**Summary Participant Information Sheet**

**Study title:** ACCORD-2: A Multicentre, Seamless, Phase 2 Adaptive Randomisation Platform Study to Assess the Efficacy and Safety of Multiple Candidate Agents for the Treatment of COVID-19 in Hospitalised Patients

**Study protocol:** ACCORD-2-004

**Study drug:** Acalabrutinib, referred to throughout the document as the “study drug”

**Sponsor of the study:** University Hospital Southampton NHS Foundation Trust, Southampton General Hospital, Southampton SO16 6YD, UK

**Investigator:** <Investigator’s Name>

Please take time to read the summary below. If you decide you are interested in taking part, you will need to sign the consent form. The study doctor or study nurse will discuss the study with you. You will have time to think about whether you wish to join the study. You will also be able to ask any questions if you are unsure about anything to do with this study. The study doctor or study nurse will answer any questions you may have. Additional detailed information is provided in the Main Participant Information Sheet, you should keep both the Summary and Main Participant Information Sheets for reference.

**Introduction**

You are being invited to take part in this research study because you have been feeling unwell with symptoms caused by a virus called SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2). The disease that the virus causes is called COVID-19.

**What is the purpose of the study?**

This research study is being done to test whether medicines which we think may work against SARS-CoV-2 might be able to help people with COVID-19. At the moment, there are very few medicines approved to treat COVID-19 and new ones are required to improve outcomes of COVID 19.

Hospitals, researchers and the UK Government are working together to see if existing treatments for other conditions or diseases or new drugs may be used to treat people with COVID-19. To do this, several treatments will be tested, one at a time, in people with COVID-19. Medications tested in this study are investigational, which means they have not been approved by health authorities, such as the European Medicines Agency (EMA), for treating COVID-19.

**What medication is being tested?**

All participants taking part in this study will continue to receive the currently accepted medical standard-of-care for COVID-19.

In this study, acalabrutinib will be tested as a potential treatment for COVID-19. Acalabrutinib is being developed by AstraZeneca AB. Acalabrutinib capsules (100mg) will be taken twice a day for 10 days. You will swallow the capsules whole with one cup of water. If you are not able to take acalabrutinib by mouth for more than 24 hours, you will need to stop taking part in the study.

During a viral infection, cells in the immune system can release substances called cytokines, which may lead to lung inflammation (redness and swelling). Acalabrutinib blocks the activity of a protein called Bruton tyrosine kinase (BtK) found on certain type of immune cells, which interferes with the release of cytokines. It is hoped this will help reduce lung symptoms in people with COVID-19

If you take part in the study, you will be randomly assigned and have a chance to receive ”acalabrutinib with standard-of-care” or “standard-of-care only”, with more people receiving acalabrutinib. About 90- 120 people are expected to receive either “acalabrutinib with standard-of-care” or “standard-of-care only”. This is Stage 1. If it is deemed that acalabrutinib should continue to be tested, about 252 people are also expected to receive either “acalabrutinib with standard-of-care” or “standard-of-care only” This is Stage 2.

**How long will I be in the study?**

You will be in the study for approximately 90 days (3 months).

**What will happen if I take part in the study and what will I have to do?**

The study consists of 3 periods:

* Screening period – up to 2 days, to check that the study is right for you
* Treatment period – up to 15 days, to receive either the study drug with standard-of-care or standard-of-care only as randomly assigned (by chance)
* Follow-up period – up to 3 months, to check how you are doing and if you have had any side effects from the study drug

If you agree to participate, you will undergo some tests to check that the study is right for you. These include:

* Pregnancy testing if you are a woman who is able to become pregnant
* Physical exam and vital signs
* Electrocardiogram (ECG): A painless test to check the health and rhythm of your heart
* Chest x-ray or CT scan to look at your lungs
* Collection of blood, saliva (spit), throat/nose swab samples for testing

If the study is right for you and you are assigned to receive acalabrutinib, you will take it by mouth twice a day for 10 days (20 doses total). You will be given the study drug as a 100 mg capsule. It will need to be swallowed whole with a cup of water (about 240 mL). The doses should be taken 12 hours apart at about the same time every day, with or without food. If you vomit after taking a dose, you should not retake it and wait until your next scheduled dose. If you are not able to take the study drug by mouth for more than 24 hours, you will need to stop taking part in the study.

You will have some tests and assessments, and be asked to provide samples, while in the hospital. These include:

* Checking your health, heart, and whether you need oxygen
* Taking blood, saliva (spit),and throat/nose samples to check your health
* Blood samples to check the amount of study drug in the body (called “pharmacokinetics”)
* Blood samples to study what the study drug does to the body (called “pharmacodynamics”)

About 341 ml (about 23 tablespoons) of blood will be taken from you over the entire study.

Some of the tests and assessments being done in this study would also be done as part of your standard-of-care for COVID-19, even if you did not participate in this study.

There is preliminary evidence that some people may be more susceptible or have worse symptoms and outcomes because of their genetic makeup; therefore, one exploratory objective is whole genome sequencing of your DNA (the “instruction book” of your body). Analysis of your DNA will allow genetic factors to be further studied.

