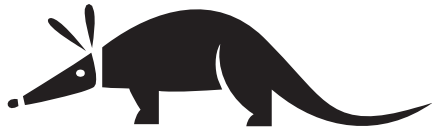
PATIENT INFORMATION SHEET AND CONSENT FORM

An evaluation of the effect of an angiotensin-converting enzyme (ACE) inhibitor on the growth rate of small abdominal aortic aneurysms	Eudract number **:** 2010-020226-17 Ethics ref : 10/H0711/80 Sponsors ref : CRO 1644



AARDVARK

Aortic Aneurysm Regression of Dilation: Value of ACE inhibitors on RisK

This patient information sheet is in two parts. **Part A** is a summary of the AARDVARK study. **Part B** gives more detailed information on the study and administration issues. Please read both sections before making your final decision.

PART A

Invitation

You are being invited to take part in a research trial. 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 if you wish with family, friends or your doctor. Do ask the research doctor or nurse if there is anything that is not clear or if you would like more information. Take as much time as you need to decide whether or not you wish to take part. Thank you for reading this.

If you agree to take part, you will be asked to fill out, sign and date this information sheet and consent form and to keep it as a useful reference on trial details and personal contacts

WHAT IS THE PURPOSE OF THE TRIAL?

You have a condition known as an abdominal aortic aneurysm**.** An abdominal aortic aneurysm is a balloon-like swelling of the main blood vessel of the body (the aorta) as it runs through the abdomen. The normal diameter of the abdominal aorta is approximately 1.8cm or about three quarters of an inch in diameter. Small aneurysms grow slowly and do not appear to cause problems until the diameter exceeds 2-3 times the diameter of the normal aorta (about 5.5cm or more than 2 inches in size).

When the aneurysm is small it is safer to monitor using regular ultrasound scanning - an ultrasound scan is a painless test that uses sound waves to create images of organs and structures inside your body. If the aneurysm reaches a large size (usually over 5.5cm), repair with an operation is recommended to avoid the serious problem of bursting: Causing significant internal bleeding (aneurysm rupture).

It is important to find treatments that help prevent an aneurysm enlarging.

One trial has shown that the use of a specific type of drug, angiotensin converting enzyme (ACE) inhibitors, which are usually used to treat high blood pressure, may reduce the risk of bursting (rupture) of large aneurysms. Therefore it has been suggested that ACE inhibitors also might slow the growth of small aneurysms. It is not clear whether these drugs, ACE inhibitors, would have their effect by reducing blood pressure or by acting directly on the aneurysm or both.

This trial will assess whether an ACE inhibitor drug called perindopril will reduce the growth rate of small aneurysms. It will also assess whether a small reduction in blood pressure levels with any drug also could reduce the growth rate of these aneurysms.

WHY HAVE I BEEN CHOSEN?

You have been asked to take part in this trial as you have an aortic aneurysm of a small size that is currently being monitored using ultrasound scans.

DO I HAVE TO TAKE PART?

It is up to you to decide if you want to take part in the research or not.

If you decide to take part you are still free to stop being in the trial and withdraw your consent at any time. In this case, your research doctor may ask you why you want to withdraw but you do not have to give a reason. You may also decide at any time that you no longer want to take the trial tablet. In such case, you can stop taking the trial drug but continue in the trial and the trial team will collect information on your health until the end of the trial.

If you agree to take part, your GP will be told that you have agreed to take part in the trial and, with your permission, will be told about the trial and the treatments you may be taking. He/she will be asked for some additional medical details about you. We may also need to contact other doctors or specialists who look after your medical care.

If you decide not to take part, the care you receive will not be affected in any way.

WHAT WILL HAPPEN TO ME IF I TAKE PART? / WHAT DO I HAVE TO DO?

Each patient in this trial must take part for a 2-year period. There are likely to be 225 patients similar to you in this trial.

You will first undergo a screening visit. At this visit we will check whether you are suitable for the study. If your blood pressure is found to be raised, we will suggest some treatment for this. We will then invite you back after 6 weeks to check if your blood pressure has lowered.

