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UNIVERSITY OF LEEDS

ARTEMIS

(Augmenting radiotherapy in rectal cancer to minimise invasive surgery)

Augmenting RadioTherapy in REctal Cancer to Minimise Invasive Surgery

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT

You will also be given a KEY FACTS sheet to help you understand the ARTEMIS trial

You should also receive your hospital's standard participant information sheets on radiotherapy or chemoradiotherapy (depending on what type of radiotherapy your treating team has recommended for you) and also chemotherapy after the radiotherapy / chemoradiotherapy which is termed FOLFOX or CAPOX.

PLEASE CIRCLE

Radiotherapy or chemoradiotherapy:
FOLFOX or CAPOX

A large-print version of this sheet is available on request.

Contents

INTRODUCTION

You have been invited to take part in a research study called "ARTEMIS".

Before you decide if you want to take part, we would like to explain why the research is being done, how we will use the information we have about you, and what the study will involve.

Please read this information carefully, and discuss with others if you like. Ask us if anything is unclear, or if you would like more information.

Once you have read this information, your doctor or nurse will talk to you about the study again and you can ask any questions you like.

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.

PART 3 gives some additional information about how your information will be used.

Please take your time to decide whether or not you wish to take part.

How to contact us

If you have any questions about this study, please talk to your doctor: <<Enter PI, nurse name >> << Contact details for site>>

Thank you for reading this information sheet.

PART 1

1.1 What is the purpose of the study?

The ARTEMIS trial is for patients who have been diagnosed as having a cancer of the lower bowel, known as the rectum. There are no definite metastases. At present, surgery is the standard treatment for rectal cancer. Some patients require radiotherapy or chemoradiotherapy to reduce the size of the cancer prior to surgery. In some cases, this treatment may be enough to treat the cancer completely and surgery may be avoided. We hope that this study – which examines the benefit of adding an additional treatment alongside radiotherapy and chemotherapy - will allow us to increase the chance of curing your rectal cancer without the need for surgery. This is known as a Complete Clinical Response (cCR). We hope this will also be associated with an improved quality of life for patients.

If patients with rectal cancer are treated with either radiotherapy or chemoradiotherapy, then in about 10 to 15% of cases the cancer disappears and such patients might then be able to avoid surgery. Surgery itself can increase the likelihood of long-term bowel or bladder problems and reduce sexual function. If chemotherapy is given after the radiotherapy or chemoradiotherapy, then the chance of the cancer disappearing completely can increase further to about 30%. This is sometimes known as Total Neoadjuvant Therapy (TNT).

The ARTEMIS study will explore the potential benefits of giving an additional drug treatment, AN0025, which works with your immune system to see if this further improves the chance of the

cancer completely responding to treatment, known as cCR. We hope this will also be achieved without significantly increasing the toxicity both with the treatment and in the long-term.

1.2 Why have I been chosen?

Your doctor has informed you that you have a rectal cancer and has recommended radiotherapy or chemoradiotherapy, followed by surgery to remove your tumour. After discussion with your doctor you have expressed an interest in possibly participating in a study aimed at trying to avoid surgery and preserve your rectum ('organ preservation'). The ARTEMIS study aims to recruit up to 140 participants with cancers like yours.

1.3 Do I have to take part?

No, your participation in the ARTEMIS study is voluntary and you may withdraw your consent to take part at any time, without giving us a reason.

If you decide to take part, you will be given this information document to keep. You will be asked to sign a consent form, but you are still free to withdraw at any time and without giving a reason.

If you decide not to take part, your doctor or nurse will be happy to talk through other treatment alternatives with you. The standard of your treatment and care will not be affected in any way if you decide not to take part.

1.4 Will my taking part be kept confidential?

If you decide to participate in the ARTEMIS study, the information collected about you will be handled strictly in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act 2018 (DPA 2018).

According to these laws, we can collect, store and use personally-identifiable information about you and your health because we are carrying out research in the public interest, to improve health, care and related services. When you agree to take part in one of our research studies, we only use your information in the ways needed to carry out and analyse the study, and in some cases to support additional, similar research.

Your anonymised data may be passed to other organisations (possibly in other countries where the data protection standards and laws are different to the UK) to monitor the safety of the treatment(s) that you are receiving; this data will have your name removed.

Please refer to Part 2 and Part 3 for further details.

1.5 What are the possible benefits of taking part?

By taking part in this study, you will receive the best available treatment for your cancer: radiotherapy or chemoradiotherapy followed by chemotherapy (You may be offered this if you do not take part in this study). You may receive the additional immunotherapy drug (1 in 2 chance). We do not know if this will increase the chance of your cancer disappearing completely compared to the current treatment.

1.6 If I want to, will I definitely be able to take part?

Unfortunately, no. Although your doctor thinks you might be suitable to take part, the research team will still need to carry out some tests and ask you some specific questions to make sure you are suitable. These are known as "eligibility screening tests". Most of these tests would happen as a part of normal clinical care, and you will have already undergone some of them.

If the eligibility screening tests show that it is not appropriate for you to take part in the ARTEMIS study, your doctor will discuss your alternative treatment options with you.

1.7 What will happen if I take part?

Before the study, you will need to have some tests, examinations and scans of your disease, to make sure that you are suitable for the study

Most of these tests are standard routine practice and include:

- Medical information about your health and physical examination.
- A flexible sigmoidoscopy, which is a flexible telescope that the doctor will use to see inside your bowel. You probably will have had this to help prove your diagnosis of a rectal cancer.
- A biopsy (a procedure where a small piece of tissue is removed from the cancer to look at under a microscope). This will be taken at the time of the sigmoidoscopy and is not usually painful.
- Blood tests to check your blood count (which includes red cells, which are responsible for anaemia if they are too low), kidney and liver function.
- Scans to assess your disease. This will include a Computerised Tomography (CT) scan (which involves exposing you to some radiation) of your thorax, abdomen and pelvis, and Magnetic Resonance Imaging (MRI) scan of your pelvis.

For the purpose of this trial, we might need to do a few more tests, depending on the practice in your clinic. If you are a woman of childbearing age, we will check to make sure that you are not pregnant. We might also need to repeat the scans to assess your disease if they were done over 6 weeks ago, and the blood tests if they were done over 2 weeks ago. You may already have completed some or all of the necessary tests as part of being diagnosed with rectal cancer. You will not need an extra biopsy or endoscopy.

If you agree to take part, we would like you to complete some questionnaires about your quality of life and how you are feeling generally. These questionnaires will be completed at the beginning of your treatment (on paper only when you are in clinic), and then 3 weeks post the end of your RT treatment, during your follow-up appointments at 4, 6, 9, 12, 18, 24 and 30 months from the start of treatment (paper or electronic versions). These questionnaires will take around 20 minutes to complete.

After you agree to enter the study, you will be treated with either A) radiotherapy or chemoradiotherapy followed by chemotherapy treatment, or, B) you will receive an additional immunotherapy tablet (AN0025) in addition to this treatment. “Immunotherapy” describes a treatment that helps the patient’s own immune system to attack the cancer and when used in combination with other treatments may increase the chance of your cancer completely disappearing. The current treatment involves attending hospital for a radiotherapy treatment planning scan (a CT scan), then a few weeks later you will start radiotherapy or chemoradiotherapy. Your team will either recommend a 5-day course of radiotherapy, or, a 5 week course of radiotherapy treatment (dependent on what they think is best for you) together with a daily chemotherapy tablet. Further CT scans will be carried out on each day of your radiotherapy treatment to help with guiding treatment. Your treatment team will explain why they have chosen radiotherapy or chemoradiotherapy to you.

Following completion of radiotherapy or chemoradiotherapy, regardless of whether you received the additional immunotherapy tablet or not, you will receive a course of chemotherapy which usually lasts 12 weeks.

Following completion of this treatment, you will then be reviewed regularly to monitor your progress, with a variety of checks including further scans, flexible sigmoidoscopies and examinations. We will also ask you to complete questionnaires asking you about your symptoms and quality of life. If your cancer completely disappears you will continue to be reviewed regularly in clinic for up to 30 months from the start of your treatment. However, if (a) your cancer does not disappear within the first 6 months, or (b) if it disappears completely within the first 6 months but then later returns, you will be considered for surgery to remove it. **All** participants in the ARTEMIS trial will be followed up until 30 months from the start of their treatment, whether they have surgery at any stage or not. After this you will probably have routine follow up visits (but no trial-related procedures) until you have completed 5 years of surveillance from the time of the initial treatment.

1.8 Who is providing my treatment and are they qualified?

The multi-disciplinary team (MDT) is headed by Simon Gollins who is a Consultant Clinical Oncologist at Royal Shrewsbury Hospital, plus senior medical colleagues from cancer centres around the UK including the Christie in Manchester. These are the same expert team who would be treating you outside of the trial were you to receive standard of care treatment.

1.9 What if something goes wrong?

As with any cancer treatment, your doctors and nurses aim to ensure that any risks are kept to a minimum. A number of different people (such as radiographers, physicists, chemotherapy nurses and doctors) check the radiotherapy and chemotherapy treatment before and during treatment, so the chance of it being delivered incorrectly is very small. Should this happen, or an unexpected problem arises during treatment, your medical team will discuss the consequences and options with you.

