To be printed on hospital headed paper

A-PREDICT

A Phase II Study of Axitinib in Patients with Metastatic Renal Cell Cancer Unsuitable for Nephrectomy

PATIENT INFORMATION SHEET

We are inviting you to take part in a research study called A-PREDICT. Before you decide whether to participate, 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. Ask us if there is anything that is not clear or if you would like more information – the contact details for your local A-PREDICT specialist can be found on page 14. Please take as much time as you need to decide whether or not you wish to take part in the A-PREDICT study.

Part 1 of this information sheet tells you about the purpose of the study and what taking part will involve for you.

Part 2 gives more detailed information about the biological research we would like to carry out on samples that we will ask you to donate if you decide to join A-PREDICT

CANCER RESEARCH UK

PART ONE

What is the purpose of the A-PREDICT study?

We are aiming to find out if a drug called axitinib might help people with cancer like yours who have not had any previous treatment. We also want to find out who will be helped the most with axitinib treatment by looking at the way your cancer reacts to the drug.

What is axitinib?

Axitinib is a new kind of drug that comes in tablet form and is taken twice a day. It is designed to stop the growth of new blood vessels which help cancer cells to get the nutrients they need. It has been found to stop or slow the growth of cancer in patients who have received it when their cancer has started spreading after being given another treatment.

Why am I being invited to take part?

Your doctor believes you may be suitable to take part in this study because it appears that you have a type of kidney cancer that has spread away from the kidney and cannot be removed by surgery. This type of cancer is known as metastatic renal cell cancer.

If you join the study, you will be one of 99 people from across the UK taking part. If the results of this study show that axitinib may help people with the same type of cancer as you have, a further larger study will be conducted to confirm which people it will help, and how long the effect of the drug will last.

Do I have to take part?

No, it is up to you to decide whether or not to take part in A-PREDICT. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are free to leave the study at any time and do not have to give a reason. Whether or not you decide to join the A-PREDICT study will not affect the standard of care you receive

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

You will need to have a number of examinations before you can join the study. Some of these are routine, but others will need to be done to make sure that it is safe for you to take part and that you have the sort of cancer that this drug may help.

They may take up to 3 weeks to complete and include:

- a physical examination, including your heart rate, breathing rate, blood pressure, height and weight
- a maximum of 20ml of your blood will be collected
- a collection of a sample of your urine
- a CT scan of your chest, abdomen and pelvis to measure the sites of your cancer
- a sample of your kidney cancer will be collected by a biopsy. You may also give permission to take another sample from an area where the cancer has spread, if your doctor feels it is safe to do so
- a pregnancy test if you are female and of child bearing age

Once these have been completed and your study doctor has confirmed that you can join the study, you will begin treatment with axitinib. You will need to take two tablets a day and return to the hospital on a regular basis to see how you are getting on. Your doctor may decide to increase your dose if he/she feels you may benefit. You will need to continue to take axitinib tablets until your doctor decides that they are no longer helping to treat your cancer.

You will be offered surgery if your study doctor feels that surgery to remove your kidney (nephrectomy), or surgery to remove sites where the disease has spread, would help you after you have started treatment.

What are the side effects of axitinib?
As with any drug, axitinib can have side effects. No-one can predict before you begin treatment whether you will have any of these, or how serious they might be.

Please let your study doctor and/or research nurse know about any side effects as soon as possible so they can advise you what to do. This may include stopping your tablets for a few days. Their telephone numbers are at the end of this information sheet (p14). There is also 24 hour support available from your hospital, to provide access to immediate medical care in the event of any serious problems.

The side effects of axitinib that have been reported in previous studies are listed below. **Not all patients will experience all of these side effects and medications can be given to make any side effects less serious or uncomfortable.**
Serious side effects:

- **2 in 10 people** receiving axitinib have developed serious high blood pressure
- **1 in 10 people** receiving axitinib have experienced severe diarrhoea or extreme tiredness
- **1 in 20 people** receiving axitinib have developed redness and severe tenderness in their hands and feet
- **1 in 33 people** receiving axitinib have experienced serious bleeding. A very small number of people have experienced serious bleeding from an enlarged blood vessel (aneurysm),that has burst
- **1 in 55 people** receiving axitinib have experienced heart failure

Around 1 in 100 people receiving axitinib have experienced embolisms or thrombosis (blood clots) in the arteries or veins or tearing and perforations of the digestive tract

Common side effects:

