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A Phase II study of Higher RadiOtherapy Dose In The Eradication of early rectal cancer

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT

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

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

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.

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.

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PART 1

What is the purpose of the study?

Patients with small (early) rectal (back passage) cancers would normally have this treated using surgery to remove the whole rectum, which is the standard treatment. However, if radiotherapy or radiotherapy given at the same time as chemotherapy ('chemoradiotherapy') is given over 5.5 weeks then this can lead to the cancer disappearing in about one third of such patients.

The APHRODITE study will explore the potential benefit of giving a higher radiotherapy dose over 5.5 weeks to see if this improves the chance of the cancer completely disappearing, while at the same time not causing too many extra side effects. In the future, this could lead to better treatment and improved quality of life.

Two main groups of patients will be included in the APHRODITE study:
Group 1: Patients who are suitable to undergo surgery but would prefer to try and cure their cancer using radiotherapy or chemoradiotherapy without having surgery, keeping surgery in reserve in case this treatment does not cure their cancer.
Group 2: Patients who are not suitable for surgery, either because surgery is thought to be too risky because they have other medical problems which would increase the risks of having surgery, or because they would have difficulty looking after a stoma (bowel bag) following surgery.

Why have I been chosen?

Your doctor has decided that you fit into **Group 1/Group 2**. *[Researcher please cross out the non-relevant Group]*

Group 1: Your doctor has informed you that you have an early rectal cancer and that standard treatment is surgery to remove the rectum and your doctor thinks that you are suitable to have surgery. However, after the APHRODITE trial has been introduced to you by your medical team, you are interested in knowing more about undergoing radiotherapy or chemoradiotherapy to try and cure your cancer without surgery, within the APHRODITE trial.

Group 2: Your doctor has informed you that you have an early rectal cancer and has recommended treating your cancer with radiotherapy or radiotherapy in combination with chemotherapy ('chemoradiotherapy'), rather than surgery.

The APHRODITE study aims to recruit 104 patients with cancers like yours, who are suitable for treatment with radiotherapy or chemoradiotherapy.

Do I have to take part?

No, your participation in the APHRODITE 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.

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 may have already undergone some of them. One of the eligibilities we may need to confirm is your MRI scan with our trial radiologists. Our trial radiologist will look at your MRI scans and assess eligibility. In order for the radiologists to confirm that you are/are not eligible we will first register you and the consent form will ask if we have permission to send the MRI eligibility scans to our radiologist in real-time. Our radiologists will then review your scan and inform the research team at your hospital. You will then if confirmed as eligible be randomised on to the trial and this process is explained fully within this patient information sheet. This process will not affect your treatment timelines and the findings will be discussed at your next hospital visit with your doctor.

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

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. All patients entering the study will need to have these tests, which need to be within certain ranges or sizes in order to allow patients to enter the study.

These tests are standard routine practice and include:

- Medical history and physical examination.
- A flexible sigmoidoscopy, which is a flexible telescope that the doctor will use to see inside your bowel.
- A biopsy (a procedure where a small piece of tissue is removed from the cancer to look at under a microscope).
- 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 chest, 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 done over 2 weeks ago.

If you agree to take part, we would like you to complete three questionnaires about your quality of life and how you are feeling generally. These questionnaires will be completed at the beginning and at the end of your treatment, then during your follow up appointments at 3, 6, 9, 12 and 24 months from the start of treatment. These questionnaires will take around 20 minutes to complete. The questionnaires will be provided by one of the research team and completed in clinic before you see your doctor.

After you agree to enter the study, you will attend hospital for radiotherapy treatment planning, then at a later date you will start the radiotherapy treatment. Following completion of radiotherapy, you will then be followed-up regularly to monitor your progress, with a variety of checks including further scans, sigmoidoscopies and clinical examinations.

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 will have 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. 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 receive is called Intensity Modulated Radiotherapy (IMRT). IMRT is able to target your tumour more precisely so that your tumour receives a very 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 either through a window or on a closed circuit television screen. The treatment is painless and the machine will rotate around you without touching you over 10-20 minutes. Treatment will occur once each weekday (Mondays to Fridays) over 5.5 weeks (28 weekday treatments in total).