The Study Management Group and independent committees will monitor the study on an on-going basis so that if there is a difference in the treatment groups this will be detected as soon as possible and the study stopped. If you experience any symptoms or side effects, you must report these to your study nurse or doctor. Their contact numbers can be found at the end of this information sheet.

1.10 What if I lose mental capacity during the study period?

This would be a very rare occurrence. It could happen to any patient whether or not they take part in this study. Regardless, if you are randomised to the intervention arm and you lose capacity, then data pertaining to safety will continue to be collected for regulatory reporting purposes and will be included in any safety analysis. This is a legal requirement.

1.11 What are the chances of my cancer disappearing completely?

If patients with rectal cancer are treated with either radiotherapy or chemoradiotherapy, then in about 10 to 15% of cases the cancer disappears and such patients might then be able to avoid surgery. If chemotherapy is given after the radiotherapy or chemoradiotherapy, then the chance of the cancer disappearing completely can increase further to about 25%.

1.12 How have the 'intensified' chemoradiation regimens to be studied in ARTEMIS been chosen and will they be better than standard treatment?

The radiotherapy and chemoradiotherapy treatments (both with further chemotherapy) used within ARTEMIS have been chosen because they have already been tested in previous studies. They have both shown promising rates of complete disappearance of rectal cancer and acceptable levels of side effects. We are hoping that one or both of the 'intensified' chemoradiation treatments with immunotherapy (AN0025), as used in the ARTEMIS trial, will be better than 'standard' treatment without this drug. However, we cannot say this for sure, without making a comparison within a large study such as ARTEMIS.

1.13 What side effects will I get and will they be greater if I am randomly selected to receive the additional treatment?

Information sheets of "standard" radiotherapy or chemoradiotherapy are detailed below but further information will be given to you by your treating team as they normally would whether you are in this trial or not. Information on standard chemotherapy with FOLFOX or CAPOX will also be given to you by your treating team. The additional side-effects of AN0025 are shown later in this ARTEMIS information sheet.

1.14 Why is treatment not available via the NHS and is there any cost?

There are well established treatment protocols for cancer in the NHS, though many new drugs and therapeutics are discovered and researched every day. These new research programmes, like ARTEMIS, have to be funded separately in order to improve patient outcomes compared to the standard of care. After being closely monitored and viewed as a success, these new treatments are then adopted by the NHS.

1.15 Can I get this treatment through my private healthcare?

No, you cannot currently receive AN0025 through your private healthcare insurance.

1.16 Radiotherapy planning and treatment

Radiotherapy treatment planning

Before your radiotherapy treatment can start, your treatment will need to be planned. You will need to attend the radiotherapy department for a CT scan of your pelvis. This is in addition to the CT scan that you had to diagnose your disease. At the visit, the radiographers may make marks on your skin to make sure the same area is treated accurately at each treatment session. These are permanent very small dots (tattoos) that are not unsightly and sometimes very difficult to find unless you look very closely in this region. After your planning scan, the physicist and your radiotherapy doctor will then carefully create your personal treatment plan using CT scan images. This planning may take 2 weeks or more to complete. You will then receive an appointment to start your radiotherapy treatment.

Radiotherapy treatment

High-energy X-ray beams are directed at the cancer from outside the body (this is known as external beam radiotherapy). The type of radiotherapy that you will most likely receive is called Intensity Modulated Radiotherapy (IMRT) (though you may receive Volumetric Modulated Arc Therapy (VMAT) or TomoTherapy dependant on what your treatment team decides is best). These types of radiotherapy are able to target your tumour more precisely so that your tumour receives a high dose of radiotherapy and normal healthy cells nearby receive a much lower dose. The radiotherapy treatment is given as a series of short, daily treatments, using equipment similar to a large X-ray machine. The radiographers will help you to get into the right position on the radiotherapy couch. Once you are in the right position, the staff will leave you alone in the

room so that they are not exposed to the radiation. They will watch you carefully on a closed circuit television screen. The treatment is painless and the machine will rotate around you without touching you, it will last 10-20 minutes. Treatment will occur once each weekday (Mondays to Fridays) over either 5 days or 5 weeks (up to 25 weekday treatments in total) depending upon the radiotherapy schedule your treating team have selected. The amount of radiation received in the ARTEMIS trial is the same as 'standard' radiotherapy treatment.

1.17 Chemotherapy treatment

This is the use of anti-cancer drugs to destroy cancer cells. For 'standard' chemoradiation, the chemotherapy drug used is called capecitabine. This is given by mouth as several tablets (typically 3 or 4 tablets) twice a day on the days when you receive radiotherapy only i.e. it is not taken at weekends unless you attend for treatment

Please tell your doctor if you are taking, have recently taken or might take any other medications.

This is particularly important if you are taking any of the following:

- **Allopurinol** (gout medicine)
- **Warfarin** (blood-thinning medicine used to treat blood clots)
- **Sorivudine** and **Brivudine** (anti-viral medicines)
- **Phenytoin** (medicine for seizures or tremors)
- **Metronidazole** (antibiotic)
- **Clozapine** (schizophrenia medicine)
- **Folic acid**

1.18 What happens if I am taking capecitabine chemotherapy tablets and I miss a dose?

If you miss a dose, do not double up the next dose. Take your regular dose at the next scheduled time and bring back any remaining tablets to clinic at the end of your treatment.

1.19 How long does the treatment go on for?

The 'standard' radiotherapy treatment will be given over 5 days or 5 weeks (25 treatments), dependent on the radiotherapy treatment course your team have chosen for you. Occasionally it may go on for slightly longer than this if you experience side effects that mean treatment must be interrupted or delayed.

Following completion of radiotherapy treatment, you will start chemotherapy 3 weeks later. Prior to starting chemotherapy you will be seen in clinic to assess any radiotherapy side effects and to ensure it is safe to start chemotherapy. Chemotherapy will last 12 weeks, although may go on for slightly longer if you experience side effects that mean treatment must be interrupted or delayed.

1.20 What is the current standard treatment?

Radiotherapy (RT) or chemoradiotherapy (CRT), both followed by chemotherapy, is sometimes known as Total Neoadjuvant Therapy (TNT). This treatment can sometimes be considered for patients with rectal cancer, dependent upon various factors which are assessed using your scan and endoscopy results.

There are two radiotherapy approaches that can be considered – 1) a 5-day course of treatment,

or, 2) a 25-day course of treatment together with chemotherapy tablets (capecitabine). This is known as chemoradiotherapy (CRT). Both types of radiotherapy are only given during weekdays and not at weekends. This may seem like a big difference in treatment, but your treatment team will explain why they have chosen radiotherapy or chemoradiotherapy to you after the MDT meeting. An MDT (Multi-Disciplinary Team) is a meeting where all of the people involved in your care discuss your case and together they decide the best treatment option for you.

Three weeks after the radiotherapy or chemoradiotherapy, a 12-week course of chemotherapy will commence. This course involves receiving 2 different drugs, which will involve a combination of intravenous and tablet medication (CAPOX: Capecitabine and oxaliplatin) or all intravenous medication (FOLFOX: 5FU and oxaliplatin). The former will be given every 3 weeks for a total of 4 cycles over 12 weeks. The latter will be given every 2 weeks for a total of 6 cycles over 12 weeks. Both types of chemotherapy are equivalent and the choice can be made after discussion with your treating team.

1.21 What is the new treatment being studied?

Adding drug AN0025 to radiotherapy or chemoradiotherapy

AN0025 is a drug which helps the patient's own immune system to attack the cancer - a form of 'immunotherapy'. A recent study in about 60 patients showed that when it was combined with 'standard' radiotherapy or chemoradiotherapy, the rates of the cancer completely disappearing was very promising. However, a larger study such as ARTEMIS is needed to confirm these findings. Within ARTEMIS, AN0025 is taken by mouth as two tablets once per day for the total duration of the treatment (radiotherapy or chemoradiotherapy + additional 3 months of chemotherapy). This will start 2 weeks prior to radiotherapy or chemoradiotherapy.