- **Around half** of people receiving axitinib experience some degree of tiredness, diarrhoea or high blood pressure
- **Around 4 in 10 people** receiving axitinib develop a loss of appetite.
- **Around 3 in 10 people** receiving axitinib experience hoarseness or voice change, redness and tenderness in their hands and feet, feel sick or lose weight
- **Around 1 in 4 people** receiving axitinib experience underactive thyroid (which may appear as tiredness, low voice, feeling cold, constipation, loss of appetite, swollen eyes or changes to the skin and hair), are sick or experience bleeding
- **Around 2 in 10 people** receiving axitinib experience shortness of breath, headache, constipation, cough, soreness or swelling of the mouth, protein in urine, lack of energy or joint pain
- **Around 1 in 10 people** receiving axitinib experience indigestion, change of taste, dizziness, weakness, pain in hands or feet, muscle pain, stomach pain, rash, dry skin or swelling or irritation of the nose, throat, eyes, stomach, lungs or other body part that produces mucus
- **Around 1 in 15 people** receiving axitinib experience mouth and nose pain, low red blood cells, dehydration, itching, hair loss or have an increase in liver enzymes in their blood

Between 1 in 20 and 1 in 333 people receiving axtinib have experienced one or more of the following: decrease in platelets in their blood, decrease in certain types of white blood cells, increase in red blood cells in their blood, increase in thyroid function, increase in the calcium, potassium or bilirubin in their blood, flatulence, haemorrhoids, burning sensation of the mouth, ringing in the ears and redness of the skin.

Everyone in this study will receive regular check ups to look out for the common side effects listed above and any other problems, so they can be treated. If you are experiencing serious side effects, your doctor may reduce the amount of axitinib you are taking. If treatment with axitinib is not causing you too many problems, your doctor may consider increasing the amount of drug you take each day. You should continue to take the same amount of axitinib each day until you are advised to change by your doctor.

Will there be anything extra I need to do if I take part in A-PREDICT?

Yes, if you choose to take part in A-PREDICT you need to visit your hospital more often than you may otherwise need to, and you will have two extra CT scans.

We will also ask that you provide blood and urine samples, and samples of your cancer, known as biopsies, three times during the study. There is currently no information available to help doctors to individually select the best treatment for people with your type of cancer. The samples you donate will help to provide this information for doctors to use in the future.

More information about what this will involve is in part 2 of this information sheet (p 12).

How many times will I need to visit the hospital?

You will be seen regularly by your study doctor and/or nurse after you join the study. Each visit will involve having medical investigations to check on your state of health. You may need to visit a different hospital for your biopsies, more details of this are provided in section 2. You will be asked to come to the hospital 2 and 4 weeks after you start treatment, and then every 4 weeks after this until axitinib is no longer helping to stop the growth of your cancer. When this happens, you will need to stop taking axitinib and your doctor will decide what is the best treatment for you. We won't ask you to have any more investigations for the A-PREDICT study, but would like to continue to collect information about how you are doing.

The table below shows what will happen at each of your hospital visits:

	Before you start treatment	2 weeks after starting treatment	4 weeks after starting treatment	8 weeks after starting treatment	12 weeks after starting treatment and every 4 weeks after that	End of treatment
A physical examination, including measurement of your heart and breathing rates, blood pressure, height and weight	✓	✓	✓	✓	✓	✓
Blood test	✓	✓	✓	✓	✓	✓
Urine test	✓		✓	✓	✓	✓
Assessment of current symptoms and treatment (if needed)	✓	✓	✓	✓	✓	✓
Biopsy of your kidney tumour for biological study	✓			✓		
Biopsy of one other disease site for biological study	✓					✓
Blood samples and urine sample for biological study	✓			✓		✓

You will have CT scans to measure how well your cancer is responding to treatment when you've been taking axitinib for 8 weeks, 4 months, 6 months and 3 monthly after this.

What else do I have to do?

Before deciding to take part in this study, you need to consider carefully how these tests and hospital visits will affect you and your family. Some tests may be uncomfortable. Please ask your hospital doctor or nurse if you have any questions about the tests and procedures. If you decide to take part, you will need to:

- sign the study consent form to show you understand what A-PREDICT involves
- attend all scheduled appointments
- take your axitinib medication twice a day, about 12 hours apart, and with food. Your medication should be stored in the bottle given to you by your study doctor or pharmacist. You need to store it at room temperature (between 15 and 30 °C)
- stop taking axitinib for one week before your 8 week check up, when you will be asked to donate samples for the biological study. Your doctor will tell you when you should start taking the tablets again.

