**Legal Representative 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”

**IRAS Number:** 282769

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

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

**Why are we asking the person you represent to take part in this study?**

The person you represent is eligible to take part in this research study because they have been feeling unwell with symptoms caused by a virus and they need to be looked after in hospital. The virus is called SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2). The disease that the virus causes in infected people is called COVID-19.

The study doctor will discuss the information in the summary information sheet, this information sheet and the separate consent form with you, as the person you represent is currently not able to make their own decisions due to the severity of their infection. This information sheet will provide additional information to that in the Summary Legal Representative Information Sheet for further understanding of this research study.

If you decide the person you represent should take part in this study, you will need to sign the consent form on their behalf. You and the person you represent will be given or emailed a copy of this information sheet and the consent formto keep.

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

At hospitals across the UK, universities, companies making medicines, 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. Some treatments act directly against the virus when it gets into the body. Other treatments help the body’s immune system (the natural defence against viral infections) to work better.

As each treatment is tested in people with COVID-19, a group of doctors and researchers will look at the results to see whether it works and how safe it is.

Acalabrutinib will be tested in 2 stages: Stage 1 and Stage 2.

* Stage 1 will test how safe acalabrutinib is when given with standard-of-care. Stage 1 will also look at whether acalabrutinib works to improve symptoms of COVID-19. The information gathered from Stage 1 will be used to see if acalabrutinib should continue to be tested in Stage 2 of the study.
* Stage 2 will continue to look at whether acalabrutinib works when given with standard-of-care and how safe it is. Stage 2 will further look at the effects of acalabrutinib on the disease, such as collecting information on whether symptoms have improved, if care in the intensive care unit is needed, and survival and health status after recovery. In Stage 2, the study doctor and researchers are investigating if acalabrutinib works to lessen the symptoms of COVID-19 or shorten the time people with COVID-19 are ill.

**What medication is being tested?**

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

Standard-of-care is considered to be all other treatments and care that the person you represent is currently receiving at the hospital for COVID-19, without any restrictions or limits.

Acalabrutinib is approved in the United States and other countries for treating certain types of blood cancers. The use of acalabrutinib in this study is “investigational”. “Investigational” means that acalabrutinib has not been approved by health authorities, such as the European Medicines Agency (EMA), for treating COVID-19.

Details of the acalabrutinib dose and how it will be administered are described in the Legal Representative Information Sheet.

If the person you represent takes part in the study, they will be randomly assigned by a computer and will have a chance of receiving one of the following:

* Acalabrutinib with standard-of-care
* Standard-of-care only

Throughout the document, acalabrutinib will be referred to as the “study drug”.

**What will happen to the person you represent during the study?**

The study doctor will tell you which stage of the study the person you represent will be in..

If the person you represent takes part in the study, they are expected to be in the study for about 90 days (3 months).

Screening period

If you decide that the person you represent should participate, you, as their representative, will need to sign the consent form. The study doctor will then collect information about them and their health.

The person you represent will have some tests and assessments to check that the study is right for them. This includes having an electrocardiogram to check how their heart is working. It will also include taking blood samples to check their overall health (including a pregnancy test for women who are able to get pregnant), and blood oxygen levels.

Blood samples will also be taken for exploratory purposes. Please see **Table 1** and section “What will happen to any samples the person you represent gives?”for more information.

These tests and assessments may be done either on the same day that treatment starts, or a day or 2 before treatment starts.

If the study is right for the person you represent, they will enter the treatment period.

Treatment period

The treatment period will last for about 15 days.

The person you represent will be randomly assigned (by chance) to receive either the study drug with standard-of-care or standard-of-care only. You and the study doctor will know if they receive the study drug or not.

The person you represent will have some tests and assessments performed daily while they are in the hospital. These include a check of their health and whether they need oxygen, and taking blood and throat/nose swab samples to check their health. Some of the tests and assessments being done in this study would also be done as part of the standard-of-care for COVID-19, even if they did not participate in this study.

During the treatment period, blood, saliva (spit), or throat/nose swab samples will also be taken for exploratory research and used as follows.

