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*To be printed on local hospital headed paper*



**Participant Information Sheet**

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| **Study Title:** **AURORA: Atezolizumab in patients with urinary tract squamous cell carcinoma: a single arm, open label, multicentre, phase II clinical trial****Researcher: Dr Simon Crabb****Sponsor Reference: RHM CAN 1665 IRAS: 1004493 REC: 22/LO/0272** |

**You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear or you would like more information before you decide whether to take part in this research. You may like to discuss it with others, but it is up to you to decide whether or not to take part. If you are happy to participate you will be asked to sign a consent form.**

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| **Contents**Part A – pages 2 to 6 - describes the purpose of this study and what will happen to you if you take part.Part B – pages 7 to 10 - gives detailed information about the conduct of the study and important contact details. |  | **How to contact us**If you have any questions about this trial or would like to discuss it further, please contact:[local investigator name][contact details] |

**Do I have to take part?** No. It is entirely up to you if you take part in the trial or not. If you choose not to take part, the care you get from your own doctors will not be affected in any way.

**If I start the trial, can I stop if I want to?** Yes. If you choose to take part in the trial, you are free to stop treatment at any point without giving a reason – the standard of your care will not be affected.

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| **Important things you need to know*** The AURORA trial is open to patients with urinary tract squamous cell carcinoma.
* The aim of this trial is to determine the activity and safety of the immunotherapy drug Atezolizumab
* The response rate of the medication on the tumour (how much the tumour shrinks) will be measured.
* You will need to sign a consent form before taking part in the trial to confirm that you understand it and agree to take part.
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**Part A: The reasons for this study and what is involved**

**What is the research about?**

Patients with urinary tract squamous cell carcinoma (UTSCC) cannot be cured with current treatments and do not have good survival outcomes compared to other cancers. We are investigating whether Atezolizumab, an immunotherapy drug that is not currently licensed in Europe for UTSCC cancer (but is licensed and used in other cancers) will allow patients with UTSCC to improve their survival rates. The trial is being sponsored by the University Hospital Southampton NHS Foundation Trust.

**Why have I been asked to participate?**

You have been invited to take part because you have been diagnosed with urinary tract squamous cell carcinoma (UTSCC). Your medical team feel that this trial may be of interest to you.

Atezolizumab is currently an experimental treatment for your cancer (SCC). This is because it has never been tested specifically in this uncommon cancer type before. However, we have some preliminary biological data from urinary tract SCC patient tumour samples that suggests that they might be expected to respond to immunotherapy treatment. We know, from the use of atezolizumab to treat other cancers including more common types of urinary tract cancer, that it is generally more tolerable and with fewer side-effects than chemotherapy. The trial is aiming to recruit a maximum of 36 patients in total.

**Alternative Treatments**

You do not have to take part in this study in order to receive treatment/care. Other options (in addition to the standard or usual treatment described above) may include, but are not limited to:

* No therapy at this time.
* Other experimental studies may be available if you do not take part in this study.

Please talk to your study doctor or usual cancer doctor about the known benefits and risks of these other options before you decide to take part in this study. Your usual cancer doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

**How will my treatment be decided?**

Everyone who agrees and is suitable will receive the same treatment if they stay on the trial.

If you decide to take part in the AURORA trial, you will be treated with atezolizumab. You will be treated with a dose of atezolizumab by intravenous (IV) drip once every 4 weeks (28 days is called a “cycle”). Treatment will be for up to a year, as long as you don’t have excessive side effects with atezolizumab or the other study procedures and there is no sign of the cancer having progressed. You will receive a maximum of 13 cycles of atezolizumab treatment.

You will be reviewed every 28 days before each treatment to establish if there have been any side effects. You may be given different medication, or have pauses in treatment, to help if these occur. At the end of treatment, the study doctor will ask you to return to the clinic for a post-treatment follow-up assessment within 30 days after the last dose of treatment. You will have clinic visits every 12 weeks during the trial, including scans, to check the status of your cancer. These will continue beyond the end of trial treatment until either the cancer has shown signs of progression or the last participant recruited into the trial has been followed up for 12 months. At that point your care will return to standard treatment options under the care of your usual oncologist. We would continue to monitor your survival status.

**What will happen to me if I take part?**

Following consent, you will undergo screening tests to ensure that this trial is right for you. Once screened eligible you will start the Atezolizumab. Atezolizumab will be administered by intravenous (IV) drip (in a vein) once every 4 weeks – this will take less than an hour and you will not need to stay in the hospital overnight. During treatment with Atezolizumab, you will have monthly blood tests and a clinic visit. This is to monitor your health and have a physical examination. If your disease worsens whilst on Atezolizumab you will stop this treatment. Your doctor will discuss the treatment options available to you. We will continue to monitor you via a process called follow-up.

