the terms used in the clinical area of the website may not be familiar to you and may seem confusing. If you have any questions about anything that you may read on the SYSTEMS-2 website, please feel free to use the 'contact' form on the website or speak to your research doctor.

Please visit WWW.SYSTEMS-2.co.uk for further information.

If during the course of the trial you have any questions regarding your participation or would like further trial specific information before making your decision please contact:

Doctor:

Name Insert *local details*

Telephone Number *Insert local details*

Research Nurse:

Name Insert *local details*

Telephone Number *Insert local details*

24-Hour / out of hours contact: *Insert local details*

If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor or nurse.

Thank you for taking the time to read this information sheet. If you wish to take part you will be given a copy of this information sheet and a signed consent form to keep.

CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

(Form to be on hospital headed paper)

Patient Identification Number for this trial:(to be obtained post registration)

Title of Project:

SYSTEMS-2: A Randomised Phase II trial of standard versus dose escalated radiotherapy in the treatment of pain in malignant pleural mesothelioma

		PLEASE INITIAL EACH BOX
1.	I confirm that I have read and understand the information sheet dated **7th March 2019 (Version 6.2)** for the above trial and I fully understand what is involved in taking part in this trial, and have had the opportunity to ask questions.	☐
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3.	I agree that relevant sections of any of my medical notes (including Community Health Index (CHI) or NHS number) and data collected during the trial may be looked at by responsible individuals from the Cancer Research UK Clinical Trials Unit (Glasgow), the trial sponsors, the regulatory authorities, and the NHS organisation where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
4.	I agree to give permission for data collected relating to me to be used for "cancer research" purposes as described in this information sheet including allowing this data to be linked to data coming from other sources such as cancer registries and medical clinical records. I understand giving consent to the use of this data as described is optional and not mandatory for participating in this trial.	☐
5.	I give my permission for a letter and information regarding my participation in this trial to be sent to my GP.	☐
6.	I agree to take part in the above trial.	☐

Consent for Blood and Tissue collection and use in future research

(This part of the study is optional - if you do not wish to give this permission, do not initial the boxes - you can still participate in the trial).

7. I give my permission to give 3 extra samples of blood for translational research purposes and to be kept for future research as described in the information sheet for the above trial. I understand how the samples will be collected, that giving samples is voluntary and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

8. I give my permission for stored tumour tissue sample that was removed during my operation and was not needed for routine diagnosis and treatment to be collected and used for future translational research purposes as described in the information sheet for the above trial. I understand I understand that I am not being asked to undergo any repeat biopsy or operation for the purpose of this.
and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

9. I agree that the blood and tissue samples and information collected about me will be stored indefinitely on behalf of the Trial Management Group and may be used in future projects which will require to be ethically approved, as described in the information sheet. I understand that my stored samples will be linked anonymised, so will not be identifiable to researchers but will be linked to my information at the Cancer Research UK Clinical Trials Unit (Glasgow) to allow my samples to be withdrawn from storage upon my request. I understand that some of the projects may be carried out by researchers other than the Trial Management Group, including researchers in and outside the EU. ☐

Please sign and date below:

Name of Patient	**Date**	**Signature**
Name of Person taking consent	**Date**	**Signature**

When completed, 1 original for patient; 1 original for researcher; 1 photocopy to be kept with hospital notes