(Form to be on hospital headed paper)

THIS STUDY HAS BEEN REVIEWED AND APPROVED BY A RECOGNISED RESEARCH ETHICS COMMITTEE

INFORMATION SHEET FOR PARTICIPANTS IN CLINICAL RESEARCH PROJECT

Title of Project: BARitOne: Biologically Adaptive Radiotherapy for Oropharyngeal Cancer

IRAS ID: 318567

Introduction

We would like to invite you to take part in our research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives, and your GP if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part.

Why have I been invited to take part?

You have been invited to take part because you have recently been diagnosed with a cancer of the back of the throat – this is called oropharyngeal cancer. Treatment for this cancer is radiotherapy over a course of 6 weeks (30 doses). You have been identified as being suitable to take part in this study.

Do I have to take part?

No, taking part in the study is voluntary. It is up to you to decide whether to take part or not after reading this information.

If you *do* decide to take part, you should keep this information sheet and sign the consent form when asked. You are still free to withdraw at any time without giving a reason. This will not affect the quality of care you receive.

If you decide ***not*** to take part, you will be offered the treatment your consultant thinks is best for you. Deciding not to take part in the study will not affect the quality of your treatment in any way.

Part 1 – What's involved: Tells you the purpose of this study and what will happen to you if you take part.

Part 2 – Supporting / further information: Gives you more detailed information about the study.

PART 1 – WHAT'S INVOLVED

What is the purpose of the study?

Six weeks of treatment with radiotherapy for cancer of the throat - oropharyngeal cancer, is carried out with the aim of long-term cancer control or cure. Unfortunately, we know that not all cancers are cured, and some cancers come back (known as recurrence) after finishing radiotherapy. If oropharyngeal cancer comes back, it usually recurs in the same place it was at diagnosis. Giving a higher dose of radiotherapy to this area might help keep the cancer under control for longer. However, increasing the dose of radiotherapy for all patients is not required. We therefore need to be able to identify the patients who will benefit from increasing the dose, which is why you are being asked to participate in this study.

Our previous research showed that a special type of scan, a diffusion weighted (DW) MRI scan, carried out before and during treatment can tell us which patients are most likely to have recurrence. MRI scanners use strong magnetic fields and radio waves to form pictures of the body. DW MRI looks at the movement of water within tissues and can identify when the radiotherapy is not working well enough by changes in this water movement.
This study will use these scans to identify which patients are at risk of their cancer coming back after radiotherapy treatment. We will use this information to decide whether to increase the dose of radiotherapy given to the cancer for the second half of treatment.

A DW MRI scan will be done before the start of radiotherapy, and repeated after 2 weeks of treatment. These scans will be analysed by the specialist team:

- If the MRI scans show that the cancer is not responding to the usual radiotherapy dose, a higher dose of radiotherapy will be given for the second half of treatment.
- If the scans show that the cancer is responding well to radiotherapy, standard treatment will continue, and the standard dose of radiotherapy will be delivered.

The scans allow patients who are at the highest risk of recurrence after treatment to be identified, so we can intensify treatment only for those who really need it. Identifying cancers in patients where the radiotherapy is not working well enough during treatment and changing the radiotherapy plan may lead to better treatment in the long term. One aim of this study is to see how practical the extra steps involved in changing the treatment plan are and work out the best way of doing this.

The study will also allow us to gather information from participants about side effects and the impact on patients' quality of life during and after treatment – an important way for us to make sure that increasing the dose of radiotherapy is acceptable.

We would also like to take some extra blood and saliva samples (before, during and after radiotherapy) from participants. The scientists in our research team will analyse these samples to look for new ways of detecting cancer and monitoring response to treatment, to try to understand why some cancers aren't controlled with radiotherapy.
An optional, additional biopsy from the primary tumour taken during radiotherapy may also help scientists work out why some tumours are cured with radiotherapy and others aren't.

The research will last for up to 2 years from when you finish radiotherapy. It will begin just before your treatment starts; continue during your 6 weeks of radiotherapy and for up to 2 years of follow up.

Please see the diagram on the final page of this information for a summary of how the study will work.

How are treatment options decided?
If you decide to enter the study, you will start treatment with the standard radiotherapy dose. If the MRI scan after 2 weeks of treatment shows that cancer is not responding, you will then receive the higher dose. The higher dose of radiotherapy will be given for the final 3 weeks of treatment. This will be decided by the specialist research team who will analyse the scans.