* Blood, saliva (spit), and throat/nose swab samples to check for SARS-CoV-2 levels.
* Blood samples to look at antibodies. Antibodies are specific proteins made by the body’s immune system (natural defence) against the viral infection.
* Blood samples to study substances produced by cells in the immune system. These substances help the immune system fight the viral infection.
* Blood samples to study substances produced by the immune system.
* Blood samples to study their DNA and RNA (the “instruction book” of your body). Researchers would like to learn how differences in genes between people with COVID-19 may affect how they respond to the study drug. DNA testing is not a general diagnostic test. The initial genetic test is not definitive and if any significant genetic findings are discovered then another genetic test will need to be conducted.
* Nose swab to study the RNA (the genetic material) of SARS-CoV-2. Researchers would like to learn more about the virus that causes COVID-19.
* 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”). This will be done by looking at biomarkers. Biomarkers are biochemical substances in the body that can be used to help diagnose a disease, measure the progression of a disease, or study the effects of a treatment.
* Additional chest X-rays or computed tomography (CT) scans may be required for safety reasons and should be considered additional to normal care outside of this research study.

We will also ask you to allow the use of their leftover samples for future scientific research and allow optional blood samples for additional research to be taken. If you do not agree, they will still be able to take part in the main study and their medical care will not be affected. Please see Table 1 and section “**What will happen to any samples the person you represent gives?”** for more information.

If the symptoms of the person you represent improve before completing all the doses of the study drug, they will not need to finish the remaining doses. After taking their last dose on Day 10 or earlier, they will stay at the hospital for at least another 24 hours. During this time, a blood sample will be taken to check their health before they are discharged from the hospital.

Once the person you represent is discharged from the hospital, they will be asked to come back to the hospital on Day 15 and Day 29 if possible. At these visits, some of the previous tests and assessments will be repeated. If they are unable to return to the hospital due to being quarantined or for other safety reasons, some of the tests and assessments may be done by telephone or the hospital may arrange for a home visit by a member of the study team.

The amount of blood taken over the entire study will be about 341 ml (about 23 tablespoons) in total. Additional blood samples may be taken for safety reasons or if there are issues processing the samples.

Follow-up period

After the treatment period, the person you represent may be asked to return to the hospital on Day 60 (after 2 months) and Day 90 (after 3 months). This is to check how they are doing and if they have had any side effects from the study drug. Additional blood samples may also be taken for exploratory research.

Alternatively, they may be contacted by a member of the study team by telephone or they may visit them at home on these days.

If the person you represent is asked to return to the hospital, their reasonable travel expenses will be reimbursed. The study team will be able to advise them on the process for reimbursement.

Please see **Table 1** for a summary of what will happen at each study visit.

**Table 1. Tests and assessments that the person you represent will have**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Day** | **Screening** | **Day 1** | **Daily Until Hospital Discharge** | **Day  15** | **Day  29** | **Day 60** | **Day 90 (End of Study)** |
| **Sign informed consent form** | **X** |  |  |  |  |  |  |
| **Check if the study is right for the person you represent** | **X** |  |  |  |  |  |  |
| **Medical history and disease details** | **X** | **X** | **X** |  |  |  |  |
| **Receive acalabrutinib 100 mg** |  | **X** | **X**  **(Days 2-10)** |  |  |  |  |
| **Receive standard-of-care** |  | **X** | **X** |  |  |  |  |
| **Physical examination (including signs, height and weight)** | **X** |  |  |  |  |  |  |
| **Targeted physical examination (based on symptoms** |  |  | **X (as needed)** |  |  |  |  |
| **Chest X-ray or CT scan** | **X** |  |  |  |  |  |  |
| **Electrocardiograma** | **X** |  |  |  |  |  |  |
| **Check vital signsb** |  | **X** | **X** | **X** | **X** |  |  |
| **Check health** |  | **X** | **X** | **X** | **X** | X | X |
| **Check for side effectsa** |  | **X** | **X** | **X** | **X** | **X** | **X** |
| **Check oxygen levels** |  | **X** | **X** | **X** |  |  |  |
| **Blood sample to check healtha** | **X** |  | **Days 3, 5, 8 , 11 (if in the hospital)** |  |  |  |  |
| **Pregnancy test for women who are able to get pregnant** | **X** |  |  |  |  |  | **X** |
| **Blood samples to check SARS-CoV-2 levelsa** |  | **X** |  |  |  |  |  |
| **Saliva (spit), throat/nose samples to check SAR-CoV-2 levelsa** |  | **X** | **Days 3, 5, 8 , 11  (if in the hospital)** | **X** | **X** |  |  |
| **Blood samples to study types of cells in the immune system (optional)a** |  | **X** | **Days 3 and 8  (if in the hospital)** | **X  (if are in the hospital)** |  |  |  |
| **Blood samples to study substances produced by the immune systema** |  | **X** | **Days 3, 5, 8, 11  (if in the hospital)** | **X**  **(if in the hospital)** | **X**  **(if in the hospital)** |  |  |
| **Blood samples to check antibodiesa** |  | **X** | **Day 8  (if in the hospital)** | **X**  **(if in the hospital)** | **X**  **(if in the hospital)** | **X** |  |
| **Blood samples for genetic (RNA) testsa** |  | **X** | **Days 3 and 8  (if in the hospital)** | **X (if in the hospital)** |  |  |  |
| **Blood (DNA) or nose swab (RNA) samples for genetic testsa** |  | **X** |  |  |  |  |  |
| **Blood samples for pharmacodynamic testinga** |  | **Xc** | **Day 3** |  |  |  |  |
| **Blood samples for pharmacokinetic testinga** |  |  | **Day 3** |  |  |  |  |
| 1. These tests or assessments are not part of the usual standard-of-care for COVID-19 and are specific to this study only. 2. Includes checking body temperature, heart rate, breathing rate, blood pressure, and blood oxygen level. 3. Will be collected before taking acalabrutinib and 4 hours after taking acalabrutinib 4. Will be collected before taking acalabrutinib, and 30 minutes, 1, 2, 4, and 6 hours after taking acalabrutinib | | | | | | | |