1.22 What treatment will I receive if I take part?

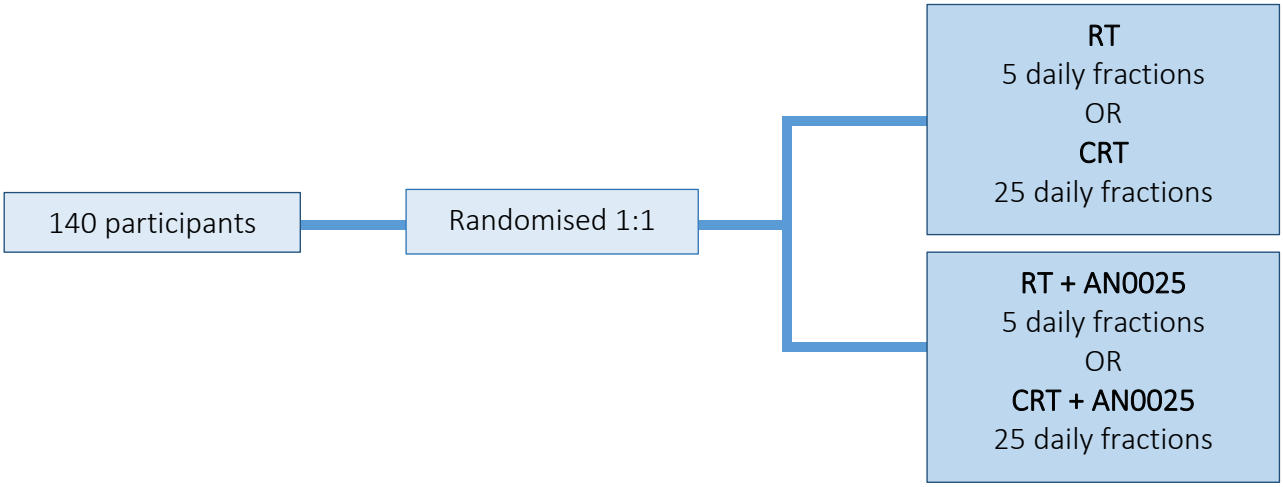
We need to make sure the groups of people receiving each treatment are as similar as possible, to be certain that the way each group responds to their treatment is due to the treatment itself rather than other differences between the groups that we do not know about.

The best way of finding out the benefits of an immunotherapy drug, alongside radiotherapy and chemotherapy treatment, is in a randomised study.

'Randomised' means that a computer will allocate you randomly (as if by the roll of dice) to receive either radiotherapy and chemotherapy (TNT), or the addition of the immunotherapy drug alongside these treatments. Neither your doctor nor you will choose which treatment you receive. In this way, a fair comparison can be made between the different treatments. There is a 1 in 2 chance of receiving the immunotherapy treatment alongside the radiotherapy and chemotherapy treatment schedules.

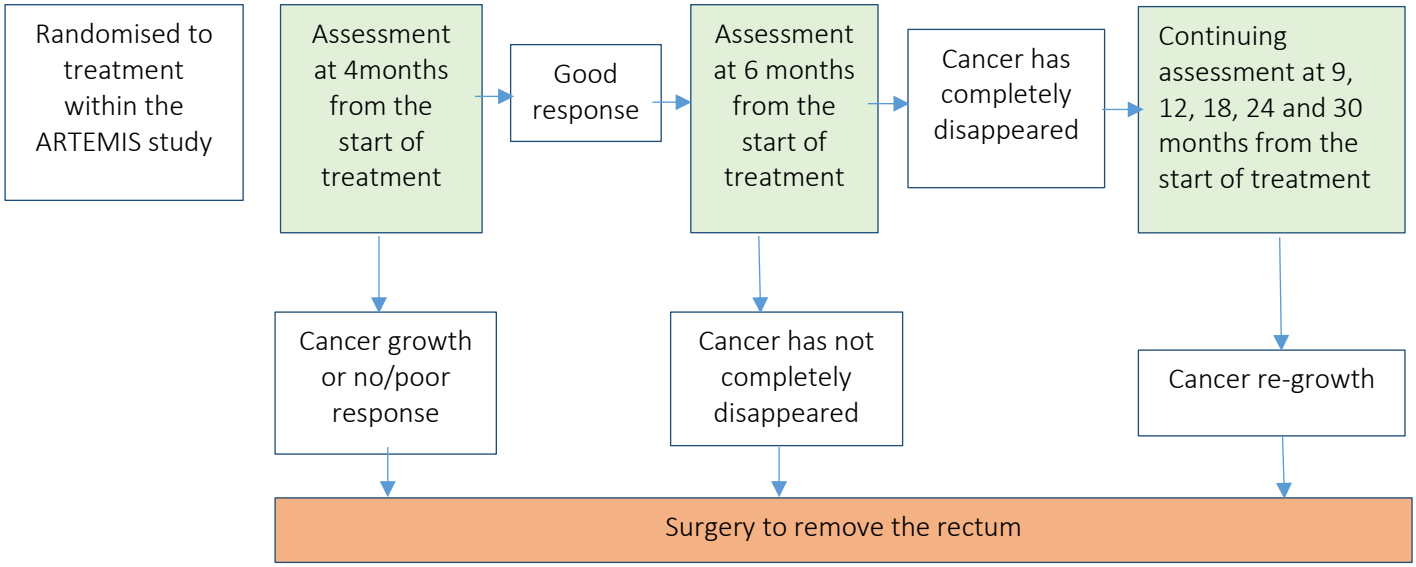
This is illustrated below:

(RT: Radiotherapy, CRT: Chemoradiotherapy, AN0025: trial drug used in ARTEMIS trial)



All participants will then receive 3 months of oxaliplatin-based chemotherapy (FOLFOX or CAPOX) starting 3 weeks after the end of the radiotherapy described above

How will I be monitored after I have finished treatment?



Assessment at 4 months: Participants will have an assessment at 4 months from the start of treatment. If there is evidence of cancer growth or a poor response to treatment, then there will be a discussion with your doctor to determine the best course of action. This most likely will be surgery.

Assessment at 24-26 weeks (6 months) following the start of treatment: Participants who have not undergone prior surgery will have an assessment at 24-26 weeks from the start of treatment. If there is evidence of some cancer still remaining (i.e. the cancer has not completely disappeared) then surgery to remove the rectum will be recommended. If however the cancer has completely disappeared, then surgery will not be recommended and participants will continue to be closely watched with regular assessments using examination, sigmoidoscopy and MRI scanning.

Assessment beyond 24-26 weeks (6 months) from the start of treatment: Participants whose cancer has completely disappeared at 6 months following the start of treatment, will then be

assessed at 9, 12, 18, 24 and 30 months to check that their cancer has not returned. These assessments will include MRI scans, and the 18 and 30 month assessments will also include CT scans). Participants will continue to be followed up by their referring surgical team after 30 months, though this will be off trial and as per standard protocol.

What happens if my cancer returns in the rectum during follow-up?

It is expected that approximately 25% of cancers that had disappeared at 6 months, will return over the following two years i.e. between 6 and 30 months. For the patients whose cancer returns, it is very likely (in approximately 90% of cases) that the cancer will start to grow again in the rectum at the site where it was originally found. For these participants surgery will be offered to remove the rectum.

Participants who undergo surgery to remove their rectum at any stage will then no longer undergo any further sigmoidoscopies or pelvic MRI scanning within the ARTEMIS study. Ongoing follow-up after surgery will be arranged by the team who performed the operation.

Quality of life questionnaires: ALL participants within the ARTEMIS trial will be asked to complete questionnaires asking about their symptoms and quality of life, regardless of whether they have surgery or not (paper or electronic versions). These will be completed at the beginning of your treatment (on paper only when you are in clinic), and then 3 weeks post the end of your RT treatment, during your follow-up appointments at 4, 6, 9, 12, 18, 24 and 30 months from the start of treatment (paper or electronic versions). This is a particularly important aspect of the study as we hope that increasing the chance of the cancer disappearing and avoiding surgery improves quality of life, for example by reducing the number of participants needing a stoma.

CT scanning: All participants within the ARTEMIS study will have a CT scan of their thorax, abdomen and pelvis at 6, 18 and 30 months following the start of their treatment (or at 6, 12 and 24 months should they undergo surgery).

1.23 What happens when the research study stops?

The study will stop two and a half years after the last participants starts treatment. After this time, the frequency at which your doctor sees you may vary slightly depending on your hospital's policy, but you are likely to be seen regularly until it is 5 years after your treatment ended.

Five years after your treatment, you are usually discharged from follow up if your cancer shows no signs of returning, but you can always contact the team if you have any concerns following discharge.

Please note that the study drug will not be available after the end of the research study.

1.24 Additional research

As part of the ARTEMIS study, we will ask your permission to use the following:

- Radiotherapy data
- Scans (such as MRI scans and CT scans)
- Original biopsy or surgery specimen (no additional biopsies are needed)
- Blood samples

- Stool samples

All samples will be stored for potential future research.

The reason why we would like to collect your radiotherapy data, your scans and biopsies and blood samples is to see if the cancer will be / has been successfully treated and understand if some patients are more likely to benefit from AN0025 than others.

The reason why we are also collecting stool samples will allow us to see how the bugs in the gut can affect the chances of successful treatment and will also understand more about how AN0025, radiotherapy and chemotherapy affect the cancer.

These samples are not compulsory, and it is your choice as to whether you agree to this or not. You can choose to withdraw your consent for your samples being used for research at any time, though this would not be possible if the sample has already been analysed by the time consent is withdrawn. Upon withdrawal of consent the samples and any analysis would no longer be used.

We will ask your permission to take some extra blood samples which are in addition to those that you might normally have taken when you are being treated and later being followed up in clinic. We will also ask you to provide some stool sample collections at the same time as the blood samples. No additional hospital visits should be necessary for the blood samples since they will be collected when you will be in the hospital as part of your radiotherapy or follow up appointments. The stool sample collection kit will be given to you at the assessment timepoints in clinic to be completed at home and posted back to the lab. For participants in the ARTEMIS study, blood and stool sample collections would be taken before starting any treatment and at various intervals for up to 30 months after treatment. A maximum of 5 sets of extra blood samples could be taken and 7 sets of stool samples. Not all hospital sites are involved in this blood sample collection. Please check with your doctor or nurse to see if this applies to you.