Treatment 1: standard dose of radiotherapy for 6 weeks
Treatment 2: standard dose of RT for 1st 3 weeks, then higher dose of radiotherapy for final 3 weeks

Blinded Study
This study is single blinded; this means you will not know which treatment you are receiving in the last 3 weeks of radiotherapy. Although the study team will know this information, you will not be told what the scans show (i.e. is radiotherapy working well enough or not) and you will not know if you receive the usual or higher treatment dose of radiotherapy in the final 3 weeks. This allows a fair comparison of both treatments, and at the end of the study we will be able to tell reliably if there are any true differences between the treatments. While we understand that you might be keen to know what the scans show, the reliability of these scans in deciding treatment is one of the things being tested and so it would be too early to give you this information during the study.

You will be informed which treatment you have received at the end of your participation, once your follow up is complete.

What will happen to me if I take part?
If you decide to take part in this study, a member of the study team will meet you at your next appointment. You will be asked to sign the consent form (attached to this document) and given a copy to keep.

Before you take part in the study, your study doctor/nurse/radiographer will examine you and ask about your medical history. The following standard tests will we be able to confirm whether you can take part in the study.

- ☐ Biopsy of tumour
- ☐ Testing of tumour for p16 and/or HPV status
- ☐ CT scan of head, neck, and chest

What elements of the study are additional to the standard treatment?
MRI scans:
The two DW-MRI scans are additional but essential to the study. The MRI scans are done in the radiotherapy department at the Beatson West of Scotland Cancer Centre. The first scan is on the same day as your radiotherapy treatment begins and the second scan is during the 3rd week of treatment.

Before each MRI you will be asked a list of safety questions by the radiographers. The MRI scans are painless, but they are noisy and some people do not like the feeling of being enclosed. To help with this you will have the option of taking a mild sedative or undergoing relaxation sessions to help manage the experience. You can stop the scan at any time by pressing a 'buzzer'. The MRI scan takes approximately 30 minutes. You will also be given an intravenous (into the vein) injection of a dye. This helps show up the cancer on the MRI scan. You will be asked to stay as still as possible while the scans are being done, but you can breathe normally. There is nothing you need to do either before or after the MRI scan in terms of diet or preparation. In the third week of your radiotherapy treatment, we will again ask you to attend for an MRI scan. The process will be the same as the scan before radiotherapy.

Increased dose of radiotherapy:
If the scans suggest that the cancer is responding to standard treatment, then this treatment will continue for the final 3 weeks (15 days) of treatment.
If the MRI scans suggest the cancer if not responding to the standard radiotherapy treatment, your treatment plan will be changed to deliver an increased dose of radiotherapy to the tumour each day for the final 3 weeks (15 days) of treatment. This will be given in the same way as your first 15 treatments. You will not notice a difference in your treatment being given. Your radiotherapy treatment will still be completed on the same date as planned as the number of doses does not change.

Questionnaires:
You will be asked to complete questionnaires about physical and emotional symptoms at different intervals (before treatment starts, when your treatment has finished, and then at 3, and 6 months after the end of treatment). This is an important way for us to make sure that increasing the dose of radiotherapy is safe, however this can take extra time during hospital visits. The research team will also record your progress in your hospital notes during routine clinic visits.

Blood and saliva samples:
Blood tests (approximately 40mls, equal to eight teaspoons) and saliva sample (a single spit into a sterile container with around 2 mL (half a teaspoonful) saliva anticipated)**:**

- ☐ **Before treatment starts**
- ☐ **Weekly during treatment**
- ☐ **Week 4 after treatment**
- ☐ **Months 3 and 6 after treatment**

Tumour tissue samples (biopsies):
You will be asked if we can keep any pieces of tissue or cancer which we may have removed surgically that are no longer needed.

These samples will be used for future studies, which may include genetic tests, to investigate improved ways of diagnosing cancer and to investigate ways that cancers develop.