Chemotherapy treatment

This is the use of anti-cancer drugs to destroy cancer cells. Chemotherapy is normally given at the same time as radiotherapy and the combined treatment is called ‘chemoradiotherapy’. In some cases, however, your doctor may recommend that you should receive radiotherapy alone without chemotherapy because they may feel that you may not be able to tolerate the side effects of chemotherapy in addition to your radiotherapy.

If you do receive chemotherapy, this will be one of two types. The choice of which type is most suitable for you will be made by discussion with your doctor. The first type is called Capecitabine. Capecitabine is given by mouth as several tablets (typically 3 or 4 tablets) twice a day on the days when you receive radiotherapy i.e. for 28 days in total. The second type of chemotherapy is called 5-Fluorouracil and leucovorin (5FU/LV), which is given intravenously through a drip over an hour, once per day during the first five radiotherapy treatments, and once per day during the 21st to 25th radiotherapy treatments.

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**

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

If you are taking capecitabine chemotherapy tablets during radiotherapy, we will ask you to complete a diary card to record when each tablet is taken and any missed doses (with reasons). If for any reason you do miss a dose then inform the team looking after you and they will advise you what you should do.

How long does the treatment go on for?

The chemoradiotherapy (or radiotherapy alone) treatment will be given over 5.5 weeks (28 treatments). Occasionally it may go on for slightly longer than this if you experience side effects that mean treatment must be disrupted or delayed.

What is the current standard treatment?

Group 1: The standard treatment for early rectal cancer, for patients who are suitable, is surgery to remove the rectum.

Group 2: The standard treatment for early rectal cancer, for patients who are unsuitable for surgery, is a combination of chemotherapy and radiotherapy ('chemoradiotherapy'). The aim of this treatment is to get rid of the cancer.

What is the new treatment being studied?

The new treatment being studied in the APHRODITE study gives some patients a higher dose of radiotherapy to their cancer over 5.5 weeks. We want to find out whether a higher dose of radiotherapy offers a better chance of getting rid of the cancer, while not causing unacceptable side effects. The higher dose of radiotherapy being tested takes no longer to give each day and is given over the same number of days as the standard dose. The only difference is that the dose given each day is slightly higher than the standard dose. We expect that the higher dose will lead to an increase in side effects during the treatment and afterwards, but may also increase the number of cancers that completely disappear and never return.

What treatment will I receive if I take part?

We need to make sure the group of people receiving the standard radiotherapy dose is as similar as possible to that receiving the higher radiotherapy dose, to make sure that the way each group responds to their treatment is due to the treatment itself rather than some other difference between the groups that we do not know about.

The best way of finding out how effective the new treatment with a higher dose of radiotherapy is, compared to the standard dose of radiotherapy, is in a randomised study.

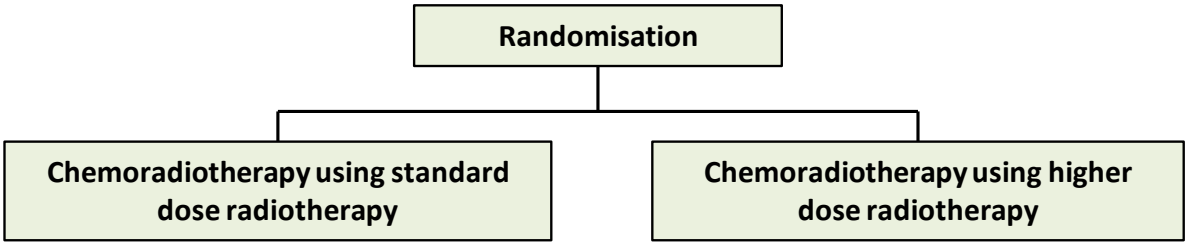
'Randomised' means that a computer will allocate you randomly (as if by the roll of dice) to receive either the standard dose or the higher dose of radiotherapy. Neither your doctor nor you will choose which treatment you receive. In this way, a fair comparison can be made. You will be twice as likely (two thirds) to go in to the higher dose radiotherapy arm than the standard dose radiotherapy arm (one third) and once randomised, you will be told which arm you have been randomised to.