We will also ask your permission to provide some stool sample collections. The stool sample collection kit will be given to you at the assessment timepoints in clinic to be completed at home and posted back to the lab. For all participants in the ARTEMIS study, stool sample collections would be taken before starting any treatment and at various intervals for up to 30 months after treatment. A maximum of 7 sets of stool samples could be taken. Not all hospital sites are involved in this blood sample collection. Please check with your doctor or nurse to see if this applies to you.

We would also like to collect your NHS/CHI/Hospital number. These numbers are your hospital patient numbers, and we would like to collect them so that we can link your data and collect information held within your electronic health records, from your GP and hospital appointments. We may use this for future research linked to this research. We would only do this once any future projects had received ethical approval. To obtain or link your health record data, we would need to send a limited amount of your identifiable data (for example, initials, data of birth, and NHS/CHI/hospital number) to the relevant NHS data provider.

We would also like your permission to share your data with approved research databases. Research databases involve collecting information about lots of patients. Authorised researchers use the information to learn new things about how to treat patients in future. You might have been asked to join a research database in the past, or you might be asked in future. If you do join a research database, we would like to save time for your hospital and for the researchers. We could do this by sharing information we have collected about you in this study (ARTEMIS). This would involve sharing your personal details (such as my initials, date of birth and NHS number) to link study information to your record in those research databases. This would only happen if you are already taking part in the research database that is requesting the information. Any contact to join a research database would come through your hospital research team and not through the University of Leeds. 1.25 What if the treatment does not help?

Sometimes the treatment does not completely get rid of the cancer. If this happens, your team will discuss the options with you. This is likely to involve MDT discussions with the surgical team to decide if surgery to remove your tumour is appropriate.

1.26 **What are the risks of taking part in this trial?**

The side effects of 'standard' radiotherapy, chemotherapy and AN0025 are described in detail in this section. As a new drug, there is not enough research to provide a truly accurate representation of the potential side effects that may occur. However, clinical testing has suggested the following to be the most commonly occurring side effects when receiving AN0025 in combination with radiotherapy. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The chance of this happening to you as a consequence of taking part in this study is extremely small.

1.27 **Potential side effects of the new treatment being studied (AN0025)**

The first-in-human study of AN0025 has been completed. In this study, the common side effects associated with AN0025 (occurring in one or more subjects out of 10, i.e. ≥10%) were fatigue, diarrhea, nausea, decreased appetite, anemia (a low number of red blood cells that can causes tiredness and shortness of breath), vomiting, abdominal pain, shortness of breath, fever, dehydration, and headache.

Another study is a multicenter, combination therapy study of AN0025 in subjects with locally advanced rectum cancer. The study showed that AN0025 was well tolerated in combination with chemoradiotherapy. The most common treatment-related side effects (reported in >10% of participants) were fatigue, diarrhea, decreased appetite, headache, nausea and paresthesia (numbness or tingling). Hypersensitivity/drug hypersensitivity has also been recognised as a common side effect of AN0025.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think they are related to the study drug.

If there are persisting side effects, your study doctor may decide to permanently discontinue your study treatment with AN0025.

The side effects listed above are the most common side effects of AN0025 (occurring in ≥10%) that have been reported only. If you would like further information about all side effects reported for AN0025, please ask your research nurse or pharmacist. AN0025 is an investigational

treatment, so there may be other side effects that we do not yet know about. You will be given any new information as it becomes available that can help you choose to continue in the study. You will be monitored for safety throughout the study.

It is also not been established how AN0025 will affect the way in which your regular medications or supplements will work. It is possible that taking AN0025 with your regular medications or supplements may change how AN0025 works. It is very important that you tell the study doctor about all the prescription or over-the-counter medications that you are taking during the study. It is also very important that you tell the study doctor about all supplements (including vitamins, herbals, and minerals) you are taking during the study.

With any medication, there is a risk of allergic reactions, such as hives, swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing, and if not treated promptly could become life-threatening.

1.28 Potential side effects of radiotherapy

If you decide to take part in the study, you must report any problems you have to your study nurse or doctor. There is a contact number provided at the end of the information sheet for you to phone if you become worried at any time.

With the technique of radiotherapy which will be used in ARTEMIS, called IMRT (Intensity Modulated Radiotherapy), we can reduce the amount of radiotherapy received by healthy tissue nearby. This means the risk of side effects is lower than other radiotherapy techniques,

When your radiotherapy is planned, we not only aim to treat the cancer as accurately as possible but we also try to minimise the amount of normal tissues and structures which receive radiotherapy. However, unfortunately you can still have side effects. With the exception of radiotherapy induced fatigue, the side effects only affect the part of the body that the radiotherapy treatment is aimed at, in this case, the rectum and surrounding structures in your pelvis e.g. bowel, bladder, skin and pelvic bones. Radiotherapy affects people in different ways, so it is difficult to predict exactly how you will feel. Some people have only mild side effects, but for others the side effects are more severe. Knowing about the side effects may help you prepare and manage any problems. Your team will review you throughout your treatment and offer support with managing any side effects which develop.

You should be aware that the side effects listed below might be worse if you receive the additional immunotherapy drug.

1.29 Acute (early) side effects of radiotherapy

The side effects that occur during radiotherapy and for a few weeks after finishing radiotherapy treatment are known as ‘acute’ side effects. They usually get worse towards the end of treatment and then start to gradually get better a few weeks after treatment has ended, but may take some months to settle back to normal.

A change in bowel function

During the course of treatment, you may notice changes in how your bowel works. You may experience a sense of needing to open your bowels urgently, diarrhoea, mucus or bloody discharge and pass more wind. These symptoms can sometimes be reduced by avoiding particular foods. Your doctor or a dietician at the hospital can give you advice about this. You may need medication to improve your bowel function, your team will discuss these options if needed.

Pain and discomfort
Occasionally you can develop pain and discomfort in the rectum and around the skin of the anus, which can be most noticeable on opening your bowels. Occasionally the skin around the anus can become sore and inflamed. This discomfort usually starts about 2-3 weeks after treatment begins and heals 3-6 weeks after it finishes. Please let the hospital staff know if you are experiencing such symptoms so that you can be prescribed medicines and creams to help.

Urinary problems
During radiotherapy, passing urine may become painful or you may pass urine more frequently. If this happens, your medical team will check you do not have a urine infection and may suggest painkillers or other tablets. Very occasionally, a fine tube (called a catheter) is put into your bladder to drain the urine if you are unable to empty your bladder effectively.

Hair loss (from radiotherapy)
Sometimes you may lose your pubic hair during radiotherapy. The hair should grow back after treatment finishes in most patients, although very occasionally the hair loss is permanent.

Fatigue (extreme tiredness)
Fatigue is a common side effect of radiotherapy. The tiredness usually starts around 3-4 weeks after treatment begins and may last for a number of weeks following treatment. Following radiotherapy, you will commence chemotherapy and this can also cause fatigue. It is important to pace yourself during this time. Your health care team will be able to give you advice on balancing rest with exercise/activities.

Vaginal irritation
The vagina can become irritated and inflamed during radiotherapy. It can be prone to infection, so please let staff know if there is an abnormal discharge or itch. Intercourse may be painful or cause bleeding and it may be advisable to not have intercourse until the skin has healed. Your nurse or radiographer can advise you and offer practical advice to help minimise symptoms.

All these acute side effects usually decrease gradually once the treatment has ended, but it may take some months for skin changes to go back to normal.

1.30 Late side effects of radiotherapy

Side effects can also occur months and years after finishing radiotherapy. Some side effects can persist years after the patient has finished treatment. These are known as late side effects and are listed below.

You should be aware that the late side effects may be increased if you are randomised to receive the immunotherapy drug alongside radiotherapy.

A permanent change in bowel function
Some people find that their bowel action is permanently altered after radiotherapy. This is due to scarring of the bowel wall, and occasionally this can be severe. Problems that can occur include:

- more frequent bowel motions
- an urgent need to pass a bowel motion
- narrowing of the bowel passage causing difficulty in passing bowel motions
- rectal bleeding due to new, fragile blood vessels formed as a result of radiotherapy
- mucus or jelly-like discharge,

- rarely, patients can lose control of bowel motions completely.

These side effects can usually be managed with lifestyle modifications e.g. diet, although you may need to take medication. Your healthcare team will be able to advise you about strategies to improve your symptoms

In very rare circumstances, patients may require surgery to form a stoma (bowel bag). Any requirement would be discussed thoroughly with you and information provided to help inform decision-making.