- talk to your study doctor first if you want to stop taking the tablets for any other reason
- only take the tablets yourself. Keep them out of the reach of children
- **tell your doctor about any other medicines that you take, even if you buy them without a prescription.** Before starting any new medication including over the counter medications or herbal supplements please check with your study team.
- avoid drinking grapefruit juice, as it can change the effect axitinib has on your cancer cells
- tell your doctor about any medical problems you have
- use an effective method of birth control to avoid becoming pregnant or fathering a child while taking axitinib and for 6 months after stopping treatment. If this happens whilst you are taking axitinib, you will need to tell your study doctor. If you need further information about effective methods of contraception for use whilst in A-PREDICT, please talk to your doctor.
- avoid breastfeeding while you are taking the study medicine
- return your medicine containers (with any left over tablets) to the study team at each visit

It is very important that you follow these requirements to continue in the study.

How long will I need to take axitinib?

Study treatment may be stopped if your study doctor finds that it is no longer helping to control your disease, you are experiencing intolerable side effects or you no longer want to continue on the treatment.

What are the alternatives for treatment?

If you decide not to take part in this study, your doctor will discuss all alternatives with you and you will be offered the best available alternative treatment. You will not be offered axitinib outside the study.

What are the other possible disadvantages and risks of taking part?

By taking part in this study you will have more CT scans than you would if you did not take part. Some of the study biopsies may be carried out under CT guidance. CT scans and CT-guided biopsies use x-rays. X-rays can cause cell damage which may, after many years or decades turn cancerous. However, for people in A-PREDICT the risk of this affecting them is small.

You will need to attend hospital more frequently than you would if you were receiving standard care. This may cause some disruption to your normal activities and home life and this should be discussed with your family and friends if it will impact on them. We will not be able to reimburse you for any extra travel expenses.

If you have private medical insurance you should check with the insurance company before agreeing to take part in this study to ensure that your participation will not affect your cover.

What are the possible benefits of taking part?
Your doctor feels that that axitinib may help to control the progression of your cancer, but we cannot guarantee it. The information we gain from this study may help us to improve treatments for patients with renal cell carcinoma in the future.

What happens when the research study stops?
A-PREDICT study will continue until after everyone who is participating has stopped taking axitinib. When you stop taking axitinib, your doctor will discuss with you your next options for treatment.

What if relevant new information becomes available?
Sometimes during the course of a research project, new information becomes available about the drugs that are being studied. If this happens, your research doctor will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your continued care. If you decide to continue in the study you may be asked to sign an updated consent form.

If new information means it would be in your best interests to withdraw you from the study, your doctor will explain the reasons and arrange for your continued care.

If the study is stopped for any other reason, you will be told why and your study doctor will arrange for your continued care.

What happens if I don't want to carry on with the study?
You are free to withdraw from A-PREDICT at any time. You do not have to give a reason and your future treatment will not be affected. Your doctor will discuss your treatment options with you and will offer the most suitable treatment available. However, if you were to withdraw, we would like your permission to continue to collect information on your progress that is routinely recorded in your medical records. This is so that the overall quality of the study is not impaired.

What if something goes wrong?
If you have a concern about any aspect of this study you should ask to speak with your study doctor or research nurse who will do their best to answer your questions.

Any complaint about the way you have been dealt with during this study or any possible harm you might suffer will be addressed. You will be closely monitored both during and after therapy and any side effects will be treated as appropriate. If you are harmed whilst taking part in this study due to someone's negligence, then you may have grounds for legal action but you may have to pay for it. If you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you. We recommend that you obtain a copy of your hospital's complaints procedure or policy if you intend to make a complaint. Concerns should be raised by speaking to a member of staff at your hospital or by talking to your local Patient Advice and Liaison Service (PALS). **[NOTE TO CENTRES: PLEASE DELETE THESE PARENTHESES WHEN ADAPTING PIS TO CENTRE SPECIFIC DOCUMENT AND REPLACE PALS INFORMATION WITH EQUIVALENT LOCAL ORGANISATION IF CENTRE IS OUTSIDE ENGLAND]**.

Will my taking part in this study be kept confidential?
All information which is collected about you during the research will be kept strictly confidential. When you join the study, your name, date of birth, postcode, hospital number and NHS or Community Health Index (CHI) number will be passed to the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) where the study is being coordinated. You will be given a unique registration number, which will be used together with your initials and date of birth on forms that the research staff will send to ICR-CTSU. All information about you will be coded with the registration number and will be stored securely. It will be treated as strictly confidential and nothing that might identify you will be revealed to any third party. Only members of the research team will have access to the information that could allow this study number to be linked to you.

