PATIENT INFORMATION SHEET

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Study Title	Prognostic value of ploidy and digital tumour-stromal morphometric analyses for guiding chemotherapy treatment for Stage II / IIIa Colon Cancer Patients (ONCOPROG_AI)
Chief Investigator	Prof David Kerr
Contact Number	01865 784743
Protocol Number	V.16.1
Sponsor Name	Oxford Cancer Biomarkers Limited (OCB)
IRAS ID	330060
Name of Research Ethics Committee	East of England – Cambridge South

If you need the writing in this document to be larger, please tell the study doctor.

Short Title: OncoProg AI

Title: Prognostic value of ploidy and digital tumour-stromal morphometric analyses for guiding chemotherapy treatment for Stage II / IIIa Colon Cancer Patients

Summary:

- **OncoProg® is a testing technology used to examine a tumour sample and predict whether the tumour is likely to re-occur.**
- **The OncoProg® test can be used on patients with stage II and Stage IIIa tumours.**
- **The OncoProg® test is carried out after surgery on a piece of tumour that has been removed from the patient.**
- **The results of the OncoProg® test will indicate the likelihood that a given tumour will re-occur.**
- **The result of the OncoProg® test is intended to be used by the oncologist and patient to inform on the likely benefits of chemotherapy after surgery to the patient.**
- **The information provided by the OncoProg® test is intended to improve treatment decision making for stage II and IIIa colon cancer patients.**
- **The study will assess whether the use of the OncoProg® test technology improves treatment decision making in a real-world clinical environment.**

You are being asked to consider joining a clinical research study. A member of the study team, who may be 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 the study.

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 continue to take part. **Taking part in this study is entirely voluntary.**

Why Is This Study Being Done?

Chemotherapy is sometimes given to patients who undergo colon cancer surgery to improve the likelihood of success of surgery and reduce the risk of the cancer coming back, however chemotherapy carries side effects including the risk of fatigue, nausea, infections, low blood cell numbers, inflammation of the mouth or gut and severe diarrhoea and not all patients will need to have chemotherapy.

In normal practice, your consultant will usually help you make the decision of whether to have chemotherapy with the results of all your tests (including scans, blood tests, and a detailed test of the tumour itself) as well as input of other specialists including radiologists and surgeons.

A new test, called OncoProg®, has been developed to help doctors decide whether chemotherapy will be of benefit to you. OncoProg® looks at tumour samples that have been made using thin slices of your tumour and takes several measurements including the deoxyribonucleic acid (DNA) content on each of the cells in the slide, as well as how the cells are arranged within the tumour to predict the risk of the tumour returning. The doctor then uses this information together with all the other results, to determine whether you are likely to benefit from chemotherapy or not. If you are likely to benefit from chemotherapy the test can help determine whether one drug, or more than one drug (combination chemotherapy) is the best option, taking into the account the risks and benefits.

OncoProg® is a UKCA/CE-marked test (which means it has general health regulatory approval to be used in patients in Europe and the United Kingdom) and has been shown to accurately determine whether colon cancer will come back in tests involving over 2,500 people with stage II and stage IIIa colon cancer. OncoProg® analyses the DNA content of the tumour cells (DNA) and how much of the tumour area consists of tumour cells versus non-tumour cells (stroma). Artificial intelligence (AI)-based methods were used in the development of OncoProg® to improve the accuracy of these analyses. The two measurements of 'DNA' and 'stroma' are then combined to provide a prediction of the risk of the tumour recurring. OncoProg® was developed by Oxford Cancer Biomarkers Ltd, a personalised medicine company that develops products based on scientific research from the University of Oxford.

For details of the clinical research used to develop the OncoProg® test please see here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5889021/

For further information on Oxford Cancer Biomarkers and how OncoProg® was developed please visit the OCB website: https://oxfordbio.com/

This current study has the aim of assessing how doctors use OncoProg® to help determine the best course of treatment for patients with stage II and IIIa colon cancer, what final decisions are reached in collaboration with patients considering their wishes, as well as estimate the cost of OncoProg® to the National Health Service (NHS).

Why have I been invited?

You have been invited to participate because you are due to undergo surgery for colon cancer, although we will not know what stage your cancer is at until after the surgery and analysis of the tumour has taken place. We are aiming to include around 250 patients into this study over the next one to two years.

Do I have to take part?

No. **Participation in the study is entirely voluntary.** You will be given time to consider taking part in the study. Your standard of care will not be affected if you decide not to take part in this study.

If you do join the study, you are free to withdraw at any time and you are not required to give a reason. This will not in any way affect any future care you will receive from your medical and nursing team.

What will happen to me first if I continue to take part?

If you decide to take part you will be asked to sign the Informed Consent Form at the end of this document. You will be given a copy of the Consent Form to take away and refer to later.

What will happen next?