Infertility (loss of the ability to have children)

Pelvic radiotherapy is likely to cause infertility in women. This is because the ovaries usually stop producing eggs after radiotherapy and the uterus is less flexible and may not be able to carry a baby to full term. Pelvic radiotherapy may also cause infertility in men. If you are considering having a child in the future, it is important to discuss your options with your doctor or nurse before treatment starts. Fertility treatments aimed at helping you to be able to have a child after your treatment has finished can be complicated. The options available to you will depend on your age, whether you already have children or a partner, and how soon your treatment needs to start. Your doctor can refer you to a fertility specialist for further discussion.

Men: Sperm can be stored for use in the future. It is important to talk to your doctor before the treatment starts. During radiotherapy, you may still produce sperm, but these could be damaged, resulting in abnormalities in the child. It is therefore very important to use barrier contraception (condoms) during treatment and for six of months after treatment has finished.

Menopause

Women who are still having periods may find that treatment brings on an early menopause because of the reduction in hormones produced by ovaries. This results in infertility and menopausal symptoms such as hot flushes and sweats may occur, which may affect sexual activity. Your doctor or nurse can give you advice on managing menopausal symptoms. It usually takes about three months for the ovaries to stop producing eggs and during this time, it is still possible to get pregnant. It is important to use contraception during radiotherapy if you are still of childbearing age.

Vaginal dryness and tightening

Women may develop dryness and narrowing of the vagina after radiotherapy. This may make sexual intercourse difficult or uncomfortable. This can often be avoided with the use of "vaginal dilators" as soon as the soreness has resolved and after treatment is finished. These are plastic devices that you insert into the vagina regularly to keep the vagina walls open. You may also need to use a lubricating jelly during sex. Your doctor or specialist nurse can give you more information about this.

Bones

During radiotherapy, the radiation passes through the bones of your pelvis including your hipbones. As such, you will be at a slightly increased risk of pain in your pelvic bones, or very occasionally breaking these bones in future. These small breaks may cause pain, requiring medication and an adjustment in physical activities, but will heal without requiring an operation. If you are concerned, please speak to your doctor about reducing the risk of these side effects.

Impotence

Men may become unable to have an erection (impotence) after treatment. It is important to let your doctor know if this happens to you, as there are ways this can be managed.

Urinary difficulties

There is a small risk of difficulties passing urine, urgency or bleeding after finishing radiotherapy. Please let your doctor know if these are an issue and treatment options can be discussed.

Skin changes
The skin in the treated area, especially around the anus, may look different long-term after any inflammation has subsided. It may be a slightly different colour than the surrounding skin, have visible blood vessels in it, or feel slightly thicker and may be prone to bleeding. This does not usually cause a problem, but if you are worried about it, please speak to your medical team. You may experience an itch, which can last for many months (it may be longer in some patients, although this is rare). Your medical team will advise on topical creams, which you can apply to minimise the dryness and soothe the itching.

1.31 Potential side effects of capecitabine chemotherapy when given together with radiotherapy

During your radiotherapy treatment, your team will regularly assess how you are managing treatment and any side effects that have developed. Alongside providing guidance or medication to help your symptoms, your team may interrupt your capecitabine if you have troublesome symptoms.

Anaemia (low red blood cells)
Red blood cells carry oxygen round the body. If they are low, you have less oxygen and can be tired and breathless. The medical team will do weekly blood tests to detect this and occasionally you may need a drip to give you extra red blood cells (blood transfusion). Sometimes, the low red blood cells are related to the tumour rather than the capecitabine chemotherapy.

Bruising and bleeding
Capecitabine can reduce the number of platelets in your blood. Platelets are cells that help the blood to clot. Tell your doctor if you have any bruising or bleeding you cannot explain. This includes nosebleeds, bleeding gums, blood spots or rashes on the skin. The medical team will do weekly blood tests to check platelets. Very occasionally, you may require a drip to give you extra platelets (platelet transfusion).

Risk of infection
Capecitabine can reduce the number of white blood cells in your blood, which is called neutropenia. White blood cells help your body fight infection. Neutropenia will make you more likely to get an infection and it may be more difficult for your body to respond to the infection

The medical team will do weekly blood tests to check for neutropenia.

Contact the hospital straight away on the contact number you've been given if you have a temperature over 37.5°C (99.5°F), you suddenly feel unwell (even with a normal temperature), or you have symptoms of an infection such as shivering, sweats, sore throat, cough, breathlessness or pain on passing-urine.

Nausea and vomiting
You may feel nauseated or vomit (feel or be sick). Medicines are given to counteract this and are generally very effective. If you continue to suffer nausea or vomiting, consult your doctor or nurse, as there are many different anti-sickness medicines available.

Hair loss (from chemotherapy)
While the radiotherapy will cause pubic hair loss, some chemotherapy drugs can cause temporary hair loss in all areas of hair. However, this is very uncommon with capecitabine.

Sore mouth
Capecitabine may make your mouth sore and cause mouth ulcers. Regular mouthwashes are

important and your nurse will show you how to use these properly. Let your medical team know if your mouth continues to be sore, as other treatments are available.

Sore hands and feet
Capecitabine can cause the palms of your hands and soles of your feet to become sore and inflamed, your medical team can prescribe a topical cream.

Sore eyes
Capecitabine can cause your eyes to become irritated, feeling gritty or sore. There is help available so please let your medical team know if this happens to you.

Chest pain
Rarely, capecitabine can cause a spasm or sudden narrowing of the coronary arteries in the heart. Although uncommon, this can lead to angina, chest pain and even a heart attack, which can be life-threatening. It is therefore important that if you do develop chest pain, to stop your capecitabine tablets immediately and call 999/attend A&E for emergency assessment.

1.31 Very rare side effects from radiotherapy or chemotherapy

There is a very small risk of developing other side effects as a result of receiving chemotherapy. These can include abnormal blood test results and blood clots. Please let the medical team know if you develop new symptoms such as shortness of breath or chest pain. Giving radiotherapy or chemotherapy, whether given as part of standard treatment or in a study, carries a very small risk of severe side effects that can rarely result in the death of the patient. This risk should be discussed with your doctor and compared with the need for treatment and its possible benefits. Early treatment of side effects is important and you should inform the clinical team promptly if you experience any.

1.32 Potential side effects of oxaliplatin with 5FU (FOLFOX) or capecitabine (CAPOX)

Both of these treatments are standard forms of chemotherapy which will have been used for many years by your treating team (who will have extensive experience in using them). They will provide their own information sheets on the regimen that has been chosen after discussion with you.

Side effects whilst the treatment is being given may include:

- Allergic reaction
- Pain along the vein
- Throat spasm

Common side effects of chemotherapy may include:

- Risk of infection
- Bruising and bleeding
- Anaemia (low number of red blood cells)
- Diarrhoea
- Feeling sick
- Tummy pain
- Numb or tingling hands or feet
- Feeling tired

- Sore mouth and throat
- Loss of appetite
- Changes to your taste
- Hair loss
- Eye problems
- Han-foot pain
- Skin changes
- Effects on the heart
- Effects on the lungs
- Muscle or joint pain
- Headaches

This patient information sheet mainly provides information about very common and commonly reported side-effects (we are unable to list all of the side effects), for more information regarding these and the less common side-effects please refer to the manufacturers' patient information leaflets, obtained from your hospital pharmacy and/or on the internet at www.medicines.org.uk. Sometimes patients may find these leaflets difficult to read. Please ask if you would like a copy from your doctor or hospital pharmacy.

1.33 Participants having surgery

Participants in the ARTEMIS study whose tumour never disappears completely and therefore have surgery at 6 months following the start of treatment are waiting longer to have their surgery than in standard practice (usually approximately three and a half months from the start of radiotherapy). Published evidence suggests that this does not increase surgical side effects or lower the chances of curing their cancer in the long term.

For participants who achieve complete disappearance of their cancer at 6 months, but whose cancer later returns, again, the published evidence shows that the chances of having successful surgery are not reduced by this longer delay.

However, despite the above evidence, it is possible that the addition of an immunotherapy tablet (such as AN0025) may increase the chance of complications following surgery and reduce the long-term chances of cure. More information is needed to assess the effect of adding this treatment alongside chemotherapy and radiotherapy. It is therefore very important to measure the outcomes of all participants in ARTEMIS, including all the participants who go on to have surgery, including surgical complication rates, success of surgery in eradicating cancer, and long-term survival and quality of life.

1.34 Contraception and avoidance of pregnancy

Male participants will be required to use barrier contraception, such as condoms during and for 6 months after finishing treatment. It is advised that men avoid having children during this time unless this is through sperm collected before the treatment started. Please speak to your doctor who will explain any concerns you have regarding infertility.

It is vital for women to avoid pregnancy during the treatment and contraceptives should be used throughout. It is important to tell your clinical care team if you are pregnant or become pregnant during treatment, as this will affect your care.

It is very likely (in both males and females) that you will be infertile after the treatment is finished. This means you will lose the ability to have children. However, if you think there is any chance

you are pregnant in the future, please speak to your doctor. Further information about the risks of infertility is provided in the 'Infertility' section, below.

Female participants require confirmation that they are not pregnant. Therefore, all women of childbearing potential must undergo a pregnancy test prior to starting treatment within the ARTEMIS study.