The recommendation of whether to add in chemotherapy on top of your radiotherapy will be made by your doctor and told to you **before** randomisation. This means that patients who are felt to be suitable for chemotherapy in addition to radiotherapy (chemoradiotherapy) will be randomised to receive either chemoradiotherapy using standard dose radiotherapy versus

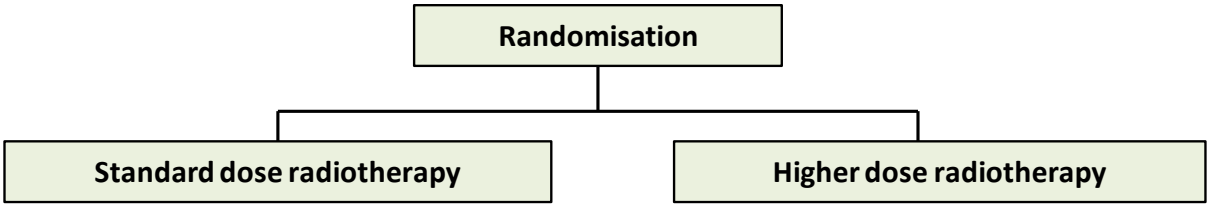
chemoradiotherapy using higher dose radiotherapy. Patients who are felt to be suitable for treatment with radiotherapy alone will be randomised to receive either standard dose radiotherapy alone versus higher dose radiotherapy alone.

This is illustrated below:

Randomisation if patient thought to be suitable for radiotherapy combined with chemotherapy (chemoradiotherapy):

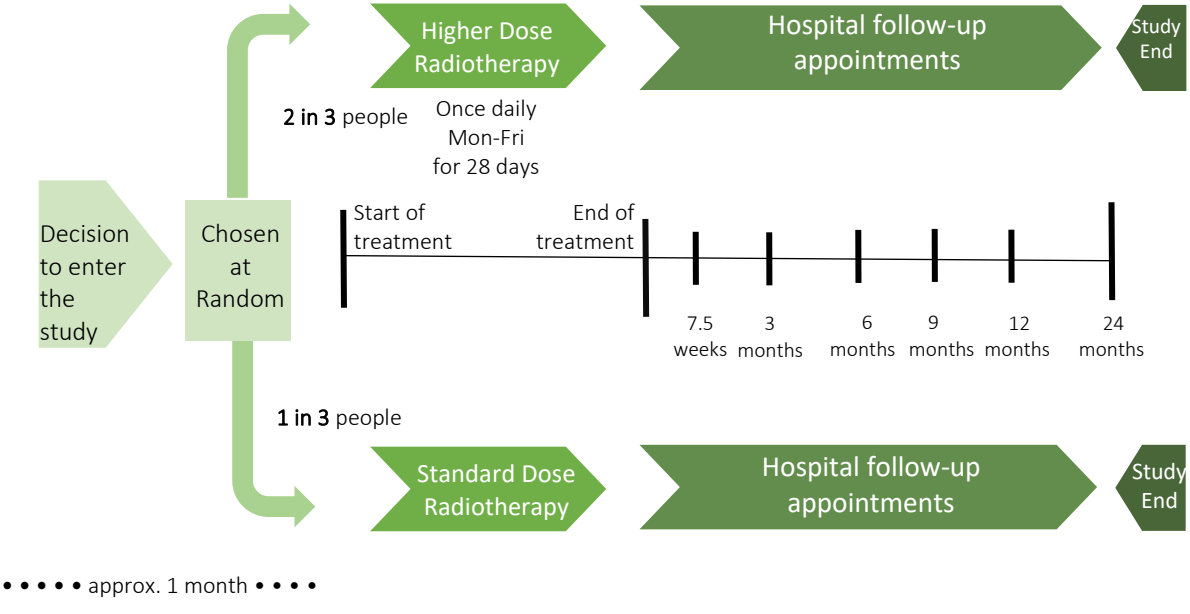


Randomisation if patient thought to be suitable for radiotherapy alone:



Study Schema

Once you have been randomised into either the standard dose radiotherapy arm or the higher dose radiotherapy arm you will follow the treatment schedule below:



• • • • • approx. 1 month • • • •

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.