Every 12 weeks, you will have CT scans (computerised tomography scan) to monitor the effect of the treatment. These are the same type of scans you would have normally to monitor your health. Only one scan is additional to the standard of care treatment offered. Should your disease worsen, you will move into the follow-up phase of the trial to be monitored for overall survival.

We will ask you to give your consent for up to 3 additional blood samples: one at the start of the trial and the others during the treatment.

A list of activities to be completed at these visits can be found at the end of this document for reference.

**COVID and Immunotherapy**

It is the doctor’s decision on whether to administer COVID-19 vaccines based on the risk of COVID-19 infection/complications and potential benefit from vaccination, general condition of the patient and the severity of COVID-19 outbreak in a given area or region and in accordance with the vaccine label. This will be discussed with you by your doctor on a patient by patient basis. If you have any questions or concerns, please ask your doctor.

**Expenses and Payment**

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

**What are the possible benefits, risks, and disadvantages of taking part?**

* You may benefit from a longer period of disease remission by having the Atezolizumab. However, this cannot be guaranteed and there may be no additional benefit for you in relation to how long your cancer is controlled.
* The information that we get from this study may help us to treat future patients with the same condition in a more effective way.
* The inconvenience, side effects and impact on quality of life is similar to that of any course of chemotherapy and immunotherapy.
* You will be helping to further our knowledge of how to treat cancer and this will also benefit society as a whole.

Radiation Risks

* During the trial, you will have contrast CT scans to assess your cancer. These tests use radiation, which has a limited increase to your risk of cancer in the future. These tests are part of standard care but you will receive one additional scan by taking part in the trial.

**Risk Explanations:**

If you take part in this study you will have 13 CT scans of your chest+abdomen+pelvis. One of these will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your tumour and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. This chances of this happening to you as a consequence of taking part in this study are extremely low.

**What are the side effects of the treatments?**

Treatments for cancer often have side effects, including some that are life-threatening. There may be additional unknown risks.

If you have any side effects linked with the study drug, your doctor may give you medications to treat the side effect(s), future treatments may be delayed, or treatment may be stopped permanently. Any important findings that develop during the research period that may impact your desire to take part in the trial will be given to you.

**Very common (may affect 1 in 10 people):**

* Physical weakness or lack of energy
* Cough
* Diarrhoea
* Nausea
* Decreased appetite
* Asthenia (lack of energy and strength)
* Itchy skin (pruritus)
* Vomiting
* Back pain
* Shortness of breath (dyspnoea)
* Fever
* Rash
* Headache
* Joint pain (arthralgia)
* Urinary tract infection

**Common (may affect 1 in 100 to 1 in 10):**

* Low platelet count (thrombocytopenia)
* Infusion related reaction
* Abnormal thyroid function (underactive thyroid or overactive thyroid)
* Low potassium levels or low sodium levels
* Increased liver enzymes in the blood (may indicate liver inflammation)
* Impaired kidney function or kidney disease (blood creatinine increased)
* High blood sugar (hyperglycaemia)
* Low blood pressure
* Stuffy nose (nasal congestion) or cold like symptoms or chills
* Dry skin
* Difficulty swallowing
* Sore throat (oropharyngeal pain)
* Abdominal pain
* Inflammation of colon
* Low oxygen in your blood (hypoxia)
* Inflammation of the lungs (pneumonitis)
* Chest discomfort or chest pain

**Uncommon (may affect less than 1 in 1000 to 1 in 1,00):**

* Diabetes mellitus
* Inflammation of the pancreas (pancreatitis) or inflammation of the kidneys (nephritis)
* Numbness, muscle weakness, pain (Guillain-Barré syndrome)
* Muscle inflammation (myositis)
* Decreased ability of your glands to produce hormones (adrenal insufficiency)
* Inflammation of the brain tissue (meningoencephalitis)
* Red, crusty patches of skin (psoriasis)
* Allergic reactions to treatment drug

**Rare (may affect 1 in 10,000 to 1 in 1,000):**

* Inflammation of the pituitary gland (hypophysitis)
* Muscle weakness (myasthenic syndrome)
* Inflammation of the middle eye (uveitis)
* Inflammation of the heart muscle (myocarditis)
* Blistering of skin or skin rashes (pemphigoid)

**Contraception and pregnancy during the trial.**

Women

If you are pregnant or breast feeding, you will not be able to enter the AURORA trial. Women who can bear children must agree to use two forms of highly effective contraception –during the study and for 6 months after the last dose of trial drug and will need to have a negative serum pregnancy test at screening and negative urine test prior to starting each treatment cycle.