If you proceed into the study, you will be asked to take half a tablet for the first two weeks (you will be provided with a pill-cutter) and one tablet each day from then onwards.

This tablet could contain the ACE inhibitor called perindopril (10mg), or another drug used to treat blood pressure called amlodipine (5mgs) or a placebo (dummy) pill.

It will be decided randomly (like the toss of a coin) if you receive the placebo or one of the blood pressure medicines so you have a one in three chance or receiving each of the medications.

This is a blinded trial which means you will not know which treatment you are receiving, although, if your research doctor needs to find out, he/she can quickly do so. Neither the trial doctor nor you may choose which treatment you receive.

To assess the effects of these drugs we will:

- Monitor your aneurysm growth by a series of ultrasound scans at either 3 or 6monthly intervals. Please speak to your study team in regards to the frequency of your visits.
- At least once a year your scans will be performed by a specialist scanner
- Measure your blood pressure at every visit.
- Collect blood samples at screening, 3 month, 12 month and 24 month visits. These samples are to check that your kidney function is normal. Approximately 1 teaspoon of blood will be collected these visits.
- Ask you to complete questionnaires to assess quality of life and other health care resources used (for conditions unrelated to your aneurysm) at the end of each year.

Each follow up visit to the hospital (every 3 or 6 months) will take approximately 30 minutes although your initial visit could take up to one hour. After this first visit you will be informed of the aneurysm size and blood pressure from your visit. There will be no need for you to attend your GP for extra visits unless any of our tests show that you may need other treatment or tests.

Reasonable travel expenses for attending a trial visit will be paid to you and you should discuss this with the trial team.

All the costs of the trial (medicines, visits and tests) will be provided for by the trial funder. Your research doctor will be compensated for his/her time and resources given to the trial however, your research doctor will not be paid for his/her involvement in the trial.

So long as you continue to take part, you will be required to:

- Attend the scheduled visits organised by your research doctor and nurses.
- You should take the trial drug as instructed by your trial doctor or research staff.
- At each visit you should bring all unused medicines and any empty medicine boxes with you.
- Bring a written list of all your medications to each visit.
- You will not have to limit your normal lifestyle or activities while you are part of the trial.
- Your GP will continue looking after you in the usual way. It is important that you tell your research doctor about any other medicine you are taking before starting the trial, because some of them may prevent you from joining the trial.
- Should you start taking a new medicine during the trial, you must tell your research doctor or nurse straight away in order to check if it can be taken safely with the trial treatment. This includes any medicines prescribed by your GP or specialist or those you may have bought yourself even herbal products or food supplements.
- You should tell your trial doctor or trial staff about any medical problems, doctor visits, hospital visits, or medical procedures that you have while you are in the trial.
- It would be a good idea to mark in your diary card details of any hospital or GP appointments with notes of any medication changes.
- You will be given a contact card with details of the trial. You should carry this card with you at all times and should you need to be admitted to hospital make sure that the hospital is aware that you are taking part in this trial so that they may contact your

trial team. If you experience any serious health problems such as a heart attack or a stroke, your trial doctor must be informed immediately.

- You should not take part in any other research trial whilst you are in this trial

POSSIBLE BENEFITS OF TAKING PART IN THE TRIAL

Your part in the trial may provide important information and allow doctors to learn more about the trial drugs and treating abdominal aortic aneurysms. During this trial you will get physical exams and your health

will be monitored. If this trial demonstrates a decreased growth rate of aneurysms for patients taking ACE inhibitor drugs, patients that have the same condition as you may significantly benefit from this trial after the resulted have been determined and made public.

For patients with very small aneurysms less than 4.5 cm (or 1.8 inches) in diameter there will be an increased frequency of ultrasound examinations over and above what is normally offered in the NHS, but benefits of more regular scans may include earlier detection of rapidly growing aneurysms or detection of aneurysms that have reached a size that requires treatment.

ARE THERE ANY SIDE EFFECTS FROM THE DRUGS USED IN THIS TRIAL?

The active drugs in this trial are small doses, expected to lower the blood pressure by a small amount (about 6mm of mercury). They should not cause any untoward effects, but in the case of side effects you should contact the trial centre or other medical help as soon as possible for advice.

