Anti-platelet Therapy in the **P**rimary **P**revention of Cardiovascu**L**ar Dis**E**ase in Patients with **C**hronic **O**bstructive **P**ulmonary **D**isease

APPLE-COPD: ICON2

Participant Information Sheet

Study Chief Investigator
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Study Principal Investigator
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Introduction

We would like to invite you to take part in a research project called "APPLE-COPD ICON2: Anti-platelet therapy in the primary prevention of cardiovascular disease in patients with Chronic Obstructive Pulmonary Disease".

Your participation in this study is voluntary. If you do not want to be in the study, this will not affect your routine care.

Before you decide if you want to be in this study, it is important that you read and understand the information on this form. Please read this information carefully and be sure to ask questions about anything that is unclear. Your doctor will answer your questions on the study or any of the information presented here. It is important to know that no study-related tests or procedures will be performed before you sign this consent form.

Why am I being invited to take part?
You are being invited to take part in this research study because you have been diagnosed with a lung condition called chronic obstructive pulmonary disease (COPD). Despite advances in care, heart disease is the biggest killer in the United Kingdom. Patients with COPD are known to be at an increased risk of heart disease and death due to heart attacks. We think one of the causes of this may be an "increased stickiness" of the blood in patients with COPD. This stickiness may give rise to more blood clot formation than normal and might happen in the heart arteries leading to a heart attack. In addition to your standard COPD inhalers, new treatments are needed to protect you against this risk. Treatments that prevent blood clot formation might protect COPD patients from future heart attacks. Medications such as Aspirin and another new blood thinning tablet called Ticagrelor are now routinely used in patients with coronary artery heart disease and following heart attacks. However, these medications have not been studied in the prevention of heart attacks in patients with COPD.

Our research question is therefore "Does the treatment of patients with COPD who may be at a higher risk of future heart attacks reduce stickiness of blood cells called platelets and reduce inflammation". APPLE COPD: ICON-2 is a carefully planned study to investigate if treating COPD patients with heart medications such as Aspirin and/or Ticagrelor will lead to reduced inflammation and/or stickiness in the blood. We hope this study will allow us to design a later larger study seeing if these treatments will ultimately lead to reduced heart attacks and death in COPD patients.

Why is the research being done?
The purpose of this study is to evaluate whether treatment with Aspirin and/or Ticagrelor will lead to less stickiness of your blood cells at 1-month and at 6-months. We will also evaluate if this has any benefit on improving your breathing capacity, reducing inflammation levels in your body and reducing any future cardiovascular events.

Do I have to take part?
You do not have to take part in this study. Your participation in this study is voluntary and you may stop participating at any time. Your decision not to take part in this study or to stop taking part, after you have started, will not affect your medical care or any benefits to which you are entitled to. If you decide to stop taking part in this study, you should tell the study doctor right away.

What will happen to me during this study?
If you agree to participate in this study, you will undergo normal routine care in the management of your COPD that is offered to any patient that presents to the hospital with your condition. If you are eligible you will be asked to read this Participant Information Sheet and sign the Informed Consent Form. A copy of the signed Informed Consent Form will be provided to you for your records. You will then be invited to attend the COPD research clinic at the Newcastle NIHR Clinical Research Facility**,** Level 6, Leazes Wing, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne, NE1 4LP where we (a member of the research team) will perform the study procedures.
In order to be in the study, you must be willing to be available and agree to have all the required tests, take the medications provided to you, and to return for follow-up clinic at 1-month, 3-months and 6-months.

If you agree to take part in this study, the following will happen:
You will be required to attend the research clinic for 5 visits (baseline, 1 month, 3 months, 6 months and at 1 - year).