Members of the research team, including ICR-CTSU staff, and regulatory authority employees may need to examine your medical records to ensure the study is being run properly and that the information collected on the forms is correct, but your confidentiality will be protected at all times. Pfizer, the company that makes axitinib, will be informed of any serious medical events that you might have on the study. They will not be able to identify you from the information they receive.

You will retain the right to ask to be shown all your personal data that has been collected for this study, and if you think anything is incorrect you may ask to have it corrected.

All the information that is sent to ICR-CTSU will be kept 20 years after the A-PREDICT study has ended.

Will information about me be shared with other researchers?

The organisers of this study would like to be able to combine information we collect about patients in this study with information collected for other studies, if in the future it is a useful way of advancing our knowledge of the treatment of cancer. If this happens, information about you may be passed to other researchers, but they would not be able to identify you from the information provided.

Involvement of your General Practitioner/Family doctor (GP)

Your General Practitioner (GP) will be informed about your participation in the study. This will ensure your GP knows that you are taking axitinib in the event of any potential side effects and/or drug interactions.

What will happen to the results of the research study?

Independent experts will review the progress of the research, and the results will be published in a respected journal as soon as there is enough information to be sure the results are reliable. Results will be also be available on Cancer Research UK's website (www.cancerresearchuk.org/cancer-help/trials/).

You will not be identified in any report or publication. The results will help to decide how to treat kidney cancer in the future.

Who is organising and funding the research?

The research study is being carried out by the Royal Marsden Hospital (Chief Investigator Dr James Larkin) and the Cancer Research UK London Research Institute. It is being coordinated by the Institute of Cancer Research Clinical Trials & Statistics Unit and is being funded by Pfizer, the company that is also providing the study drug for free. The funding helps to cover the cost of including you in the study, the laboratory tests and helps support the study staff. None of the researchers are personally benefiting from this grant.

Who has reviewed the study?

Cancer Research UK have reviewed A-PREDICT and support the aims of the study. A-PREDICT has also been approved by the London – Brent Research Ethics Committee on behalf of all hospitals in the UK who take part. Their approval

means they are satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits, and that you have been given the right information to decide whether to take part.

What happens now?

Your doctor or nurse will be happy to answer any questions. Once you have reached your decision let your doctor or nurse know. If you choose to join the A-PREDICT study you will be asked to sign a consent form and will be given a copy to keep together with this information sheet.

Part Two
Looking at biological samples

If you agree to join A-PREDICT we will ask you to donate samples of blood, urine and samples of your cancer (biopsies). These will be collected before you start treatment, 8 weeks after you join the study, and when you stop treatment.

What does having a biopsy involve?

A biopsy is the removal of a small piece of tissue from the tumour in your kidney or other area where the cancer has spread to.

All biopsies in A-PREDICT will be taken using a biopsy needle through the skin, and should take about 30 minutes to do. You will only have one needle puncture for each biopsy.

The doctor taking the biopsy will use either a CT scanner or an ultrasound machine to see where the tumour is. You will have a local anaesthetic first to numb the area. It may still be painful or a little uncomfortable afterwards, but this should be mild and painkillers such as ibuprofen should help. You will need to stay in hospital for up to 4 hours after the biopsy, to make sure that there are no immediate complications. There may be a small amount of bleeding, which is normal and your doctor or nurse will make sure this has stopped before you go home.

Your doctor or nurse will give you information about how to care for the biopsy wound. The area will be covered with either a sticking plaster or a gauze pad. If your biopsy wound starts to bleed when you get home and it does not stop please contact your doctor. The wound may have some stitches that need to be removed after a few days and your doctor or nurse will give you information about how to arrange this.

A biopsy is an invasive procedure and there is a very small risk of perforation of a blood vessel and there is a risk of infection. These complications may be life threatening but the risk is less than 1 in 10,000.

Who will do the biopsy?

Biopsies for the A-PREDICT study will usually be taken at the hospital your study doctor is based at.

If you are invited to participate in A-PREDICT at a hospital which is not able to take biopsies, you will need to travel to another hospital which is participating in the study. Your study doctor will explain if this is the situation at your hospital and where you would need to travel to.

What sort of samples will I be asked to donate?

Before treatment

Four extra samples will be taken from your kidney tumour at the same time as the sample normally taken to confirm the type of cancer you have. If you have given your doctor permission, up to five samples will also be taken from another area where your cancer has spread to.