1.35 What are the different scans that I will have?

CT scan

A CT scan (computerised tomography scan) creates images of the inside of the body using X-rays. Please ask your doctor if you wish to know more about this.

MRI scan

An MRI scan (magnetic resonance imaging scan) uses strong magnetic fields to create images of the inside of your body. It is a bit noisy and occasionally people can find it a little claustrophobic. There are no X-rays involved. Please ask your doctor if you wish to know more about this.

1.36 What are the risks involved with the scans I will have as a part of the study?

CT scans involve X-rays (radiation). These procedures use ionising radiation to form images of your body and provide your doctor with clinical information. Within this study, you will receive between ten and thirty CT scans. One will be carried out before starting treatment to assess whether your cancer has spread to other organs away from the rectum and to help plan the radiotherapy (CT planning scan). Further scans will be carried out on each day of your radiotherapy treatment to help with guiding treatment (five or twenty-five scans depending on whether you are receiving SCRT or LCCRT). Additionally, scans will be carried out at 6, 18 and 30 months following treatment to check for any cancer spread (or 6, 12 and 24 months if surgery has been received to treat the cancer). This is the same as if you were not in the study. One CT scan corresponds to about 8 years' exposure to the natural background radiation that we all receive throughout life. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. The chance of this happening to you as a consequence of taking part in this study is extremely small.

1.37 Contact Details

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

If you wish to keep up-to-date with the progress of the ARTEMIS study, we will provide the hospital site where you attend your appointments, with newsletters about the study. Please ask your research nurse for a newsletter at your next hospital appointment, they will be happy to provide you with one. Alternatively, you may wish to visit the ARTEMIS website, where you will be able to view our newsletters along with an overview of how the study is evolving.

You may also find it helpful to contact Macmillan Cancer Support, an independent cancer information charity (freephone: 0808 808 00 00; address: 89 Albert Embankment, London, SE1 7UQ; website www.macmillan.org.uk).

Information service about cancer and cancer care for people with cancer and their families by Cancer Research UK (Tel: 020 7061 8355; website https://www.cancerresearchuk.org/about-cancer).

You will also find information on the Yorkshire Cancer Research website http://www.yorkshirecancerresearch.org.uk/; address Jacob Smith House, 7 Grove Park Court,

Harrogate, HG1 4DP.

If you would like further information about clinical research, the UK Clinical Research Collaboration (a partnership of organisations working together on clinical research in the UK) have published a booklet entitled ‘Understanding Clinical Studies’. Contact UKCRC: Tel: 0207 670 5452; website www.ukcrc.org

This completes Part 1 of the Information Sheet. If the Information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Parts 2 and 3 before making any decision.

PART 2

2.1 What if relevant new information becomes available?

Sometimes during the course of a study, new information becomes available. If this happens, your doctor or nurse will tell you about it and discuss with you and confirm whether you want to continue in the study. If you decide not to continue, your doctor or nurse will continue your care if this is necessary. If you decide to continue, you may be asked to sign an updated consent form. Occasionally on receiving new information, your doctor or nurse may consider it to be in your best interest to withdraw you from further study treatment.

2.2 Will there be information available where I can see updates on the trial?

The ARTEMIS website will provide information on significant trial updates as and when they occur. The ARTEMIS website can be accessed at https://ctru.leeds.ac.uk/artemis/

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

You can stop taking part in this study, or any part of it, at any time and without giving a reason. However, we would like to know the reason if you are willing to say. Before deciding to stop, you should talk to your study doctor or nurse. They can advise you and may be able to deal with any concerns you may have. If you decide to stop taking part at any time, it will not affect the standard of care you receive.

If you decide to stop taking your study treatment, you are likely to receive the 'standard' treatment instead (the treatment that would have been recommended if you had not entered the trial initially). Trial visits and assessments can still go ahead, if you agree to this.

If you decide to stop study visits or assessments, in order to make sure the research is still reliable, we will need to keep the information we have already collected about you, and include it in the study analysis.

2.4 What happens to my data if I stop taking part in the study?

You have the right to stop participating in any aspect of this study at any time. If you do, we will need to keep the data that we have collected so far. And if you do, it is really important for the reliability of the research that we still find out how you are from time to time. We will therefore continue to ask your doctor or nurse for updates about you, unless you clearly tell us that you don't want this. We may also be legally required to continue collecting some information about side-effects of treatments you have received.

If you decide to stop taking part in the study, we will need to keep any information we have already collected about you, and include it in the final study analysis. This information will help answer some important research questions. It is very important that once we have the information, we do not tamper with it or destroy it. If we did, it could make the study less reliable or accurate, or mean that we could not comply with other laws which protect people participating in clinical studies. However, to safeguard your rights, we will make sure that we only keep the information about you that we really need to keep.

We will also need to continue collecting some limited information about you. Again, this is important because it helps us to ensure that the results of the study will be reliable. Unless you specifically tell your doctor or nurse that you do not want us to, we will continue to ask your hospital for some information about your health. This may be from your routine hospital visits, via your GP or through other contact between you and your hospital. This won't involve you committing any further time to the study.

If you say you do not want us to collect further information, we will not ask your hospital for any. However, it is important you know that if many people leave the study early, this could make the study results, which you and others have given time to, more difficult to interpret.

In some cases, we may be required to collect some limited information about side effects you may have as a result of taking part in the study, even if you have told us you did not want to provide further data for the study. This will only be collected if required by the regulatory authorities, and if we collect it, we will collect only the minimum possible amount of personally-identifiable information.

2.5 Who has organised, reviewed and funded the research and who will be supervising it?

The trial has been organised and sponsored by the University of Leeds through the Clinical Trials Research Unit (CTRU), in conjunction with other cancer centres across the UK. The study is funded by Adlai Nortye. Overall, the trial will be supervised by the University of Leeds.

2.6 What if there is a problem?

Harm and Complaints:

Every care will be taken in the course of this clinical study to reduce the chance of harm to you. However, in the unlikely event that you are injured as a result of participating in the study, which is being managed and insured/indemnified by the University of Leeds, then compensation may be available, although you may have to pay your related legal costs. The hospital where you receive your treatment has a duty of care to you whether or not you agree to participate in the study and the University of Leeds accepts no liability for negligence on the part of your hospital's employees. If you wish to complain about any aspect of the way you have been treated, please contact your research doctor in the first instance.

Any claims will be subject to UK law and must be brought in the UK. If you have private medical insurance, you should tell your insurer that you are taking part in research. They will let you know if it affects your policy.

Regardless of this, if you wish to complain, or have concerns about any aspect of the way, you have been approached or treated during the course of the study; the normal National Health Service complaints service is available to you. These are unique to individual NHS trusts. Your study nurse or doctor can give you this information.

2.7 How will my information be used?

The information needed for study purposes will be entered directly into a secure database or collected on paper forms by a member of the study team at your hospital.

Paper forms will be sent (using standard Royal Mail post or by a very secure file transfer) from the hospital to the University of Leeds Clinical Trials Research Unit (CTRU). Paper records will be securely locked in filing cabinets. You will be allocated a study number, which will be used along with your date of birth and initials to identify you on each paper form. Your full name and signature will be included on your consent form and a copy of this will be sent to the CTRU by post or secure file transfer so we can check you have definitely agreed to take part in the study.

If you choose to complete the quality of life questionnaires on paper, a member of the study team will ask you to complete these when you come to clinic. If you choose to complete the questionnaires online, your mobile telephone number and/or email address will be collected on the contact details form so that CTRU can send you the questionnaires electronically and send you text or email reminders. This form may be sent to the CTRU by post or secure electronic transfer.

Every effort will be made to ensure that any further information about you that leaves the hospital will have information removed so that you cannot be recognised from it. This information will usually be removed by a member of the study team at your hospital, but may also be removed by the CTRU upon receipt.

Your GP, and the other doctors involved in your clinical care, will be kept informed of your participation in this study, but otherwise all information about you and your treatment will remain confidential.

Some of the treatment plans, scans and photographs of the inside of the bowel from selected participants may be sent to other hospitals to be looked at by other doctors. This is to ensure that treatments and results/reports are consistent across hospitals. These will be sent via standard hospital processes (such as by electronic transfer). We will remove your information from your scans so that it will not be possible for staff at other hospitals to identify you.

Authorised individuals from the research team, the University of Leeds, or the regulatory authorities may look at your healthcare records to check that the study is being carried out correctly.

The information collected about you may be shared with other research teams to answer new research questions in the future. Information will be limited so that you cannot be identified. When the study is finished, the results will be published in a medical journal, but no individual participants will be identified.

PART 3

3.1 General Information

The study is being carried out in the United Kingdom and the University of Leeds is the Sponsor for this study. We will be using information from you and/or your medical records in order to undertake this study and the University of Leeds will act as the data controller for this study. As a publicly funded organisation, we have to ensure that it is in the public interest when we use personally identifiable information from people who have agreed to take part in research. This means that we are responsible for looking after your information and using it properly. The University of Leeds will keep identifiable information about you for 25 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.