Following surgery, a number of tests will be done which will include confirming what stage of cancer you have. If you have stage II or IIIa, the OncoProg® test will be conducted in addition to the current standard of care tests. OncoProg® will generate a report that assesses the risk of the cancer returning.

If your cancer is not stage II or IIIa then you will not be eligible for the study, and so OncoProg® will not be conducted, and you will exit the study. You will continue to receive the gold-standard of care on the NHS.

The Oncologist will discuss with you what the best treatment is for you using the current standard of care tests alone, then they will look at the results of the OncoProg® test and see if your original decision is still the best treatment, or if the treatment should change.

For example, if the risk of recurrence was low, then perhaps the risks of chemotherapy would outweigh the benefits of chemotherapy and you must consider if chemotherapy is still considered the best treatment option. However, in cases where the risk recurrence was high you may wish to consider additional (combination) chemotherapy options as the benefits of chemotherapy would outweigh the risks of side effects. The Oncologist will discuss the risks and benefits of the treatment options with you so that you can agree the best course of treatment together.

There will be no additional visits to the hospital outside the current standard of care required if you take part in the study.

For a summary of how this study will integrate with the standard care pathway please refer to Figure 1 on Page 7 of this document.

How will we use information about you?
We will need to use information from your medical records for this research project.
This information will include your

- Initials
- Date of Birth (D.O.B)
- NHS number
- Name
- Cancer status

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a participant identification number (PIN) instead.
We will keep all information about you safe and secure.
Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. No follow up data will be collected after your withdrawal from the study.
We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

What are the possible benefits of taking part?

In the UK, around half of stage II colon cancer patients receive chemotherapy, however it is estimated that most (up to 80%) of these patients may not need chemotherapy as it does not lead to them having better quality or longer, cancer-free lives, and puts them at risk of side of effects from chemotherapy such as fatigue, nausea, infections, low blood cell numbers , inflammation of the mouth or gut (mucositis) and severe diarrhoea.

OncoProg® provides additional information about the tumour which may be useful to your doctor to determine the best treatment for you. On an individual level, this gives you and your Oncologist an additional tool to help consider the benefits versus the risks of the treatment options after surgery. This study could help patients and Oncologists in the future make the best possible post-surgery treatment decision and may also help improve the efficiency of the NHS.

What are the possible disadvantages and risks of taking part?

No test is 100% accurate. It is possible that your doctor's treatment recommendation is changed after taking into consideration the OncoProg® results to give more, or less, or no chemotherapy than would have been given if only the current standard-of-care test results were conducted. There is the possibility that the cancer may return if no chemotherapy or less chemotherapy is given. There is no way of knowing whether the cancer would have returned, or would not have returned, if the treatment decision had not been changed on the basis of OncoProg®.

The OncoProg® technology has been tested on over 2,500 patient tumour samples and the doctor is recommending the treatment decision based on OncoProg® plus other tests, your medical history, health and age, and after discussing the risks and benefits with you.

The Oncologist deciding the treatment with you, does not benefit from this study and was not involved with the development of OncoProg®.

What if new information becomes available?

Sometimes during a research project, new information becomes available about the test or technology that is being studied. If this happens, your 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 standard care to continue. If new information comes to light which alters the content of this study, and if you decide to continue in the study, you may be asked to sign an updated consent form.

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?

A report will be written recording all the anonymous information collected during the study. This information will be analysed to determine if OncoProg® has provided sufficiently useful extra information to help improve clinician/patient decision making and over use of chemotherapy and if its use will save or cost the NHS money. It is likely that this report will be published in a medical journal. We will also make a patient-friendly summary of our results which will be placed on our website (www.oxfordbio.com).

Your participation in the study, or the study itself may be stopped at any time by the investigators if they feel it is necessary for health and safety reasons. Such an action would not require your consent, but you will be informed if such a decision affects you, and the reason(s) behind it.

What happens if I change my mind during the study?

Participation in this study is voluntary and you may leave the study at any time without affecting your future care and without giving any reason.

What if something goes wrong?

You will receive the best medical care available during and after the study and we do not expect that your participation in this study will result in any harm to you at all.

If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints procedure mechanisms will be available to you. Your doctor will give you further information if necessary.

Will I be paid for taking part in the study?

You will not receive any payment for taking part in this study.

Will I have to pay anything to take part in the study?

You will not be expected to pay for any tests you undergo as part of this study.

Will my taking part in this study be kept confidential?

In the study, any information collected about you will be anonymised and be treated as strictly confidential. You will be given a Study Number that is unique to you. No one outside of your clinical team treating you will know any of your personal identifiable details.

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 by name during these presentations. Data sent to other groups in the UK and abroad will not include information that identifies you by name (your study number will be used only) and agreements will ensure that the data is treated confidentially.

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.

What will happen to the results of the research study?