After you are discharged from the hospital, you may have up to 4 additional visits to the study centre. If you are not able to visit, a member of the study team may call or come to see you at home.

We will also ask you to allow the use of your leftover samples for future scientific research and provide optional blood samples for additional research. If you do not agree, you will still be able to take part in the main study and your medical care will not be affected.

Additional detailed information about the study tests and assessments is provided in the Main Participant Information Sheet.

**What are the risks or benefits of taking part in the study?**

Although there is no guarantee that you will benefit from taking part in this study, it may be possible that the treatment helps symptoms improve. However, your condition may stay the same or worsen, during your participation in this study. Acalabrutinib may also involve risks to your future health that we currently don’t know about.

The following side effects have been reported for acalabrutinib

**COMMON** (occurring in more than 1 in 10 people)

* Headache
* Nausea (upset stomach)
* Diarrhoea (loose stool)
* Constipation (hard stool)
* Feeling tired
* Dizziness
* Other infections
* Bruising
* Joint and muscle pain
* Skin rash
* Low white blood cells
* Low iron in the blood
* Vomiting or stomach pain
* Bleeding

*If you suffer any of these side effects (or any others not listed) or you think you are experiencing a side effect during this study, please tell your study doctor immediately.*

In addition to the risks of taking the study drug, there are other risks that are associated with taking part in the study and some of the study procedures.

Imaging: The information from certain tests already performed by the clinical team to help manage your condition will be collected and used to understand your condition and response to treatment – this includes chest X-ray or computed tomography (CT) scan. Additional chest X-ray or computed tomography (CT) scan may have important safety benefits for you, but should be considered additional to your normal care outside of this research study.

Pregnancy:

We do not know how the study drug effects pregnancy during the first 3months. Because we do not know how the study drug may affect a developing foetus, or whether it will cross to a baby through breastmilk, women who are pregnant may not participate in this study. Women who are producing breastmilk must agree not to breastfeed their child during the study and for at least 3 months after finishing the study drug (they may continue to make breastmilk away from the child during this period, but this milk must be discarded). If you are a woman who is able to become pregnant, you will be advised to use an effective method of birth control whilst taking the study drug, and for at least 3 months after you have finished in order to prevent pregnancy. If you become pregnant during the study, please tell the study doctor immediately.

If you are male and taking the study drug, with a female sexual partner who may become pregnant, you must use a condom and your partner should use an effective form of contraception during the study and for at least 3 months after you have finished taking the study drug. You should not donate sperm during the study and for 3 months after you have finished taking the study drug.

The acceptable forms of contraception to use in this study include:

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| --- | --- |
| **If you already use any of the methods below, you may continue to do so:** | **Otherwise, you will need to use one of the methods below:** |
| For women:* intrauterine device (IUD/IUS)
* bilateral tubal occlusion
* depot contraception (implant/depo-provera)
* oral contraceptive pill with a barrier method (condoms used by your partner)
* abstinence (if part of your usual and preferred lifestyle)

For men:* vasectomy
* condoms
* abstinence (if part of your usual and preferred lifestyle)
 | * male or female condom (preferably with spermicide)
* cap, diaphragm or sponge (preferably with spermicide)
* combination of male condom AND either cap, diaphragm or sponge (each with spermicide)
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You will be monitored closely throughout your participation.

**What if something goes wrong?**

University Hospital Southampton NHS Foundation Trust, as the research Sponsor, has arrangements in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial. The study doctor can advise you of further action and refer you to a doctor within the NHS for treatment, if necessary.

**What alternative treatments are available?**

Your taking part in this study is voluntary – you do not have to take part to be treated for your condition. There are no currently approved treatments for COVID-19. However, your study doctor will discuss with you any other investigational drugs or supportive treatments that may be available. They will also discuss their risks and benefits. If you decide not to take part in this study, it will not affect your ability to receive medical care.

**What happens when the research study stops?**

You will receive the study drug with standard-of-care, or just standard-of-care while taking part in this study. When you have finished taking part in this study, you will not continue to receive the study drug. The care you receive after the study has ended will be the usual care given to individuals recovering from COVID-19 according to their medical needs after recovery.

If you have a reaction to the study drug, if you do not follow study team instructions, or if it is decided that it is safer for you not to participate in the study, then your participation may be stopped at any time by the study doctor or Sponsor without your consent.

If the study is stopped, you will be told and your study doctor will make arrangements for the continuation of your care.

**What else do I need to know?**

* You do not have to take part in this study. Taking part in the study is completely voluntary and if you do decide to be involved, you can choose to withdraw at any time for any reason without it affecting your medical care and legal rights.
* If information becomes available that could change your decision to be in this study, you will be told immediately. You can always decide whether or not to continue being in this study and will be free to withdraw at any time without giving a reason.
* The study Sponsor is responsible for looking after your information and using it properly. All information will be treated confidentially.
* If you require any further information about the trial or your rights as a trial participant, please contact, the study doctor or research team on XXXX.

**Please do not hesitate to ask the study team any questions you may have about the study at any time. You will be given the Main Participant Information Sheet to review for further, detailed information.**