Unwanted effects of treatment

Male patients will be required to use barrier contraception, such as condoms during chemoradiotherapy 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. Whilst some men will be infertile soon after treatment, many will not. 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 likely 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 clinical verification of non-pregnancy. Therefore, all women of childbearing potential who are at risk of becoming pregnant must undergo a pregnancy test prior to randomisation on the APHRODITE study.

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 IMRT, there is little normal tissue in the treatment area. This means the risk of side effects is lower than non-IMRT techniques, but unfortunately you can still have side effects. As with any external beam radiotherapy, the side effects only affect the part of the body that the radiotherapy treatment is aimed at. Radiotherapy affects people in different ways, so it is difficult to predict exactly how you will react. 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.

You should be aware that the side effects listed below might be worse if you get the higher dose of radiotherapy.

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.

Diarrhoea

During the course of treatment, you may notice changes in how your bowel works. You may experience diarrhoea, mucus or jelly-like 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. Most of the time the diarrhoea can be controlled by tablets, but your team will discuss other options if it becomes very troublesome.

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 clears up 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 difficult and it may sometimes be difficult to control passing urine. If this happens, your medical team will treat any 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 to relieve pain or symptoms.

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. Generally, by around 8-12 weeks, most people feel their energy levels returning, although this can be a longer period for some. 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.

Late side effects of radiotherapy

Side effects can also occur months and years after finishing radiotherapy. Some side effects can still be a problem years after the patient has finished treatment. These are known as late or ‘chronic’ side effects and are listed below.

You should be aware that the late side effects may be increased if you receive the higher dose of radiotherapy.

Bowel problems

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, 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, an urgent need to go to pass a motion, but nothing

comes out, or occasionally patients can lose control of bowel motions completely. These side effects can usually be managed, although you may need to take medication. Your healthcare team will be able to advise you to minimise any bowel effects that you experience.

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 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 put into the vagina twice a week keep the vagina walls open and supple. 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 goes 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. 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 problems

There is a small risk of difficulties passing urine, urgency or bleeding from the renal (kidney) / urinary system after finishing radiotherapy. Please let your doctor know if these are an issue, because both can be treated.

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.

Potential side effects of chemotherapy

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 pick this up and occasionally you may need a drip to give you extra red blood cells (blood transfusion).

Bruising and bleeding
Chemotherapy 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
Chemotherapy 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.

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 or pain on passing urine.

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

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 uncommon with the drugs you will receive in this study.

Sore mouth
Chemotherapy drugs 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
Chemotherapy can cause the palms of your hands and soles of your feet to become sore and inflamed. There is help available so please let your medical team know if this happens to you.

Sore eyes
Chemotherapy 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.

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, heart problems or 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.

What are the different scans that I will have?

CT scan
A CT scan (computerised tomography scan) is a standard test used to create 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.

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 other clinical information. Within this study, you will receive one CT scan, which is carried out before starting treatment to assess whether your cancer has spread to other organs away from the rectum. 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.

How is my condition monitored?

You will be seen weekly throughout your chemoradiotherapy treatment and will be able to call for advice at any time.

Once your treatment is complete, you will then be followed-up with a telephone appointment 2 weeks after the end of your chemoradiotherapy treatment. Following that, your cancer team in the outpatient clinic at 3, 6, 9, 12 and 24 months will then see you from the start of your chemoradiotherapy. Some of these visits will involve MRI scans or sigmoidoscopies (flexible

telescope to see inside your bowel). Your team may choose to have you come back more often for check-ups, if they think it will be best for you.

What are the possible benefits of taking part?