At the research clinic: You will undergo the following procedures by the research team:

1. We would like to ask you a few questions about how you are feeling using quality of life questionnaires
2. Calculate your future risk of heart disease using an electronic online calculator called the QRISK 2 score calculator.
3. A 30 mls blood sample will be taken.
4. We will perform a lung function test using Spirometry, an ultrasound scan to measure the thickness of your neck artery, and we will measure how stiff your arteries are using a specialised blood pressure cuff (this involves some pressure on your arm but no needles.)
5. You will be randomly allocated to one of 4 treatment groups (1. Aspirin & Placebo (dummy tablet), 2. Ticagrelor & Placebo, 3. Placebo alone, 4. Aspirin and Ticagrelor). Neither you or the study team can chose which treatment arm you get- this is chosen at random using a computerized system. During the study no one will know which treatment arm you get.
6. We will ask you to take your allocated medication for 6-months.
7. Following your baseline visit we will ask you to return for follow up visits: at 1-month (you will undergo further blood tests and we will review your medications), 3-months (we will review your medications), 6-months (we will review your medications, you will also undergo the procedures listed in 3 and 4 above) and at 1 year (we will evaluate your health and well-being).

How long will I be in the study?
Once you have undergone the above additional procedures, your treatment will continue as per normal routine care. However, we will follow you up at 1-month, 3-months, 6-months and at 1-year.

During the 1-year follow-up, we will collect additional information about your wellbeing. This can be done at the research clinic or via telephone.

What will happen to me when the study ends?
You will continue to receive routine normal care like any other patient with your condition under the care of your chest physician.

What are the possible benefits of taking part in this study?
There are no direct benefits to you for participating in this study. However, your participation in this study may add to the medical knowledge about how to treat COPD patients who are at risk of future heart problems. At present there is very little information in the literature about the best ways of treating COPD patients at risk of future heart problems. Information learned from this study may benefit you and others in the future.

What are the possible risks or side effects of taking part in this study?
The additional risks as a result of participation in the study are explained below if you agree to take part in the study.

1. We would like to ask you a few questions about how you are feeling using quality of life questionnaires
   No risk to you with regards to answering simple questions specific to the study.

2. Calculate your QRISK2 score (this is based on simple questions).
   No risk to you.

3. Blood samples.
   No risk beyond usual blood sampling: samples will be obtained by experienced research team members.

4. Lung function tests using Spirometry, an ultrasound scan to measure the thickness of your neck artery using an ultrasound machine and we will measure how stiff your arteries are using a specialised blood pressure cuff.
   No risks to you with Spirometry as you already have had this done as part of routine care.
   No risk is anticipated to you undergoing an ultrasound scan of your neck arteries (other than slight pressure with the placement of the probe in your neck area).
   No risk to you with regards to measuring the stiffness of your arteries using a blood pressure machine.

5. You will be randomly allocated to one of treatment 4 groups (1. Aspirin & Placebo, 2. Ticagrelor & Placebo, 3. Placebo alone, 4. Aspirin & Ticagrelor). These medications are licensed and already in use for patients with heart disease. They have some recognized side effects as specified below.

   Aspirin:
   Low dose (75 mg) Aspirin is a very commonly used medication to treat patients with heart disease. With Aspirin there is a very small risk of allergic reactions, indigestion and bleeding with more serious bleeding (bleeding in stomach, gut, or brain) occurring in approximately 7 in 1000 at 1 year of treatment.

Ticagrelor:

Likewise Ticagrelor is another medication that has been well tested previously and is routinely used in patients with coronary heart disease. The following side effects of Ticagrelor were reported in studies of patients with coronary artery disease.

a) ***A very small risk of worsening breathlessness (approximately 1 in 100 stopped Ticagrelor treatment because of breathlessness, smaller changes in breathlessness seen in approximately 14%),***
b) ***A slowing of the heart rate (approximately 1 in 20 had a slowing of the heart rate, much less approximately 1 in 100 needed pacemaker implantation)***
c) ***Any bleeding approximately 12 in 100, approximately 9 in 100 bleeding requiring blood transfusion, and fatal bleed approximately 0.3% in one year.***

However 10 – 20% of patients with COPD have an increased risk of cardiovascular adverse events without any treatment, and therefore the benefit of therapy with the above medications likely outweighs the risks.

What will happen to the blood samples in the future?