**What will the person you represent have to do?**

* The person you represent should follow the instructions the study doctor or other study team members give them.
* The person you represent should take the study drug as instructed.
* The person you represent should attend all scheduled study visits, or arrange for telephone follow-up after they go home from the hospital, if their circumstances prevent them from returning to the hospital.
* The person you represent should answer all questions completely and honestly.
* The person you represent should not take part in any other studies while they are taking part in this study, unless the study doctor advises it is safe for them to be co-enrolled to another study where they receive a study drug.
* The person you represent must follow the guidance for pregnancy and use an effective form of birth control during the study as described in the Summary Legal Representative Information Sheet.

**What will happen to any samples the person you represent** **gives?**

As part of this study, blood, saliva (spit), and throat/nose swab samples will be taken from the person you represent. These samples will be used for exploratory research to learn more about SARS-CoV-2 and how the study drug works.

If you agree to **optional** blood samples for additional research to be taken, these blood samples will be used to study the types of cells in the immune system.

You do not need to agree to these samples being taken. It will not affect the person you represent’s participation in the study or the medical care they receive.

After processing, samples will be sent to the approved academic or commercial researchers through a sample access process managed by The UKCRC Tissue Directory and Coordination Centre (TDCC), a publicly funded tissue directory initiative hosted at Nottingham University, England.

By gathering more data on individuals with COVID-19 and linking this to their medical records and medical history, researchers will be able to understand more about COVID-19 in each individual testing positive for SARS-CoV-2, how SARS-CoV-2 infects people, and why some people have worse symptoms and outcomes than others. This will provide insights for new treatments and the development of new tests that can be used for diagnosis and also to help understand if people become immune and for how long.

The virus itself may be changing as it spreads through the population and studying the viral genome in the samples of the person you represent will allow research into this. This information is extremely valuable for public health planning purposes and for developing new tests, vaccines and treatments.By taking part in this study, the person you represent is asked to do the following:

* Grant access to their medical records (past and future)).
* Provide blood, saliva (spit), and throat/nose swab samples.
* Agree that these samples can be used by approved researchers, possibly outside the UK, that may include for profit companies as well as academic institutions.
* Allow the storage of any residual (leftover) samples for future healthcare related research studies. Samples will be given to researchers through a managed access process where only approved researchers with approved projects will be given access.
* Allow us to store, process and share their coded data (without personal identifiers) with approved researchers. Data may be stored in the cloud and will follow all security procedures and compliance with privacy regulations.

**Will the person you represent be told results of their samples being used for exploratory research ?**

Generally, we will not tell the person you represent the results of the tests done on their samples or their DNA, and it is unlikely they will benefit directly from the results of these exploratory studies. However, if we learn of something that is thought to be medically significant, to them and/or their family, and they agree, the person you represent and their GP can be notified of this information. Medically significant results can sometimes have implications for treatment options, or they might be of importance to other family members. For the safety of the person you represent , any such results from this study would be checked and their GP and/or a specialist service would discuss them with you or the person you represent.