The University of Leeds will collect information about you for this research study from the hospital you are receiving treatment from. This information will include your name, date of birth and health information, which is regarded as a special category of information. We will collect this information for trial purposes. More Information on the University of Leeds privacy policy for research participants can be found in the following link:

https://dataprotection.leeds.ac.uk/research-participant-privacy-notice/

We know that some people want to know more than others about how their information is used. You can therefore choose how much detail you'd like:

- You can look at the quick access guide, below. You should definitely read this, even if you do not look at the appendix and comprehensive guide mentioned below.

- If you have particular questions or concerns, you should look at the optional appendix. This is available at the end of this information sheet.

- If you would like more detailed explanations about anything, including why we need to do things in a certain way, you can find it in our comprehensive guide. You do not have to read it before taking part in this study, but you might want to look at specific sections if you have particular concerns. This is available at https://ctru.leeds.ac.uk/ctru-comprehensive-privacy-guide/ or you can ask for a printed copy from your study doctor or nurse. This can also be made available in large print or other formats, if you need them.

The text in each of these documents is laid out in the same order, so you can easily find more detail.

All of these documents have been written with the help of patients and the public to help make sure they are clear and accessible. As in the rest of this patient information sheet, whenever we say 'we' or 'us', we mean the study team at the Clinical Trials Research Unit, University of Leeds (https://ctru.leeds.ac.uk/).

You can find more general information from the NHS about how people's information is used in research at https://www.hra.nhs.uk/information-about-patients/.

3.2 **A quick access guide to how we will use your information in ARTEMIS**

- You can read more about each of the points below in the optional appendix in the participant manual. Use the reference numbers to find the relevant section in the optional appendix.

- If you agree to take part in this study, we will collect information about you and your health. We will use this to run the study, produce the study results, and to help make sure you and other people taking part in the study are safe. The information we will collect will include:

    - Information from you and from your hospital medical notes

    - Information from analysing biological samples you give (e.g. optional tissue, blood and stool samples)

    - images from MRI scans and CT scans

    - Your contact details (email address and/or phone number) **(1)**

    - **Your NHS number (England and Wales) or CHI number (Scotland)**

- Your information will be collected by the Clinical Trials Research Unit at University of Leeds (https://ctru.leeds.ac.uk/), who are running this study. The University of Leeds will have overall responsibility for how your information is used in this study, including making sure that all information is kept secure. **(2)**

- We will keep all your information secure at all times. **(3)** The only people at the University of Leeds who will see your information are the people who need to run or analyse the study, or check how the study has been run. **(4)**

- We may use the study information for additional research projects within the University of Leeds. We will only do this for worthwhile research projects with all appropriate ethical approvals. If people outside the original study team are involved, they will only receive the minimum information needed for the new project, and they will not receive any clearly identifiable information (such as your name).**(5)**

- We will sometimes need to share your information with people outside the University of Leeds. This is so that we can run the study, keep you and others safe, comply with laws and other rules around research, and support further research in the public interest. We will never sell your information, or pass it on to people who will sell it. Information that we share will never be used to make decisions about future services available to you, such as insurance. **(5)**

- You can usually ask organisations to give you a copy of information they hold about you, or to correct your information. However, this does not apply when your information is used for research in the public interest like this, because allowing you to access or change the information could harm the quality of this research. Your contact details are different though - it's vital that you tell your study doctor or nurse if these change at any point. **(6)**

- To comply with laws and other rules about research, we need to keep your identifiable information until at least **6-12 months** after the study has finished. **(7)**

- You can usually ask organisations to delete your information or restrict how your information is used. However, allowing you to delete or restrict your information could harm the quality of this research, which is being done in the public interest. If you stop

taking part in the study, we will therefore need to keep the information we already have about you. **(8)**

- If you decide to stop attending your study visits for any reason, we will keep collecting information from any other hospital visits you have, if they are relevant to the study. This way you can keep contributing to the study without giving any more of your time, if you want to. If you are not happy with this, you can ask us to stop collecting more information about you at any time. If you tell us you want us to stop collecting your information, we will still be legally required to collect information about any serious side-effects you may experience. **(8)**

- If you have questions or concerns about how your information is used that aren't answered by this document or by talking to your study doctor or nurse, you can contact the University of Leeds Data Protection Officer. If you are still not happy, you can contact the Information Commissioner's Office. You can find out how to contact these people in the **optional appendix** and the **comprehensive guide**. For any questions or concerns that are not to do with how your information is used in this study, please contact your nurse or doctor as you usually would. **(9)**

Optional appendix: more about how your information will be used

This optional extra section of this participant information sheet is about how your information will be used if you agree to take part in this study. It gives you more detail than the **quick access guide** above. It is in the same order as that, so that you can easily find what you need. If you have questions or concerns after reading the quick access guide, you should look at this optional appendix, or the sections of it that interest you.

If you still have questions after reading this appendix, or would like more detail about anything, you should look through our **comprehensive guide** to how your information is used. You do not have to read it before taking part in this study, but you might want to look at specific sections if you have particular concerns. It is available at https://ctru.leeds.ac.uk/ctru-comprehensive-privacy-guide/ or you can ask for a printed copy from your study doctor or nurse. This can also be made available in large print or other formats, if you need them.

You should read through these sections as much as you would like to. After doing that, if you are interested in participating in the study, you can find the informed consent form at the end of this document.

A. What information will be collected, and what will it be used for?

If you agree to take part in this study, we will need to collect and use some information about you and your health. We will only use what we need to run the study, to produce the results of the study and to make sure you and other people taking part in the study are safe.

This research is in the public interest, which means our results will be used to improve the healthcare of patients in the future. Because of this, if you agree to take part in the study, we will be able to use information about you, including sensitive information about your health**, ethnicity, sex life and your genetic characteristics (this means information about your DNA from biological samples you will have given).**

Specifically, the ways we will use information about you are:

1. We will use information from you and your medical notes to run the study, to produce the study results and to confirm it is safe and appropriate for you to join the study. We will also collect information about your health from your study doctor or nurse and your medical notes to help make sure you and others are safe.
2. We will collect a copy of your signed consent form so that we can be sure you have agreed to take part in the study.
3. We will collect information about you and your health directly from you on study questionnaires. We will use this information to produce the study results.
4. The team at the hospital will use your postcode to determine the deprivation ranking of the area where you live. The deprivation rank is measured using factors such as education, employment and income. Collecting this data will help us understand who is and isn't taking part in our trial. This will help us to design more inclusive trials in the future. Your postcode will not be shared with the CTRU and is only used by the team at the hospital to calculate the deprivation rank.
5. We will collect information about optional tissue, blood and stool samples you will give in the study. The tissue and stool samples will be sent to Leeds Institute of Medical Research and the blood samples will be sent to the CRUK National Biomarker Centre. All samples will be labelled with your unique study identification number, date of birth and initials.
    - If you agree to provide samples for future research, these will be sent to **lab(s).** If other researchers in the future want to use the samples for worthwhile research in the public interest, they will be sent the samples and your unique study identification number. The other researchers may also ask us for other information about you for their research (see section 5, below), but they would not be able to see who you are from the information they have, even when they combine the results of analysing your samples with the other information we share with them.
6. Sometimes we need to ask doctors who work with us to give us advice on specific medical situations. To help the doctors do this, we might need to collect copies or scans of parts of your medical notes. These will have any details that could identify you removed before they are sent to us.
7. In this study, we need to check that radiotherapy is being given in the same way at different hospitals. To check this, we may need to send some information about your

radiotherapy to a specialised team at a hospital in the UK. This won't include any information that might identify you.

8. If you join this study, we would like to send you study questionnaires and reminders to complete study questionnaires. To do this, we will need to collect your email address / phone number. You can choose which details to provide and we will only use it for the purposes mentioned here.

If you want to find out more about any of these, please refer to the **comprehensive guide** to how your information is used.

B. **Who is collecting my information?**

Your information will be collected by the Clinical Trials Research Unit within the Leeds Institute of Clinical Trials Research, University of Leeds. You can find out more about our work at https://ctru.leeds.ac.uk/.

University of Leeds has overall responsibility for what information is collected, how it is collected, and making sure people's information is used securely and correctly. If you want to contact someone within the University about how your information has been or will be used, you can see section 9, below. See the **comprehensive guide** for more about what this means for you.

C. **Will my information be kept secure?**

We will take all necessary measures to ensure that information about you is sent and stored securely by us or by anyone acting on our behalf.

Most of your information that we need for the study will be sent to us by post. Study forms only show your initials, date of birth and your unique study identification number. Your completed consent form will also be sent to us so that we can be sure you have agreed to take part in the study. This will be sent separately to rest of the study forms.

Your study doctor or nurse will enter most of the information needed for the study directly into our secure study database. Your study doctor or nurse will also send us some information by post. This will include your completed consent form, so that we can be sure you have agreed to take part in the study. This will be sent separately to any other study forms.

Sometimes we will also get information about you by email or fax. Emails will never contain your name, only your trial identifying number and sometimes your initials and date of birth.

Finally, some particularly sensitive documents, such as safety report forms will be sent to us via a 'secure file transfer'. This means information is sent by the internet in a very secure way.

Information stored in our databases or other electronic storage locations is held very securely, in a way that would make it very difficult for any unauthorised people to access it.