Research biopsy:
Provided you agree, an additional research biopsy (tissue sample) will be carried out during radiotherapy. This will be done under local anaesthesia (an injection into the area to numb it). It is important that you tell the doctor which tablets you take before you have the biopsy, in particular any tablets that thin the blood. The first step is to numb the area for the biopsy by injection, which takes about 5 minutes to work. This means that the biopsy will be painless. Sometimes after the biopsy the area can be cauterised to stop bleeding. The whole process (local anaesthetic injection, biopsy and cautery) usually takes around 15 minutes from start to finish. When the local anaesthetic wears off after a few hours, there usually is relatively little in the way of pain or swelling. Occasionally it is necessary to take simple painkillers like paracetamol or ibuprofen. Usually, any discomfort only lasts a few days. The effects of the biopsy will be closely monitored by the research team.

You can still take part in the study even if you do not want us to take your blood, saliva, and tissue samples.

What elements of standard care may I not receive if I agree to take part in this study?
You will receive all standard care if you take part in the study or not. Radiotherapy is the standard treatment for your type of cancer. You will still receive this if you do not wish to take part in the study. If you do take part in the study you may receive a higher dose of radiotherapy for the second 3 weeks of treatment. Everything about the rest of your treatment is unchanged.

What will be the side effects of any treatment I receive in this study?
Radiotherapy treatment can cause side effects because of the healthy tissue around the cancer being exposed to some of the radiation. This means that radiotherapy to an oropharyngeal cancer can cause side effects on the surrounding organs such as the lining of the mouth and throat, and the salivary glands.

We have listed the side effects of all the areas of treatment and tests you may receive whilst taking part in the study; these apply to both the research treatment (higher dose radiotherapy for second 3 weeks of treatment) and standard treatment (which you would receive whether you too part in this study or not). The side effects may be more severe with the research (higher dose) treatment.

Side effects associated with radiotherapy treatment:

Tiredness. Most patients feel extremely tired after radiotherapy and plenty of rest is recommended. Tiredness can continue long-term.
Skin soreness. The area where radiotherapy is given (face and neck) may become red and sore after during treatment (like sunburn). The team can prescribe creams to manage this.
Skin fibrosis: In the long term your skin can become thicker and darker.
Dry mouth: Your saliva can become thick and sticky. In the long term you may need to rinse your mouth frequently with water or use artificial saliva.
Oral mucositis: This is an inflammation of the lining of your mouth causing sores, pain and possible infections that are usually treated with pain killers and antibiotics. Mouth washes will be prescribed to help with these symptoms.
Poor appetite and weight loss: It is important that you do not lose significant amounts of weight). Eating 'little and often' is recommend. It is very likely you will be referred to a dietician for nutritional advice.
Swallowing problems: Your swallowing can become difficult. Most patients will need to change their diet (for example soft food only). During treatment or within 3 months after the end of treatment you may need a temporary feeding tube through your nose or your stomach. The need of the feeding tube in the long term is quite rare (less than 10% of patients).

Alteration of your taste: Your taste will change. Most patients describe their food tasting "metallic" or "like cardboard". In the long term, most patients report minimal taste changes or complete recovery.
Osteradionecrosis of the mandible: your jawbone can be affected by radiotherapy (this happens in less than 10% of patients). You may develop pain, infections or tooth loss. There is no specific treatment for this condition. Some patients can benefit from pain killers and vitamins. In rare cases surgical treatment is required.

We cannot predict whether you will have some, all, or none of the side effects, or how severe they will be. Modern radiotherapy techniques allow us to reduce harm to the surrounding healthy organs, while delivering the high doses of radiotherapy to the tumour.

Possible side effects associated with study tests:

Blood sample collection: This may cause small amount of bleeding and temporary discomfort or you may feel faint. If this happens please tell the person taking the blood so that they can make sure you lie down until you are feeling better. Sometimes a bruise or redness develops at the site where the needle was inserted (but this will clear after a week or two). Please inform your study doctor or research nurse if you experience any reactions at the injection site.

DW-Magnetic Resonance Imaging scan: Prior to a Magnetic Resonance Imaging scan, a dye will be injected into one of your veins using a small needle or plastic tube. You may feel local warmth or pain in the area where the dye is injected. Side effects from the dye may include nausea, vomiting or headache. Allergic reactions are rare.

Research Biopsy: This may cause pain, bleeding and bruising at the site of the biopsy. The biopsy can also cause a sore throat or infection at the biopsy site.