Common side effects (ie. those that are experienced in 1-10% of patients) specific to each drug that may be experienced are noted below. A full list of the side effects is available in the appendix of this information sheet. Investigation of any of symptoms you experience may be discussed with the study medical team.

Drug	Side Effects
Perindopril (ACE inhibitor)	• Cough - If the cough is intolerable you will be told to stop the drug and you will be switched to another blood pressure drug called losartan which has a lower incidence of cough. You can continue on the trial receiving this drug. • Hypotension (low blood pressure) • Gastro-intestinal problems (nausea, vomiting, indigestion, diarrhoea, constipation, abdominal pain)

	• Allergic symptoms – rash, runny nose, nasal congestion, sore throat • Headaches • Muscle cramps • Vision disturbance • Tinnitus (ringing in the ears)
Amlodipine (Calcium channel blocker)	• Headache • Ankle swelling • Dizziness • Abdominal pain • Nausea • Tiredness • Flushing
Losartan	• Dizziness • Vertigo • High potassium levels in the blood

ALTERNATIVE TREATMENTS

At present there are no treatments used routinely to try to prevent the enlargement of aneurysms. However, it is thought however that stopping smoking and treating high blood pressure and raised blood fats are all beneficial. We will contact your GP so he may give you treatment to lower your cholesterol (blood fats). This is likely to be with a medication called a statin.

ARE THERE ANY SIDE EFFECTS FROM REGULAR ULTRASOUND SCANS?

The ultrasound examinations do not cause any harm. Ultrasound scans are simple, pain-free, non-invasive tests that can image the aneurysm and measure the size and, by comparing to previous scans, measure the growth rate. The test is very quick and will take 10-20 minutes. We will ask you to eat a small meal only before the scan, as large meals can lead to excess gas in the gut and obscure the aneurysm from view.

It is likely that you will have had an ultrasound scan previously for the diagnosis or monitoring of your aneurysm. This ultrasound examination will not be noticeably different to previous scans.

We will ask you, as part of this trial to undergo ultrasound scans at 3 or 6monthly intervals (slightly more frequently than many hospitals ask the majority of patients to undergo scans). Following this scan we will give you the results and you will have the chance to ask any questions.

BLOOD TESTS may sometimes cause some bruising and discomfort.

WHAT WILL HAPPEN IF MY ANEURYSM GROWS TO A SIZE THAT NEEDS INTERVENTION?

Your GP and vascular surgeon will be informed immediately and options for aneurysm repair will be discussed with you. If you proceed to have an aneurysm repair, we will not ask you to attend any further appointments as part of this trial and the drug treatment may be stopped.

PART B

WHO IS THE SPONSOR OF THE TRIAL?

This research is funded by the National Institute of Health Research. There is no funding from any industrial or pharmaceutical company. The research is organised and sponsored by the Imperial College. Your local hospital will be compensated for the work performed and services used at your local hospital. This trial will be co-ordinated from the Imperial College Clinical Trials Unit, London, and take place at hospitals and AAA screening centres in and around London and Coventry.

WHAT HAPPENS WHEN THE RESEARCH TRIAL STOPS?

At the end of the trial you will be informed which of the treatment arms you were assigned to. Further drug treatment will not be available from the trial centre but your GP will be notified and you may request to continue the medication. We shall tell you the results of the trial as soon as possible. Regular examination of your aneurysm will continue at your local aneurysm follow up clinic.

WHAT IF NEW RELEVANT INFORMATION BECOMES AVAILABLE?

Sometimes we get new information about the treatment being studied. If this happens, your trial doctor will tell you and discuss whether you should continue in the trial. If you decide not to carry on, your trial doctor will make arrangements for your care to continue (aneurysm surveillance). If you decide to continue in the trial he may ask you to sign an agreement outlining the discussion. If the trial is stopped for any other reason, we will tell you and arrange your continuing care (aneurysm surveillance).

WILL MY GENERAL PRACTITIONER BE INFORMED?