The participation of the person you represent in the research will help research efforts to understand COVID-19 and for the development of drugs and tests that could help many other people in the future.

**What could be the side effects of the study drug?**

All medicines may cause some side effects in some people. It is very important that the person you represent report any changes to their health to the research team, as soon as possible.

We will ask the person you represent about any side effects or other health issues occurring during the study, as described in the Summary Legal Representative Information Sheet, and continue to check on these, if they do happen.

*If the person you represent suffers any of these side effects (or any others not listed) or the person you represent thinks they are experiencing a side effect, during this study, please tell the study doctor immediately* (see ‘Who should I contact for more information?’).

**What are the possible disadvantages or risks of taking part?**

It is possible that the symptoms of their condition will not improve during the study or may even worsen. The study drug may also involve risks to their future health that we currently don’t know about.

There are other risks associated with the COVID-19 infection and the use of supplemental oxygen, but they are not specific to this study.

Please refer to the Summary Legal Representative Information Sheet for further information

**What if I have a question?**

If you have a question, concern or complaint about any part of this study, you should ask to speak to the study doctor or a member of the research team, who will do their best to help (see ‘Who should I contact for more information?’).

If you have any questions about their rights as part of the research, or any concerns or complaints about the research that you do not want to discuss with the study doctor or research team, see ‘Who should I contact for more information?’.

If the person you represent suffers a serious illness or injury during this study, please contact the study doctor immediately (see ‘Who should I contact for more information?’).

**Compensation for study related injury**

The participation of the person you represent will be covered by the NHS Indemnity Scheme, which will cover any study-related injury or clinical negligence.

**What if something goes wrong?**

The investigators recognise the important contribution that participants make to medical research, and make every effort to ensure their safety and well-being. University Hospital Southampton NHS Foundation Trust, as the research Sponsor, has arrangements in place in the unlikely event that the person you represent suffers any harm as a direct consequence of their participation in this trial.

In the event of harm being suffered, while the Sponsor will cooperate with any claim, the person you represent may wish to seek independent legal advice to ensure that they are properly represented in pursuing any complaint. The study doctor can advise them of further action and refer them to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment which may be provided if they needed to be admitted to hospital.

**What if new information about the study drug becomes available?**

Sometimes new information about the study drug is received. You will be told if any relevant new information becomes available that may affect your willingness to allow them to carry on taking part in the study. If this happens, the study doctor will contact you as soon as possible, and will discuss whether they should continue in the study. If you decide they should not carry on, their study doctor will make arrangements for their care to continue. If you decide they should continue in the study you may be asked to sign a new consent form.

Also, if new information becomes available, the study doctor may stop the participation of the person you represent. If this happens the reasons will be explained and arrangements made for their care to continue.

**What will happen if I do not want the person I represent to carry on with the study?**

The person you represent can stop taking part in the study at any time without giving any reason. This will not affect their future treatment or their relationship with the study doctor. If you wish the person you represent to stop taking part, please tell the study doctor immediately. Even if they stop taking the study drug for any reason, it is important for us to continue to monitor their health and some routine measurements will continue (such as blood pressure, whether or not they are in Intensive Care, or breathing for themselves, etc). If the person you represent has already been released from the hospital, they may be asked to return to the study centre for an end-of-study assessment. They may also be asked for permission to be contacted at a later date by their doctor to collect minimum additional data about their condition. If you do not wish us to collect such new information, we will not do so but will still use the information that has already been collected.

If you wish the person you represent to stop taking part in this study, you can ask that any samples taken from them in this study are not to be stored for further research. Instead, their samples will be destroyed.

**Will taking part in this study by the person you represent be kept confidential and how will their personal information be used?**

The study doctor and research team will collect, record and use personal information about the person you represent for the study purposes. The personal information collected during the study may include sensitive information about the person you represent, their physical or mental health or condition, and health information about them in medical records, and other personal information such as their name, address, telephone number, age, and gender. It may also include information related to the tests and procedures done in the study, including from any blood or tissue samples taken from them, or that they donate voluntarily during the study. This information is stored in their personal medical records at the study centre.

This study will also collect information about the race and ethnicity and/or the full date of birth of the person you represent.