* Female patients must agree to use two highly effective forms of contraception for example; combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable), intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion, vasectomised partner, sexual abstinence effective from the first administration of all study drugs, throughout the trial and for six months afterwards are considered eligible. .

Please be aware that if you become pregnant during the trial, you will not be able to continue taking the trial treatment but follow-up will continue. Additional consent will be sought to follow-up the pregnant participant/pregnant partner until the birth of the baby. Highly effective contraception options will be discussed with you by your study doctor.

You must refrain from any egg donation from the start of your trial treatment, throughout the trial and for 6 months after finishing treatment.

Men

If your partner is pregnant or breast-feeding, we advise you to use barrier method contraception to make sure that the baby is not exposed to the trial drug. If you have a partner of childbearing potential, you must agree to use two forms of highly effective contraception from the start of your trial treatment, throughout the trial and for 6 months after finishing treatment.

Male patients with partners of child-bearing potential who agree to take measures not to father children by using one form of highly effective contraception for example; combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable), intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion, vasectomised partner, sexual abstinence effective from the first administration of all study drugs, throughout the trial and for six months afterwards are considered eligible..

You must refrain from any sperm donation from the start of your trial treatment, throughout the trial and for 6 months after finishing treatment. Highly effective contraception options will be discussed with you by your study doctor.

**Future fertility** – immunotherapy can affect your ability to have children in the future so, you may wish to discuss this, and the possibility of storing eggs/sperm, with your doctor.

**What data will be collected?**

We will be using information from you and your medical records in order to undertake this study. Research staff at your treating hospital will enter the data relating to your disease and the trial treatment onto an electronic database. The data will be identified by your unique trial ID number only. The University Hospital Southampton (UHS) and Southampton Clinical Trials Unit (SCTU) are responsible for looking after your information and using it properly. They will keep your non-identifiable research data for 25 years after the study has finished.

Non-identifiable data will be collected using an electronic system. This software is hosted on secure servers in the UK, EU, and USA. Access to this data will be strictly controlled by the SCTU and no third parties will be granted access to the servers holding your research data. All applicable Data Protection legislation will be obeyed by UHS and SCTU.

Data held from your trial visits are stored in a secure database called an eCRF (electronic Case Report Form). The data is entered by the research team at your hospital. The data is also pseudo-anonymised in order to protect your identity; this means the data will undergo a de-identification procedure where your personal identifiable data (e.g. name, full date of birth) are replaced with one or more artificial identifiers. Therefore, you will be referred to solely as this unique reference number for the duration of the trial.

However, a few other identifiers, including month and year of birth and initials, are collected in the eCRF for the following reasons:

* Your month and year of birth – required to calculate age at consent to make sure patients are eligible to participate in the study. Day of birth is omitted to minimise the personal data being collected and reduce identification.
* Your initials are collected to help trial monitors and your local hospital research team check their records to ensure research is being conducted properly and that the correct data is being collected and stored for each consented individual. This is particularly helpful when reconciling data from multiple sources: paper case report form components and eCRF components.

**What will happen to the samples I give?**

At the start of the trial, a pre-existing section of your tumour (called an archival tumour sample) will be sent for analysis at the Southampton WISH Lab for storage and analysed at the Southampton Experimental Cancer Medicine Centre (ECMC), hosted within the Wessex Investigational Sciences Hub Laboratory. Should there be any tumour remaining at the end of the analysis, these can be returned to the original hospital which supplied the tumour initially. You will not need to have a biopsy as part of the AURORA trial treatment. The tissue sample will be stored at the Southampton Tissue Bank which has a Human Tissue Authority (HTA) Licence.

If you no longer want your archival tumour sample to be used in this research, you should tell your study doctor.Your study doctor will notify the sponsor who will ensure the samples are returned to the hospital from which they were obtained if needed, or destroyed. If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done. Please note that there may not be a tumour sample remaining following the testing for the trial. The blood samples will be sent to the Southampton WISH Lab for storage and analysed at the Southampton Experimental Cancer Medicine Centre (ECMC), hosted within the Wessex Investigational Sciences Hub Laboratory. All the samples that you provide as part of the study would be pseudo- anonymised so that it would not be possible to identify you. Part of your samples may also be used in future ethically approved studies. The blood samples will be stored at the Southampton Tissue Bank which has a HTA Licence.