Your GP (or other health care practitioner) will be notified of your participation. We will seek consent for this. We will, in turn, notify your GP (or other health care practitioner) of any other problems that occur as a

result of this trial. You will be informed of the measurements of blood pressure and aneurysm size after each visit. If the aneurysm grows to a significant size during the trial period, your GP (and vascular surgeon) will be notified urgently.

WHO HAS REVIEWED THE TRIAL?

The trial has been reviewed by the Imperial Clinical Trials Unit at Imperial College and by the Health Technology Assessment group of the National Institute of Health Research. All human research is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and received favourable opinion by a Research Ethics Committee.

WITHDRAWING CONSENT FROM THE TRIAL

Your participation in this trial is voluntary. You can choose at any time to ***withdraw*** your consent for this trial (take yourself out of this trial). Your decision will not affect your ability to receive medical care for your disease. You will not lose any rights or benefits to which you are otherwise entitled.

For the purpose of this trial, the sponsor and its agents and representatives (including the trial doctor, institution and its representatives) reserves the right to verify your survival status by way of your medical records, public records or contacting your physician or the named alternate contact person(s) if the law permits.

WHAT IF THERE IS A PROBLEM?

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Insert name and contact details). The normal National Health Service complaint complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Office.

WILL MY TAKING PART IN THE TRIAL BE KEPT CONFIDENTIAL?

If you agree to take part in the research, all personal information collected during the trial will be kept strictly confidential. It will be used only for the research and for submission to Regulatory Authorities in a way so they will not be able to identify you.

Your medical records and other personal information created during the trial may be looked at by representatives of the sponsor, people working on behalf of the sponsor such as monitors of the trial, members of the ethics committee, and from regulatory authorities and auditors to check the research is being carried out correctly.

Any information from your medical records will always be kept strictly confidential.

All information about you which leaves your research doctor's site will not be able to be traced back to you. Any transfer of this information will be done according to the rules and regulations protecting personal information.

With your agreement, your research doctor will inform your general practitioner or other medical practitioners who may be treating you of your participation in the trial

You will be allowed to have a look at your personal information to check it is correct. If you wish to do so, you should ask your research doctor**.**

You will only be told details of which specific medicine you had been taking once the trial is over and when the results are ready.

If you decide to leave the trial early, any information collected on you up to that point will still be used.

You have the right to check the accuracy of data held about you and correct any errors.

Procedures for handling, processing, storage and destruction of information about you are compliant with the Data Protection Act 1998.

Information about you will be kept for 15 years after the end of the trial, and will be disposed of securely after this time.

THE RESULTS OF THE TRIAL

The results from this trial may be published in medical journals or used in scientific reports, but your name or any other confidential information will never appear.

You may have a copy of the results should you wish. You will need to speak to your research doctor about this at the time.

Finally, you will be told which type of medicine you have been taking.

You should note that you would not be identified in any report/publication unless you have given your written consent.

THE ETHICS COMMITTEE BELOW HAS APPROVED THE PROTOCOL

The Ethics Committee of West London REC 2 has given a favourable opinion to the trial on 14th February 2011

CONTACTS AT SITE

Should you have questions about the trial or the trial products, or in the case of an emergency please contact:

Research Doctor	
Research Nurse	
Address and telephone	
Emergency contact number	

Full list of side effects

Drug	Side effects
Perindopril (ACE inhibitor)	Common (affecting 1- 10% of people who take this drug) : • Cough - If the cough is intolerable you will be told to stop the drug and you will be switched to another blood pressure drug called losartan which has a lower incidence of cough. You can continue on the trial receiving this drug. • Hypotension (low blood pressure) • Gastro-intestinal problems (nausea, vomiting, indigestion, diarrhoea, constipation, abdominal pain) • Allergic symptoms – rash, runny nose, nasal congestion, sore throat • Headaches and dizziness • Muscle cramps • Vision disturbance • Tinnitus (ringing in the ears) Less common (affecting less than 1% of people): Mood or sleep disturbances. Acute swelling of the throat and face. Inflammation of the pancreas which could cause pain in your abdomen. Inflammation of the liver and jaundice have been reported. Altered blood levels of liver tests, other chemicals in the blood, lowering of white cells and anaemia have occurred in patients taking this group of drugs.
Amlodipine (Calcium channel blocker)	Common (affecting 1- 10% of people who take this drug): • Headache • Ankle swelling • Dizziness • Abdominal pain