The race and ethnicity of the person you represent is considered sensitive personal information under data protection law. The results of this study will be grouped by race and ethnicity. This will help to decide if race and/or ethnicity affect if the study drug works and how safe it is in different populations.

The full date of birth of the person you represent needs to be collected because it is required to calculate their age at entry into the study.

If you decide that the person you represent would agree to give this information, their race and ethnicity and/or their full date of birth will be collected and entered into the same database where the other data about them will be entered, stored, and protected during this study.

The privacy and personal information of the person you represent will be protected. Any information about them that is collected during this study will remain confidential. The Sponsor estimates that their personal information will be stored for approximately 15 years after the end of this study.

All information which is collected about the person you represent in records that leave the study centre for the purposes of analysis, and medical, laboratory, statistical or regulatory activities related to the study research will be identified only by their study subject number. Their full name or any other directly identifiable information about them will not be included in these records. Only the study doctor and study centre will have access to information that can link them to their study subject number; this information will not be shared outside of the study centre unless necessary for safety purposes.

During the study, the collected personal information of the person you represent including their medical files may be disclosed to the Sponsor, its representatives assisting with the study research, including the central laboratory, study monitors, and to auditors, government or regulatory health authorities. Their records will be kept secure at all times and treated in accordance with UK law

The samples of the person you represent, the data derived from any analyses of those samples and the personal information found in their health records will be collected by IQIVA, an organisation working with the Sponsor of this study to perform clinical research studies. The information from the study may be published or sent to regulatory authorities in the UK or other countries. The identity of the person you represent will not be released except with permission, unless necessary for the vital interests of their safety. Data, including linked medical record data, will be collected into a research database which will be made accessible to approved researchers through a managed access process governed by a scientific advisory board of experts.

By signing the consent form, you, on behalf of the person you represent, are giving permission for the processing and use of the personal information of the person you represent for this study. The samples and information of the person you represent will not be released for other uses without their prior consent, unless required by law. You are also giving permission, on behalf of the person you represent, for the processing of their personal information or any part of it to be transferred to people and organisations (mentioned above) outside their country, where personal data protection laws may be different to those in their own country. If their personal information is accessed or processed outside of their country, the Sponsor will ensure that the privacy and confidentiality of their information is protected according to the data protection laws and regulations applicable in their country. The Sponsor needs to manage the records of the person you represent in specific ways for the research to be reliable. This means that they won’t be able to let you or the person you represent see or change the data they hold about them. You or the person you represent can object to any further processing of their information by applying to their study doctor.

The study doctor will tell the family doctor (GP) of the person you represent about their taking part in the study and may ask them for medical information about them.

The results of this study will be used to make informed clinical decisions for developing new treatment uses for these medications. If you want the results to be made available, please talk to the study doctor.

**Who has reviewed the study?**

All research studies are reviewed by an independent group of people, called a research ethics committee to protect the safety, rights, well-being and dignity of the person you represent. This study has been reviewed and has been given a favourable opinion by the Research Ethics Service of the UK NHS Health Research Authority.

The Sponsor, Regulatory Authorities or the Ethics Committee may stop the study at any time where there is good reason.

**Who should I contact for more information?**

If you have any questions about the person you represent’s participation in the study, please contact the study doctor or research team. Within the European Community, the processing of the personal information of the person you represent will be carried out under the responsibility of the data controller. The data controller for this study is the University Hospital Southampton NHS Foundation Trust, who is the Sponsor of this study. If you have any questions about personal data protection rights of a participant in this study, or a complaint about the use of their personal information, please liaise with the study doctor or research team. The team will then be able to direct your questions to the Sponsor’s Data Protection Officer or the Sponsor’s Data Representative as needed.

Study Doctor Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Study Doctor Phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Study Nurse Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Study Nurse Phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

(where applicable)

24 hours Emergency Contact Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

24 hours Emergency Contact Phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[England only] Patient Advice and Liaison Service (PALS) Number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[Non-England] Independent Advisor Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[Non-England] Independent Advisor Phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

The person you represent also has the right to complain about the collection, processing, use, and disclosure of their personal information to a supervisory authority. The supervisory authority may be the national data protection authority of their country, the Information Commissioner’s Office, or the national data protection authority of the EU Member State where the Sponsor, or their EU Data Representative, is located.

**Thank you for reading this and considering if the person you represent will take part in this study.**