It will take us about 2 years to get all the results of this study and publish them. When we have completed this, the samples will be destroyed (all samples destroyed by 5 years).

What if new information becomes available?

Your doctor will tell you about any important new information learned during the study that might be of relevance to you.

Expenses and Payments

You will not be paid for taking part in this study. However, your travel expenses will be reimbursed for your visits to the clinic. Taxis to and from visits can be arranged by a member of our team. You may choose to use your own method of transport, in which case we will reimburse the costs associated with your travel such as bus/train fares and/or parking tickets.

What other treatments are available?

If you agree to participate in the study, you will receive all treatments that are currently provided and are available to all NHS patients with your similar condition. However, you will receive additional comprehensive evaluation using the additional tests specified above.

Confidentiality of Study Records and Medical Records

You have a right to privacy, and all information that is collected will be kept confidential to the limit that is possible by law. Your data such as study records, information about your general health, your cardiac status or concomitant medication, and all other relevant information specific to the investigations you undergo as part of the study will be collected by the doctor. Electronic data will be stored in a secure password protected database designed specifically for the study. Paper data collection forms will be stored in study specific filing cabinets that will be locked under the supervision of the Principal Investigator and the nominated study research team members.

You will be identified only by a unique code number and information about the code will be kept in a secure location and access limited to research study personnel. The study doctor and the study staff will have access to the code list. The data will be coded, stored, and protected for at least 10 years after completion/discontinuation of the study.

Will my GP be informed of my participation in the study?

With your permission, your GP will be notified of your participation in APPLE COPD: ICON-2 study along with your hospital discharge summary letter.

Who is organising and funding the research?
This study is funded by the pharmaceutical company Astra Zeneca as an educational research grant to Dr. Vijay Kunadian Senior Lecturer at Newcastle University and a Consultant Interventional Cardiologist at the Freeman Hospital.

Names of Contacts for Questions about the Study
If you have questions regarding any of the above information or your taking part in the study, please contact:

Chief Investigator and Consultant Interventional Cardiologist:
Dr. Vijay Kunadian MBBS, MD, FRCP
Tel.: +44 191 2085797
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Principal Investigator and Consultant Respiratory Physician:
Dr. A De Soyza MBChB, PhD
Sir William Leech Centre, Freeman Hospital, High Heaton, Newcastle-upon-Tyne, NE7 7DN
Tel: 0191 2231608
Email: anthony.de-soyza@ncl.ac.uk

If you have any concerns about any aspect of this study, you should ask to speak to the study doctor/research team on **0191 282 0070** and they will do their best to answer your questions.

If you are unhappy or wish to make a formal complaint, you can do this through the hospital complaints department or PALS:
Freepost: RLTC-SGHH-EGXJ
North of Tyne PALS, The Old Stables, Grey's Yard
Morpeth
NE61 1QD
Tel: 0800 0320202 or Email: northoftynepals@nhct.nhs.uk

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APPLE-COPD: ICON2

Patient Informed Consent Form

Participant ID: |___|___|___|___|___|

Study Chief Investigator: Dr. Vijay Kunadian Consultant Interventional Cardiologist
Study Principal Investigator: Dr. A De Soyza, Consultant Respiratory Physician

Please initial box

- I have read and understood this information sheet (Version 3.0, dated 27/06/2016) and have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. ☐
- I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without harming my future medical care or losing any benefits to which I might be otherwise entitled. I also understand that the investigator in charge of this study may decide at any time that I should no longer participate in this study. ☐
- I agree to my data being used and processed as described in this information sheet and understand it may be transferred outside of the UK and EU. ☐
- I understand that relevant sections of my medical notes and data collected during this study may be looked at by individuals from regulatory authorities or from the NHS trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
- I agree to my GP being informed of my participation in this study. ☐
- By signing this consent form, I have not waived any of my legal rights or released the parties involved in this study from liability for negligence. ☐
- I have read and understand the above information. I agree to participate in this study. ☐

Study Participant: Print Name	Study Participant: Signature	Date

Person taking consent: Print Name	Person taking consent: Signature	Date