You will be monitored closely for these and any other side effects. You will have regular appointments with the study doctor, nurse, or radiographer. You will also have a telephone number to contact the research staff if you are concerned about possible side effects.
Where possible, other treatments may be given to you to make side effects less serious or uncomfortable. Many side effects go away after the study treatment is reduced or stopped but in some cases side effects can be serious, long lasting, or permanent (even with standard treatment).

Although we are able to target the radiotherapy accurately to the tumour we know that side effects still occur as the healthy tissue around the cancer is exposed to some radiation. The chances of more serious side effects may be slightly higher with the increased dose of

radiotherapy than the standard dose. Experts designing this study and reviewing the study independently think that this is very unlikely.

What are the possible benefits of taking part?
There may or may not be direct medical benefits to you from taking part in this study. A potential benefit may be a higher chance of your cancer being kept under control or cured. Some patients benefit from the increased support during monitoring during studies from the regular contact with the study team.

What are the alternative treatments?
It is up to you whether you wish to take part in this study. If you would prefer not to take part, your doctor will explain the standard treatment that is available to you.

PART 2 – SUPPORTING / FURTHER INFORMATION

What if new information becomes available?
Sometimes during a study, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your study doctor will arrange for your care to continue. If you decide to continue you may be asked to sign an updated consent form.

Also, on receiving new information your study doctor might consider it to be in your best interests to withdraw you from the study. If this happens, they will explain the reasons and arrange for your care to continue.

Stopping the study
You can choose to come off the study at any time without needing to give a reason. Your study doctor may also decide to take you off the study if it is no longer appropriate for you.

What if something goes wrong?
If you have a concern about any aspect of this study, you should ask to speak with the study doctor, radiographer or nurse who will do their best to answer your questions.
In the event that something does go wrong, and you are harmed during the research and this is due to someone's negligence, then you may have grounds for a legal action for compensation but you may have to pay your legal costs. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during this study, the normal National Health Service complaints mechanism will still be available to you. If you do have a complaint, then please contact *(Insert local complaint department details here including contact name, number and address prior to printing patient information sheet on local headed paper).*

If you have insurance cover such as travel, life, critical illness, or income protection, you may wish to check with your company before agreeing to take part in this study to ensure that participation in the study will not affect your insurance cover.

Will my taking part in the study be kept confidential?
You can be assured that any data collected during this study and any of the results published will not identify you personally. Your medical records will only be available to the study doctors, your hospital consultant, responsible individuals from the Cancer Research UK Clinical Trials Unit (CTU), Glasgow, the study Sponsor(s), and the regulatory authorities. The purpose of this would be to check that the study is being carried out correctly.

We will inform your general practitioner (GP) of your participation in this study. The information that will be exchanged includes details of your diagnosis, an overview of the study and the treatment you will receive, the expected side effects, prohibited medication and any update on your progress. Contact details will be given to your GP if he/she has any questions or concerns about the study or if he/she has any concerns if you were to become unwell.

The CRUK CTU (Glasgow), which is co-ordinating the study, will collect your initials, date of birth and Community Health Index (CHI) number at the time you are registered on to the study. This information will be stored securely and will be kept strictly confidential, with access provided only to authorised personnel.

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

What will happen to any samples I give?
The blood and saliva samples we collect will be sent to the lab at the Beatson Institute for Cancer Research.

You will also be asked to consent for the research team to collect stored cancer tissue that was removed at the time of your biopsy or operation and was not needed for your routine diagnosis or treatment. The tissue sample will be sent to research laboratories. The additional research biopsy will be sent to the lab at the Beatson Institute for Cancer Research.

They could be used for other ethically approved and relevant investigations conducted by qualified researchers in academic or commercial organisations (in the UK, or worldwide). These studies may include analysis of genetic material from the tumour (DNA).

What will happen to the results of the study?
The results of this study will be presented at scientific and medical conferences and published in a medical journal. However, patients will not be personally identified in any reports or publications produced from this study. If you would like to obtain a copy of the published results, please check the Cancer Research UK website or ask your study team.

Who is organising and funding this research?
The study is being sponsored by NHS Greater Glasgow and Clyde and coordinated by the Cancer Research UK Clinical Trials Unit (Glasgow), which is based at the Beatson West of Scotland Cancer Centre in Glasgow. Financial support will be provided by the Beatson Cancer Charity.