If you no longer want your blood samples to be used in this research, you should tell your study doctor. Your study doctor will notify the sponsor who will ensure the samples are returned to the hospital from which they were obtained if needed, or destroyed. If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

The blood samples will be used to see how the Atezolizumab is affecting your tumour i.e. how your tumour is responding to the treatment.

**What will happen at the end of the trial?**

At the end of the trial treatment you will continue to have hospital visits every 12 weeks in order that CT scans can be completed and your doctor can undertake a physical exam. Following the final visit and check-up, you will return to standard of care treatment at your local hospital. Your doctor will discuss future care with you.

**Part B: Further information**

**What if new information becomes available?**

Sometimes we get new information about the treatment being studied. If this happens and it affects your participation in the study, your doctor will discuss the information with you. If, on the basis of this information, you decide not to continue with the study, your doctor will make arrangements for your continued care. If you decide to continue in the study, you may be asked to sign another consent form. It may be that your doctor feels that you should withdraw from the study. If this happens, they will arrange for further treatment if required. If the study is stopped for any reason, you will be informed, and further care arranged.

**What happens if something goes wrong?**

If you have a concern about any aspect of this study, you should contact your research doctor/nurse as soon as possible. Your clinical research team will do their best to help you and answer your questions. [Insert site phone number].

If you wish to complain, or have any concerns about the way you have been approached or treated during this trial, the normal complaints system will be available to you; this service is called the Patients Advice and Liaison Service (PALS) in England and Wales. The service available to patients in Scotland is the Health Boards Complaints Team. For the contact details and further information please check [www.nhs.uk](file:///%5C%5Csoton.ac.uk%5Cresource%5CMedicine%5CCTU%5CTrials%5C07%20Trials%20in%20development%20for%20submission%5COELIXIR%20TRIALS%5C1.%20CRUK%20APPLICATION%202019%5C3a%20Rise%5Cwww.nhs.uk%20) or your local trust’s website.

[Delete as appropriate]

Local PALS contact details [insert here]

Local Health Boards Complaints Team contact details [insert here]

The study Sponsor, the University Hospital Southampton NHS Foundation Trust (UHS), takes overall responsibility for the trial. If you remain unhappy or have a complaint about any aspect of this study, please contact the Research Governance Manager at researchmanagement@uhs.nhs.uk.

Please be aware that if you are harmed as a result of taking part in the AURORA trial, there are no special compensation arrangements. The University Hospital Southampton NHS Foundation Trust provides clinical trials indemnity insurance for negligence in its management or design of the trial. If you are harmed because of someone’s negligence, you may be able to take legal action, but you may have to pay your own legal costs.

**Will my participation be kept confidential?**

Yes. Your participation and the information we collect about you will be kept strictly confidential. Your family doctor/health care provider will be informed that you are taking part in a study so that you can be provided with appropriate medical care.

University Hospital Southampton NHS Foundation Trust is the sponsor for this study. The sponsor and the Southampton Clinical Trials Unit (SCTU), who are acting on behalf of the sponsor, will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that the sponsor and SCTU are responsible for looking after your information and using it properly. The Southampton Clinical Trials Unit will keep non-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.

You can find out more about how we use your information at <https://www.southampton.ac.uk/ctu/about/index.page>

[Insert name of local NHS site] 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 the sponsor, the SCTU and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [Insert name of local NHS site] will pass these details to the sponsors along with the information collected from you and your medical records. The only people in the sponsor organisations and the SCTU who will have access to information that identifies you will be people who need to 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.

[Insert name of local NHS site] will keep identifiable information about you from this study for 25 years after the study has finished.

Non-identifiable data, managed by the Southampton Clinical Trials Unit, will be held on servers located in the UK, EU, and USA and access will be strictly controlled and all applicable Data Protection legislation will be abided by. In collaboration with the Southampton Clinical Trials Unit a selection of laboratories across the UK will have strictly controlled access to your anonymised data. This information will contribute to a better understanding of this disease and will be used by investigators who will not have access to any data that will identify you.

With your permission, we will tell your General Practitioner (GP) that you are taking part in the AURORA trial. Your medical records will be available to those involved in your clinical care and authorised individuals from the Sponsor or the Sponsor’s delegates from the Southampton Clinical Trials Unit and Regulatory Authorities.

When you agree to take part in a research study, the anonymised data collected during the study may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

If you require any further information or assistance regarding how your personal data is used, please contact the University Hospital Southampton NHS Foundation Trust Data Protection Officer at dataprotection@uhs.nhs.uk

**NHS Digital**

NHS Digital collects data from across health and social care in the England and there are equivalents in the other devolved nations For patients in Scotland, your Community Index Number (CHI) number will be used. With your consent, during the trial, NHS Digital, or the applicable service in your area, may provide information about whether your disease has come back and your survival status to the Southampton Clinical Trials Unit (SCTU) upon request. We will use your NHS number/CHI number to request this information. The Southampton CTU is registered under the Data Protection Regulations to hold such information on a confidential basis.