Results of this study are likely to be published in medical journals, used for scientific presentations, and may also be forwarded to health 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 doctor.

What will happen to my tissue sample?

Your tissue sample will not be retained for the purposes of this study. Any remaining tissue will be destroyed or returned to the hospital providing your treatment.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' Oxford Cancer Biomarkers Limited is the sponsor for this study. It is the data controller, and is responsible for looking after your information and using it properly.

We will be using information from you, your hospital, NHS England and any other NHS registries in order to undertake this study and will use the minimum personally-identifiable information possible.

We will store any research documents with personal information, such as consent forms, securely at the Oxford Cancer Biomarkers for a maximum of 5 years after the end of the study, as part of the research record. We will keep any other identifiable information about you for 5 years after the study has finished. Your digitised samples will not be retained by Oxford Cancer Biomarkers for use in future research.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://www.hra.nhs.uk/information-about-patients/

You can find out more about how we use your information on our website www.oxfordbio.com/privacy-policy by contacting the study team.

Who is organising and funding the research?

The study is being organised and run by doctors at the University Hospitals Birmingham NHS Foundation Trust. It has been funded by the government AI in Health and Care Awards. More information about this funding can be found here : https://www.gov.uk/government/news/thousands-of-patients-to-benefit-from-quicker-diagnosis-more-accurate-tests-from-ground-breaking-ai-research

Who has reviewed the study?

The study has been reviewed by a Research Ethics Committee and The University of Birmingham NHS Foundation Trust R&D.

What if I have more questions or haven't 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 study or at any time during the study. Further information on clinical trials can be found here: *https://www.nhs.uk/conditions/clinical-trials/*

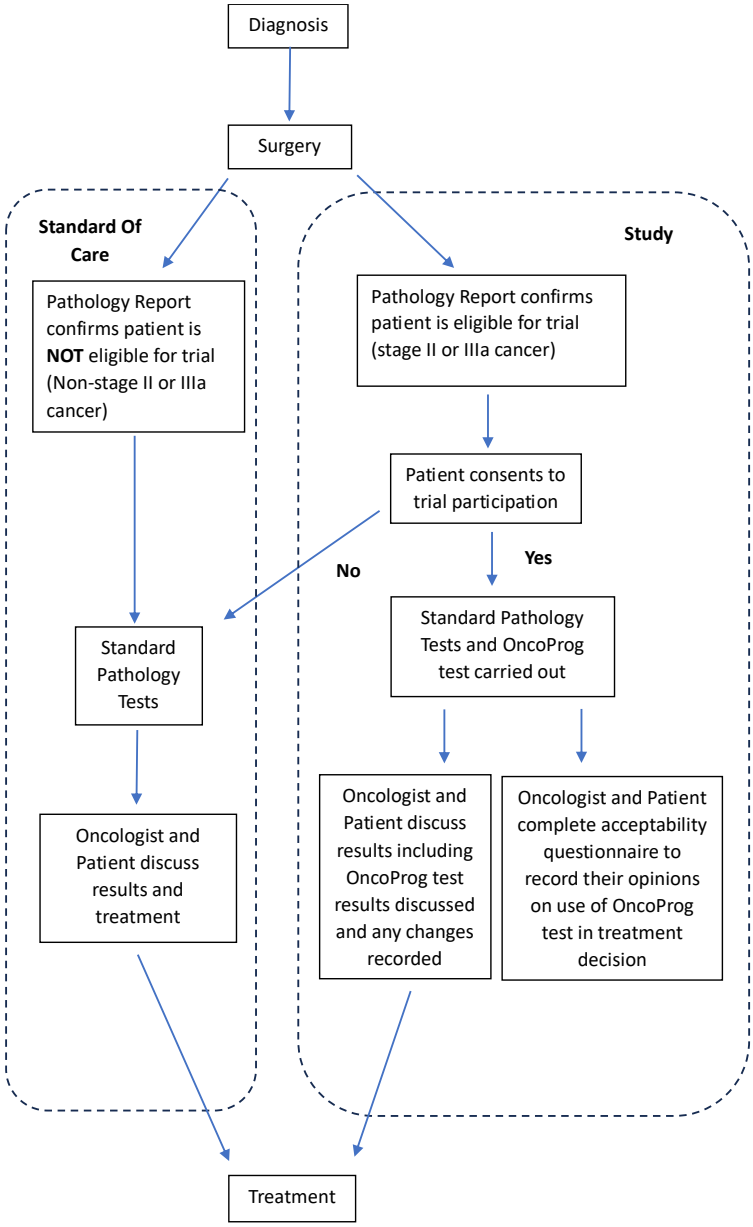

Figure 1. OncoProg AI study workflow. Diagram shows standard of care pathway and integration of OncoProg® study.

Thank you for reading this information sheet.

Your local contact is: _____

Tel:

Email :