If the sample from your kidney tumour shows that you have the type of cancer suitable for treatment with axitinib, you will then be registered into the study. One in ten people will not have the sort of cancer that axitinib may help. If you have a different type of cancer, we will still ask your permission to collect the samples you have provided, and your doctor will talk to you about alternatives to joining the A-PREDICT study.

If you do join the A-PREDICT study, you will be asked to donate two blood samples (the same amount as 4 teaspoons) and a urine sample before you start treatment with axitinib

8 weeks after joining A-PREDICT

Another biopsy of your kidney tumour will be performed, collecting up to 5 samples. Two blood samples and urine sample will also be collected.

It is important that you stop taking axitinib one week before this biopsy is done. You will be able to restart treatment 2-3 days after your biopsy, once the wound has healed.

When you stop axitinib treatment permanently

A biopsy of the area where the disease has got worse will be performed, or if this is not possible, a biopsy of your kidney tumour will be taken, collecting up to 5 samples. Two blood samples and a urine sample will also be collected.

Samples from routine surgery

We would like to ask your permission to collect samples from any surgery you may have to remove some of your cancer, if this is carried out whilst you are in the A-PREDICT study. This surgery may involve the removal of your kidney, or surgery on a site where the cancer has spread to.

Routine diagnostic samples

We would also like to ask your permission to request from your hospital the samples that are routinely collected as part of your diagnosis.

What will happen to my blood and tissue samples?

All samples collected as part of the biological sample study will be sent to the Francis Crick Institute (FCI) (formerly Cancer Research UK's London Research Institute). The FCI may work with other laboratories and researchers, in the UK and abroad, on the analysis of your samples. The researchers will not be able to identify you in the course of this work.

The scientists at the FCI will look at the samples you provide to find biological markers that may help to predict how well axitinib treatment will work for individuals. This will involve looking at the genetic information from the samples of your cancer and in your blood and urine, and how these change in response to treatment.

There is currently no information available to help doctors to individually select the best treatment for people with your type of cancer. The samples you donate will help doctors understand how treatment with axitinib works and if it will be beneficial to other patients with your cancer to use in the future. We may in the future share the information we gain from the samples you provide, including genetic details, with other researchers investigating this type of cancer. You will not be identifiable from this information. Please initial the consent form if you are happy for this information to be shared.

If you give your permission, after the A-PREDICT study is complete, your samples will be stored for use in future studies. Any future studies using your samples will be reviewed and approved by a Research Ethics Committee.

What information about me will be sent with my samples?

The samples you donate as part of A-PREDICT will be sent to the FCI labelled with your study registration number, gender and date of birth. This will maintain your confidentiality whilst allowing biological information to be compared to how well axitinib treatment works for you.

Further information

Macmillan is a registered charity providing information, emotional support and publications about all aspects of cancer for cancer patients and their families. They have published useful booklets about (1) kidney cancer (2) individual treatments

and (3) clinical trials in general. You can contact one of their specialist cancer nurses on, 0808 808 00 00.

You can learn more about clinical trials on the Cancer Research UK's patient website (www.cancerhelp.org.uk).

Thank you for interest in our research.

Your specialist is: _____

Contact phone numbers: _____

A-PREDICT Consent Form

MREC Study No: 12/LO/0639 Patient Trial ID: ……

Name of Clinician: ……

Please initial box

1. I confirm that I have read and understand the patient information sheet version 5 dated 12/06/2019 for the above study and have had the opportunity to ask questions. ☐
2. I consent to donating the biological samples described in the A-PREDICT patient information sheet version 5 dated 12/06/2019. ☐
3. I consent to the genetic sequencing of my donated samples. ☐
4. I agree to take part in the A-PREDICT study once all tests confirm I am suitable to participate. 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. ☐
5. I agree to my name, date of birth, postcode, hospital number and NHS or Community Health Index (CHI) number being sent to the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) when I join A-PREDICT. ☐
6. If I withdraw from the study, I consent to my doctor providing authorised researchers with basic clinical information that would be routinely collected and written in my medical records *(optional)*. ☐
7. I understand that sections of any of my medical notes may be looked at by responsible individuals from the research team or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
8. I agree to my GP being informed about my participation in this study. ☐
9. Data sharing: I grant advance authorisation for the possible future sharing of information collected about me with other organisations, with the understanding that I will not be identifiable from this information *(optional)*. ☐
10. I grant advance authorisation for possible future research on my stored samples, with the understanding that I will not be identifiable from these samples and that prior approval of an ethics committee will be obtained *(optional).* ☐

Name of Patient	Date	Signature
Name of person taking consent (if different from researcher)	Date	Signature
Researcher (PI)	Date	Signature