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

How have patients and public been involved in this study?
The study proposal and patient information sheet for this study was presented to patient representatives who are part of the Cancer Research UK RadNet Glasgow patient and public involvement group. A patient representative from the group is a member of the research management team and also reviews patient documentation.

Who has reviewed this study?
This study has been reviewed by several head and neck cancer and radiotherapy specialists during its development. All research in the NHS is also looked at by an independent group of people, called a Research Ethics Committee. West of Scotland Research Ethics Service have reviewed and approved this study to confirm that this study considered the 'rights and protection of patients' health. In addition, the study has been reviewed by the Research and Development Department of NHS Greater Glasgow and Clyde.

Contact for further information
If you have further questions about your illness or about clinical studies, please discuss them with your doctor.
If you would like independent advice or further information you may also find it useful to contact:

Macmillan Cancer Support, an independent patient advisory group (freephone 0808 808 0000); website http://www.macmillan.org.uk, Head Office Address: Macmillan Cancer Support, 89 Albert Embankment, London, SE1 7UQ

Cancer Research UK provide a wide range of information for people with cancer: Freephone: 0808 800 4040, and website: About Cancer | Cancer Research UK

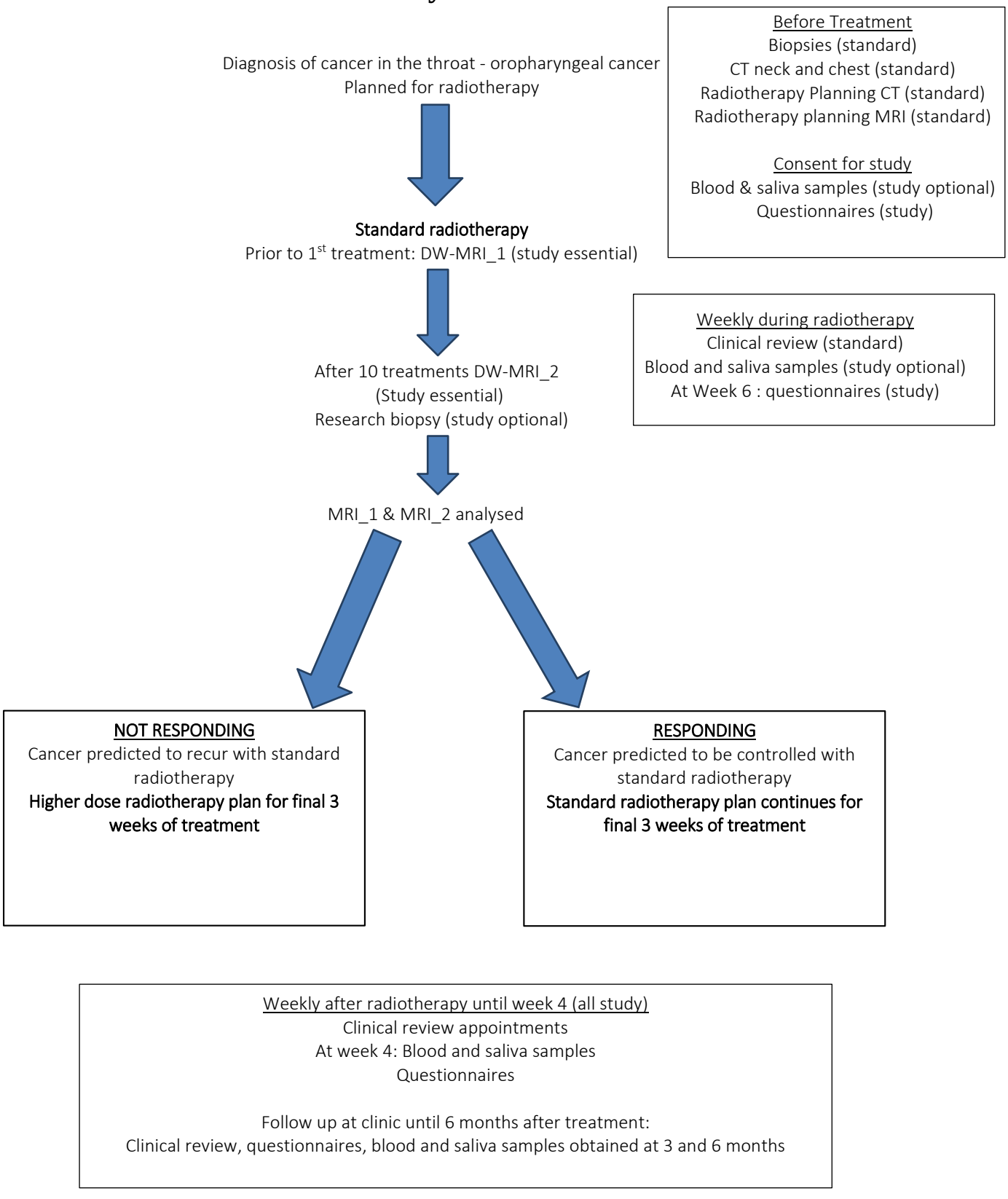
If during the course of the study you have any questions regarding your participation or would like further study specific information before making your decision please contact:

Doctor:	
Name	Dr *Claire Paterson*
Telephone Number	*0141-301-7066*
Research Radiographer:	
Name	*Lisa Hay*
Telephone Number	*0141-301-9901*
Email	Lisa.Hay@ggc.scot.nhs.uk

24-Hour / out of hours contact:
The National Cancer treatment Helpline (CTH)
(**For patients on or 6 weeks post treatment 8pm-8am):** 0800-917-7711
If you find the wording difficult to understand or would like us to explain things to you once more, please feel free to ask your doctor, radiographer or nurse.

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

Study Flow


Before Treatment
Biopsies (standard)
CT neck and chest (standard)
Radiotherapy Planning CT (standard)
Radiotherapy planning MRI (standard)
Consent for study
Blood & saliva samples (study optional)
Questionnaires (study)
Diagnosis of cancer in the throat - oropharyngeal cancer
Planned for radiotherapy
Standard radiotherapy
Prior to 1st treatment: DW-MRI_1 (study essential)
Weekly during radiotherapy
Clinical review (standard)
Blood and saliva samples (study optional)
At Week 6 : questionnaires (study)
After 10 treatments DW-MRI_2
(Study essential)
Research biopsy (study optional)
MRI_1 & MRI_2 analysed
NOT RESPONDING
Cancer predicted to recur with standard radiotherapy
Higher dose radiotherapy plan for final 3 weeks of treatment
RESPONDING
Cancer predicted to be controlled with standard radiotherapy
Standard radiotherapy plan continues for final 3 weeks of treatment
Weekly after radiotherapy until week 4 (all study)
Clinical review appointments
At week 4: Blood and saliva samples
Questionnaires
Follow up at clinic until 6 months after treatment:
Clinical review, questionnaires, blood and saliva samples obtained at 3 and 6 months

CONSENT FORM FOR PATIENTS/ VOLUNTEERS IN CLINICAL RESEARCH PROJECT

(Form to be on hospital headed paper)

Patient Identification Number for this study:
(to be obtained at registration)

Title of Project:

BARitOne: Biologically Adaptive Radiotherapy for Oropharyngeal Cancer
IRAS ID: 318567

		Please initial box
1.	I confirm that I have read and understand the patient information sheet Version X, date XXXX for the above study, that I fully understand what is involved in taking part in this study, and that I have had the opportunity to ask questions.	☐
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3.	I agree that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from the Cancer Research UK Glasgow Clinical Trials Unit, the study Sponsors, the regulatory authorities and the NHS organisation where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
4.	I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers.	☐
5.	I give my permission for a letter and information regarding my participation in this study to be sent to my GP.	☐
6.	I agree to take part in the above study.	☐
7.	I give my permission for samples from stored tumour tissue that was removed during my operation/biopsy and was not needed for routine diagnosis and treatment to be collected and used for future research purposes as described in the information sheet for the above	☐

study. I understand that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected.

10. I give my permission to have two DW-MRI scans as part of this study ☐

Optional consents:

(If you do not wish to give this permission, do not initial the box - you can still participate in the study).

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

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

13. I give my permission to have an additional research biopsy for future research purposes as described in the information sheet for the above study. I understand how the tissue sample will be collected, the possible side effects, that giving samples is voluntary and that I'm free to withdraw my approval for use of the samples at any time without giving a reason and without my medical care or legal rights being affected. ☐

Please sign and date below:

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

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