Research Data

We will be using information from you and your medical records in order to undertake this study. We are responsible for looking after your information and using it properly. The Southampton Clinical Trials Unit will keep your non-identifiable research data for 25 years after the study has finished.

In order to properly manage your data and ensure the research is reliable and accurate, your rights to view, change or move the research information we collect about you are limited. You can find out more about how we use your information on the Southampton Clinical Trials Unit website at <https://www.southampton.ac.uk/ctu/about/index.page>

Your clinician’s research team will collect information from you and your medical records for this research study in accordance with our instructions. Only members of the research team at your NHS Trust and responsible members of the University Hospital Southampton NHS Foundation Trust and Roche (the company supplying the drug) may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may look at your medical and research records to check the accuracy of the research study. All of these people have a duty to keep your information strictly confidential.

Your NHS Trust will keep identifiable information about you from this study for 25 years after the study has finished.

Consent Forms

A copy of your consent form, containing your name and initials, will be sent to the Southampton Clinical Trials Unit for confirmation of your consent. This form will be kept securely, as detailed above, for the duration of the trial. A copy will also be provided to the Southampton Tissue Bank Southampton for confirmation of your consent.

**Impact on Insurance**

Participation in any research study has the potential to impact any insurance cover that you may have (e.g. travel insurance, protection insurance (life insurance, income protection, critical illness cover) and private medical insurance) and it is advised that you seek expert advice on these issues, where necessary.

**Do I have to take part?**

No, it is up to you to decide to join the study. We will describe the study in detail and go through this information sheet with you. If you agree to take part, we will ask you to sign a consent form with the doctor. You are free to withdraw at any time, without giving us a reason.

**What happens if I change my mind?**

You have the right to change your mind and withdraw at any time without giving a reason and without your participant rights (or routine care if a patient) being affected. Your withdrawal from the study will not affect the standard of care that you will receive in any way.

**What will happen to the results of the trial?**

At the end of the trial, any results will be analysed and presented at national or international meetings and will also be published in a medical journal. Your personal details will remain strictly confidential. Research findings made available in any reports or publications will not include information that can directly identify you without your specific consent. An information sheet detailing the findings of the trial will be sent to your hospital medical team and asked to share this with the participants of the trial.

**Who is organising and funding the trial?**

The trial is being coordinated by the Southampton Clinical Trials Unit. The trial is being funded by Cancer Research UK with the investigational drug being supplied by Roche. The Sponsor is University Hospital Southampton NHS Foundation Trust. The study has been ethically reviewed by the Chelsea Research Ethics Committee and regulatory reviewed by the Medicines and Healthcare products Regulatory Agency (MHRA).

**Where can I get more information?**

If anything is unclear regarding this study information, please contact:

[Named site nurse] Research nurse, [insert site name] on Tel [……]

Dr [insert name site] PI, [insert PI name], Tel [insert number site specific]

In an **EMERGENCY**, please contact:

[Insert site-specific contact details]

Thank you for reading this information sheet. If you decide to take part in the study, you must personally initial, sign and date a consent form.

We will give you a copy of this information sheet and your signed consent form to keep. We will keep a second copy of this document with the research records on this trial and place a third copy in your hospital records.

**Schedule of trial visits:**

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| **Visit:** | **Screening**  | **Cycle 1 Day 1**  | **Cycle 2 Day 1**  | **Cycle 3-13****Day 1**  | **End of treatment Visit** **(28 days from final dose)**  | **Follow-Up Phase****(every 12 weeks)**  |
| Archival Tissue Sample sent for analysis | X |  |  |  |  |  |
| Informed Consent  | X |  |  |  |  |  |
| Eligibility Evaluation | X |  |  |  |  |  |
| Medical History  | X |  |  |  |  |  |
| Physical Exam  | X | X | X | X | X | X |
| Treatment with Atezolizumab  |  | X | X | X  |  |  |
| Pregnancy Test (serum test at screening, urine test prior to each cycle) (WOCBP) | X | X | X | X  |  |  |
| CT Scan  | X |  |  | X |  | X |
| Blood tests  | X | X | X | X | X | X |
| Quality of Life Questionnaires  | X |  |  | X |  | X |

Your study medical team will review the answers you provide in your Quality of Life Questionnaires. If you raise any issues, your doctor or nurse will be able to assist you or provide further information on an appropriate care pathway.