Group 1: By taking part in this study, you will receive radiotherapy or chemoradiation rather than surgery. If your cancer is cured by this treatment then the main benefit is that you may avoid surgery altogether. If you receive the higher dose of radiotherapy, it is possible that this will benefit you still more by reducing the chance of the cancer coming back compared to the standard radiotherapy dose. However, we are not sure of this and the aim of the study is to try to find this out.

Group 2: By taking part in this study, you will receive the best available radiotherapy/chemoradiotherapy treatment for your cancer in the standard radiotherapy dose arm of the study. If you receive the higher dose of radiotherapy, it is possible that this will benefit you by reducing the chance of the cancer coming back compared to the standard radiotherapy dose. However, we are not sure of this and the aim of the study is to try to find this out.

What are the possible disadvantages and risks of taking part?

Group 1: The radiotherapy/chemoradiotherapy may not cure your cancer and you may then need to undergo surgery to remove your rectum and cancer. This would mean that you experience the possible side effects of radiotherapy and chemotherapy (described earlier) but need the surgery anyway. It is possible that side effects following surgery, may be worse in patients who have undergone previous radiotherapy/chemoradiotherapy. There is a risk that short- and long-term radiotherapy side effects may be worse with the higher dose of radiotherapy, and require more treatment. One of the important aims of APHRODITE is to accurately record these potential side effects. Although similar high doses of radiotherapy have been used in other research studies, the long-term side effects that occur years after radiotherapy have not been studied in detail.

Group 2: There is a risk that short- and long-term side effects of radiotherapy (described earlier) may be worse with the higher dose of radiotherapy, and require more treatment. One of the important aims of APHRODITE is to accurately record these potential side effects. Although similar high doses of radiotherapy have been used in other research studies, the long-term side effects that occur years after radiotherapy have not been studied in detail.

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 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 one of the treatments turns out to be much worse than the other, then this will be detected as soon as possible and the study stopped. If you experience problems, you must report these to your study nurse or doctor. Their contact numbers can be found at the end of this information sheet.

What happens when the research study stops?

The study will stop two years after the last patient 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.

Additional research

We will also ask permission to use, your radiotherapy data, MRI and CT images along with your stored tumour biopsy sample, which we would like to analyse, including analysis of the tumour DNA, as part of this future research. This work is aimed at trying to predict which future patients might benefit from higher dose chemoradiation and who might not. This work may involve genetic analysis of your stored tissue. The use of your radiotherapy data, MRI, CT image and tumour biopsies is not compulsory and it is your choice whether to agree to this or not. You may also have been asked to take part in a separate questionnaire study about people's preference for cancer treatment. If you take part in the preference study, we may ask your permission to share the information from this study (APHRODITE) with the researchers in the preference study.

Will my taking part be kept confidential?

If you decide to participate in the APHRODITE 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.

Please refer to Part 2 for further details.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. One way we do this is by following the UK Policy Framework for Health and Social Care Research (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/).

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 APHRODITE study. We will provide the hospital site, where you attend your appointments 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 APHRODITE website where you will be able to review our newsletters, along with and overview of the study via this Website Address

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 www.yorkhsirecancerresearch.or.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 Studys'. 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 Part 2 before making any decision.

PART 2

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 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.

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

You may withdraw from the study at any time. You do not need to provide any reason if you withdraw consent from further study treatment.

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

Need to know: 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've 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 what 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.

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

Yorkshire Cancer Research (YCR), following detailed peer review funds the APHRODITE study. The study is being organised by the University of Leeds, through the Clinical Trials Research Unit (CTRU), who will collect and analyse your data. The University of Leeds also sponsors the study.

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 because 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. You can also contact the University of Leeds, Head of Research Integrity and Governance, Mrs Clare Skinner, Faculty of Medicine and Health Research Office, Level 9, Room 9.29, Worsley Building, Clarendon Way, Leeds, LS2 9NL or by email at governance-ethics@leeds.ac.uk.

Any claims will be subject to UK law and must be brought in the UK.

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.

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.

Will my taking part in this study be kept confidential?

If you decide to participate in the APHRODITE study, the information collected about you will be handled in accordance with the General Data Protection Act and Data Protection Act (DPA 2018). The information needed for study purposes will be collected on paper forms and sent

by fax, email or secure electronic email 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 fax, post, email or secure electronic transfer.