D. **Who will see my information in the research team?**

We will make sure that the only people at the University of Leeds who can see your information are people who need to run or analyse the study.

See **Part 2** of this information sheet for more on who may see your medical notes and other confidential information if you agree to take part in this study.

E. **Who else will see my information?**

There are some specific situations where we need to share information with other people or other organisations. We will always do this carefully and only when it's really necessary. We will avoid sharing information that could identify you whenever possible. We will never sell your information, or pass it on to people who will sell it. We will only share information when it is necessary for the study, necessary to protect your safety or the safety of others, or in the public interest. Information we share will not be used to make decisions about future services available to you, such as insurance.
We will share your information for the following reasons. You can find out more about these in the **comprehensive guide.**

- To run and analyse parts of the study, we need to share your information with collaborators (such as doctors, statisticians or other experts) outside the University of Leeds.
- To keep you and other people safe, we will need to share some information about health-related events you may have with authorised organisations. None of these organisations will be able to identify you from this information.
- To report to authorised people about the progress of the study, we will need to share some basic information with some authorised organisations, including the Research Ethics Committee that has approved this study. None of these organisations will be able to identify you from this information.
- To allow other researchers to carry out future research in the public interest. We will only share your information for worthwhile research with all appropriate approvals. We will only share your information in such a way that researchers outside the University of Leeds will not be able to identify you.
- We may also use study information for additional research projects within the University of Leeds. We will only agree to do this for worthwhile projects with all

appropriate approvals, and we will not share any clearly identifiable information with researchers outside the original study team.

- Due to storage space limitations, we will store information securely away from the University of Leeds for a period after the main part of the study is over. The archiving companies we use to do this for us will only store your information and will not access it or see your details.

See **Part 2** of this information sheet for more on who may see your medical notes and other confidential information if you agree to take part in this study.

F. **Can I see my information, or ask you to correct it?**

Usually, when an organisation or a company has information about you, you can ask to have access to that information at any time, or ask them to correct it if it needs correcting. However, this does not apply in the same way to information used for research in the public interest, because allowing people to access or change their information could harm the quality of the research. You therefore cannot ask to access or correct information we have about you. However, most of the information we will collect will also be in your medical notes, which you can get access to if you want to. You should speak to your study doctor and nurse if you would like more information about care you have received.

If you have provided us with contact details for use in the study (email address, phone number) it is important that we find out about any changes to these. Please let your study doctor or nurse know about any changes so that they can let us know. Otherwise, we might lose contact with you or send messages for you to your previous contact details.

G. **How long will my information be stored for?**

If you agree to take part in this study, we will need to keep your information for at least **6-12 months** after the end of the study. We need to do this in order to comply with laws and other rules about research, which say it must be possible to check the results of the research for a period of time after it has finished. We will keep your information secure during all this time. For practical reasons, we may ask reputable archiving companies to store information securely on our behalf, away from the University of Leeds.

At the end of this period, we will securely destroy your information.

H. **What will happen if I stop taking part in the trial?**

If you decide you would like to stop all your study visits for any reason, we will need to keep the information we have about you to make sure the results of the study are reliable.

Usually, when an organisation or a company has information about you, you can ask them to delete it, or not use it for a certain purpose. However, this does not apply in the same way to information used for research, because it would harm the quality of the research if people could delete or remove their information. We also need to comply with laws and other rules about research that say we need to keep all information used in research for a period of time after the research finishes. If you agree to take part in this study, it will therefore not be possible for us to remove or delete your information later on, although you can ask us to collect no further information after a given time.

Some other things you should know about what will happen to your information if you stop taking part:

- If you stop all study visits, you should discuss with your study doctor and nurse. If you still occasionally go to your hospital for routine visits, we would like to hear from your study doctor or nurse about these visits, if they are relevant to this study. This way, you can still contribute to the study and help make the study results more reliable, without giving any more of your time. However, you can tell your study doctor or nurse that you do not want any more information sent to us, and they will make sure your wishes are respected.
- If you tell us you do not want us to collect any more information about you, we will still be legally required to collect information about any serious side-effects you experience, or health events that might be related to the treatment you have received. This is so that doctors using the same treatment have all the information they need about possible side-effects.
- If you stop attending your study visits without telling anyone at your hospital, or you change your contact details or move house and do not tell your hospital, they will lose contact with you. If this happens, we may ask your study doctor or nurse to contact your GP to check if you are OK and still happy to take part in the study.

If you want to know more about what might happen to your information if you stop taking part in the study, including *why* we need to use your information in the ways we do, please see the **comprehensive guide.**

I. **What if I have concerns about how my information is being used?**

Your study doctor or nurse should be your first contact for any questions about your participation in this study. If you still have questions that they cannot answer, and which are not answered by any of these documents, you can contact the University of Leeds Data Protection Officer (the University's main contact for anything to do with how your information is used). You can do this using any of the details below. If you do contact them, please mention the name of this study (ARTEMIS) and the Clinical Trials Research Unit.

- Email: DPO@leeds.ac.uk
- Telephone number: +44 (0)113 243 1751

- Postal address for data protection issues: University of Leeds, Room 11.72 EC Stoner Building, Leeds, LS2 9JT

If you are not happy with the response to any queries or complaints, or believe your information is being used incorrectly or unlawfully, you should contact the Information Commissioner's Office:

- General website: ico.org.uk
- ICO contact webpage: ico.org.uk/global/contact-us
- Telephone number: 0303 123 1113
- Postal address: Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire, SK9 5AF

Delete this line, then print on Trust/Hospital headed paper

Participant ID:	Initials:
Date of Birth:	NHS/Hospital/CHI Number:
EudraCT Number: 2021-005716-57	Principal Investigator:

ARTEMIS

PARTICIPANT CONSENT FORM

Please initial each box

1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation in this study is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected. I understand that even if I withdraw from the above study, the data and samples collected from me will be used in analysing the results of the study and in some cases further information about any unwanted effects of my treatment may need to be collected by the study team. ☐

3. I understand that my healthcare records may be looked at by authorised individuals from the study team, regulatory bodies or Sponsor in order to check that the study is being carried out correctly. ☐

4. I agree to a copy of this Consent Form being sent to the Clinical Trials Research Unit (CTRU). ☐

5. I will allow any information or results arising from this study to be used for healthcare and/or further medical research upon the understanding that my identity will remain anonymous wherever possible. ☐

6. I understand that if during this study my clinical care team determine that I have lost my ability to make my own decisions, no further study intervention will be given. I agree that the information collected up until this point will remain on file and will be included in the analysis. ☐

7. I agree that my GP, or any other doctor treating me, will be notified of my participation in this study. ☐

8. I agree to take part in the study. ☐

The following points are OPTIONAL:

	Please initial to confirm	
	Yes	No
I agree to complete the quality of life questionnaires and understand that my email address and/or telephone number will be passed to the CTRU if I choose to complete the questionnaires online, for the sole purpose of issuing these questionnaires.	☐	☐
I give permission for optional surplus samples from my cancer biopsies that have been stored in the hospital pathology laboratory to be retrieved and used in the future for colorectal cancer research, including genetic research.	☐	☐
I understand that my optional tissue sample is a 'gift' that may be used in future research that receives ethical approval. I understand that my sample and data collected from it may be shared on a collaborative basis with researchers in the UK and potentially, centres abroad, including those outside the European Economic Area.	☐	☐
I give permission that my radiotherapy data, CT and MRI scans and photographs of my bowel may be used in future research. I understand that my sample and data collected from it may be shared on a collaborative basis with researchers in the UK and potentially, centres abroad, including those outside the European Economic Area.	☐	☐
For participating centres only: I give permission for up to 5 additional sets of translational blood samples to be collected, to be used in future colorectal cancer research, including genetic research. I understand that my sample and data collected from it may be shared on a collaborative basis with researchers in the UK and potentially, centres abroad, including those outside the European Economic Area.	☐	☐
For participating centres only: I give permission for up to 7 stool samples to be collected, to be used in future colorectal cancer research, including genetic research. I understand that my sample and data collected from it may be shared on a collaborative basis with researchers in the UK and potentially, centres abroad, including those outside the European Economic Area.	☐	☐
I agree for my details (which could include initials, date of birth and NHS number, hospital number or CHI number for Scotland) to be submitted to central UK NHS bodies, so that information about my health status may be obtained by the CTRU if necessary.	☐	☐

	Yes	No
I agree that information collected about me in this study can be shared with researchers running approved research databases. I understand this would involve sharing my personal details (such as my initials, date of birth and NHS number) to link study information to my record in those research databases. This would only happen if I am already taking part in the research database that is requesting the information.	☐	☐

Participant:

Signature……

Name (block capitals)……

Date……

Investigator:

I have explained the study to the above named participant and he/she has indicated his/her willingness to participate.

Signature……

Name (block capitals)……

Date……

(If used)Translator:

Signature……

Name (block capitals)……

Date……

(If used) Witness:

Signature……

Name (block capitals)……

Date……

(1 copy for participant; 1 for the CTRU; 1 held in participant notes, original stored in Investigator Site File)