	• Nausea • Tiredness • Flushing Less common (affecting less than 1% of people): Gastro-intestinal disturbances, dry mouth, taste disturbances, low blood pressure, faintness, chest pain, shortness of breath, rhinitis, mood changes, general weakness, tremor, pins and needles, disturbances when passing urine, impotence, breast swelling, weight changes, muscle pains and cramps, back pain, joint pain, visual disturbances, ringing in the ears, skin irritation, rashes, sweating, hair loss and skin discolouration.
Losartan	Common (affecting 1- 10% of people who take this drug): • Dizziness • Vertigo • High potassium levels in the blood Less common (affecting less than 1% of people): Gastro-intestinal disturbances, chest pain, palpitation, general swelling, shortness of breath, headache, sleep disorders, skin rash with irritation and swelling.

Study Title	**An evaluation of the effect of an angiotensin-converting enzyme (ACE) inhibitor on the growth rate of small abdominal aortic aneurysms**		
Subject #		*Site #*	
Name of Research Doctor			

Please **initial** box if you agree with the following:

I, ***(forename and surname)***

freely agree to take part in the study. ☐

- I have been given the Patient Information Final 8 dated 01/07/2012 to read as well as a full explanation by . . . . . of the aims, the procedures and possible risks of the study. I was able to ask him / her questions regarding all areas of the study and these questions have been answered to my satisfaction. I have been given the name of a person to contact if I have any questions during the study. ☐
- I have had sufficient time to think about taking part and I agree to cooperate with the research team. I will inform them immediately if I have any problems. ☐
- I understand that I am free to leave the study at any time, if I want to without having to give a reason and that my decision will not affect the standard of care I receive. ☐
- I understand my identity will never be disclosed and any information collected will remain confidential. I agree that my medical records and other personal data generated during the study may be examined by representatives of the sponsor and by people working on behalf of the sponsor, members of the Ethics Committee and by representatives of regulatory authorities. I agree that I will not seek to restrict the use to which the results of the study may be put. ☐
- I agree to my GP being informed of my participation in the study ☐

Participant/Legal Representative	**Person responsible for collecting the informed consent**
Date:	*Date:*
Signature:	*Signature:*

Name:	*Name:*

Give one signed original information and consent form to the participant and keep the other signed original in the study file.

Study Title	**An evaluation of the effect of an angiotensin-converting enzyme (ACE) inhibitor on the growth rate of small abdominal aortic aneurysms**		
Subject #		*Site #*	
Name of Research Doctor			

Please **initial** box if you agree with the following:

I, ***(forename and surname)***

freely agree to take part in the study. ☐

- I have been given the Patient Information Final 8 dated 01/07/2012 to read as well as a full explanation by . . . . . of the aims, the procedures and possible risks of the study. I was able to ask him / her questions regarding all areas of the study and these questions have been answered to my satisfaction. I have been given the name of a person to contact if I have any questions during the study. ☐
- I have had sufficient time to think about taking part and I agree to cooperate with the research team. I will inform them immediately if I have any problems. ☐
- I understand that I am free to leave the study at any time, if I want to without having to give a reason and that my decision will not affect the standard of care I receive. ☐
- I understand my identity will never be disclosed and any information collected will remain confidential. I agree that my medical records and other personal data generated during the study may be examined by representatives of the sponsor and by people working on behalf of the sponsor, members of the Ethics Committee and by representatives of regulatory authorities. I agree that I will not seek to restrict the use to which the results of the study may be put. ☐
- I agree to my GP being informed of my participation in the study ☐

Participant/Legal Representative	**Person responsible for collecting the informed consent**

Date: *Signature:* *Name:*	*Date:* *Signature:* *Name:*

Give one signed original information and consent form to the participant and keep the other signed original in the study file.