When your Quality of Life data will be kept in a secure filing area at the University of Leeds.

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.

Your data will be entered onto a secure database held at the CTRU in accordance with the 2018 Data Protection Act.

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.

Some of the treatment plans and scans 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, Royal Mail or courier). 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 may look at your healthcare records from the research team, the University of Leeds, or the regulatory authorities 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.

University of Leeds confidentiality

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 15 years after the study has finished.

Your rights to access change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

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 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 link https://dataprotection.leeds.ac.uk/wp-content/uploads/sites/48/2019/02/Research-Privacy-Notice.pdf

If you have any concerns about the way your personal data is being processed or have a query about the information in this document, please contact the University of Leeds Data Protection Officer using any of the following details:

- **Email:** DPO@leeds.ac.uk;
- **General postal address**: University of Leeds, Leeds LS2 9JT, UK;
- **Postal address for data protection issues:** University of Leeds, Room 11.72 EC Stoner Building, Leeds, LS2 9JT;
- **Telephone number:** +44 (0)113 243 1751.

The data controller registration number provided by the Information Commissioner's Office is Z553814X.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (https://ico.org.uk/).

University of Leeds will keep personal information about you from this study for 15 years after the study has finished.

NHS data confidentiality

Your hospital will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from University of Leeds and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your hospital will pass these details to University of Leeds along with the information collected from you. The only people in the University of Leeds who will have access to information that identifies you will be people who need to contact you or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

NHS will keep identifiable information about you from this study for 15 years after the study has finished.

What will happen if I lose mental capacity during the study period?

This is expected to be a very rare occurrence. It could happen to any patient whether or not they take part in this study. If this did occur, no further study treatment would be given and data collection for the study would stop. Data collected up until this point will remain on file and will be included in the study analysis.

Involvement of the General Practitioner/Family Doctor (GP):

Your GP, and the other doctors involved in your healthcare, will be kept informed of your participation in this study.

What will happen to the results of the research study?

When the study is complete, the results will be made openly available to the scientific community and will be published in a medical journal. Your personal information will be protected and kept confidential at all times and no individual participants will be named in any

published material. If you would like to obtain a copy of the published results, please ask your doctor. We will prepare a lay summary, which will be available to patients when submitting the results to a journal.

Who has reviewed the study and who will monitor it?

The NHS Health Research Authority and Research and Development (R&D) department at your hospital. An independent NHS Research Ethics committee has also reviewed and approved the study.

The study is also supervised by two independent committees called the Data Monitoring and Ethics Committee (DMEC) and the Study Steering Committee (TSC). These committees include experienced cancer doctors, statisticians and a patient representative.

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

Participant ID:	Initials:
Date of Birth:	NHS/Hospital Number:
ISRCTN: 161585514	Principal Investigator:

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 and give permission for my MRI scans to be sent to the trial team radiologists after registration in real-time to confirm eligibility. ☐

4. 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. ☐

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

6. 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. ☐

7. I will allow any information or results arising from this study to be shared anonymously with researchers at the University of Leeds conducting the study “How do patients make decisions about rectal cancer treatment?” I understand that my identity will remain anonymous. ☐

8. 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. ☐

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

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

The following points are OPTIONAL.

	Please initial each box	
	Yes	No
I give permission for surplus samples from my cancer biopsy that have been stored in the hospital pathology laboratory to be retrieved and used in the future for colorectal cancer research, including genetic research.	☐	☐
	Yes	No
I understand that my 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 outside the European Economic Area.	☐	☐
	Yes	No
I give permission that my endoscopy photos, radiotherapy data, CT and MRI scans may be used in future research. I understand that my radiotherapy data scans may be shared on a collaborative basis with researchers in the UK and potentially, centres, abroad, including outside the European Economic Area.	☐	☐

Patient:

Signature……

Name(block capitals)……

Date……

Investigator:

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

Signature……

Name(block capitals)……

Date……

(If used) Witness:

Signature……

Name(block capitals)……

Date……

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