# An international multicentre randomised controlled trial to assess the effect of Appendectomy on the Clinical Course of UlceRativE colitis; UK Arm

## PATIENT INFORMATION SHEET

## Version 4.0; 3rd June 2021

## Summary of the invitation to take part in a research study called ACCURE-UK 2

- Your medical team have identified that you are potentially suitable to enter a trial of a new treatment for your Ulcerative Colitis (UC).
- This hospital is taking part in a study called **ACCURE-UK 2**, which aims to find out whether removing the appendix (with a minor surgical operation called an appendicectomy) can reduce the chances of flare-ups of UC in the future.
- One group of patients in **ACCURE-UK 2** will undergo an appendicectomy operation in addition to their tablet medications for UC. The other will simply carry on with their tablet medications.
- Patients will be allocated to both groups at random (like tossing a coin) to make sure the two groups are comparable.
- You do not have to take part in **ACCURE-UK 2,** and if you decide not to, no-one will think badly of you and this will not affect the quality of your care in any way.
- Please take time to think about whether you want to take part in the **ACCURE-UK 2** study. More details are provided below and your medical team will be happy to answer any questions.

## An invitation to take part in a research study called ACCURE-UK 2

We would like to invite you to take part in a research study called **ACCURE-UK 2**. Joining the study is entirely up to you. Before you decide whether or not you wish to take part in **ACCURE-UK 2**, you need to understand why the research is being done and what it will involve for you.

- **Part 1** below tells you the purpose of this study and what will happen to you if you take part.
- **Part 2** gives more detailed information about the conduct of the study.
- **Part 3** gives information on additional research within the study.

Please take time to read this information carefully and ask us if there is anything which is unclear or on which you would like more information. Take your time to decide whether or not you wish to take part.

# PART 1

### What is the purpose of the ACCURE-UK 2 study?

ACCURE stands for: **A**ppendicectomy to impact upon the **C**linical **C**ourse of **U**lce**R**ativ**E** colitis. The ACCURE study was developed by researchers at the Academic Medical Centre (AMC), University of Amsterdam in the Netherlands. **ACCURE-UK 2** is the UK arm of a group of studies that are being run here and in the Netherlands. The University of Birmingham is the sponsor for the UK arm.

The overall aim of the research is to find out whether removing the appendix (appendicectomy) can reduce the chances of a patient experiencing further flare-ups of their Ulcerative Colitis (UC) in the future months.

### Why is this research study being undertaken?

Most UC patients remain on long-term medication to maintain their lifestyle and prevent flare-ups of disease. Even on this maintenance medication, over one third of patients who have had a flare-up of their disease will suffer from another attack within the following twelve months. If this happens, many will require escalation of their medication, including taking steroids. These flare-ups also carry additional impact upon patients' ability to work and undertake childcare, as well as on their overall quality of life. Doctors are constantly looking for new ways to manage UC, including developing new drugs to try to prevent or limit disease activity.

There is some evidence that the appendix has a role in the regulation of inflammation within the bowel, and that removing the appendix may have an impact upon disease activity in UC patients. This evidence is not yet strong enough to recommend that all patients with UC would benefit from having their appendix

removed. We feel that this is an interesting and exciting potential treatment option for UC, and aim to explore it further within this research.

## Why am I being invited to take part in ACCURE-UK 2?

Your medical team have identified you as being potentially eligible to enter the **ACCURE-UK 2** trial because you have proven ulcerative colitis and have experienced a flare-up (relapse) of your disease symptoms within the last twelve months, but your disease is currently inactive (in remission).

You also have not previously had your appendix removed and have not been involved in any other trial of a new treatment for UC within the last six months. If any of these facts are not true, please inform the research team as this will probably mean you are not suitable for this trial.

The medical teams involved in your UC care are collaborators in the **ACCURE-UK 2** study as they feel the study asks an important question. As such they are inviting all of their eligible patients to take part in the trial. Your doctors think that taking part in **ACCURE-UK 2** is a good option to help find out if the new treatment might work to help patients suffering from UC.

## Do I have to take part?

No. Taking part in any research is voluntary. If you decide to take part you will be given this information sheet to keep and later asked to sign a consent form, but you are still free to withdraw at any time and without giving a reason. If you decide not to take part you don't have to give any reason but if you are willing to tell us we would like to know. Your care will not be affected in any way and you will receive the standard care you would otherwise be given at this hospital. Your gastroenterologists, surgeons and nurses will be happy to talk through any questions you may have regarding **ACCURE-UK 2**.

## What does removal of the appendix (an appendicectomy operation) involve?

To remove a patient's appendix requires a minor operation (appendicectomy) performed under general anaesthetic. The appendix is a small, finger-shaped organ protruding from the large bowel in the lower right side of your abdomen (tummy). In this trial the operation would be undertaken by a consultant specialist colorectal surgeon, using a laparoscopic (keyhole) technique. This would normally be a day-case operation, meaning you will be able to go home on the same day, but an overnight stay in hospital may be required in some cases.

The surgeon will make three small cuts on the tummy (1-3 cm each) to perform the surgery to remove the appendix. The operation takes around 30-45 minutes. Patients will feel some pain relating to the wounds and the operation site and this can last for up to two weeks after surgery. The most common complication after appendicectomy is a superficial infection in one of the wounds, and this occurs in around 5% (one in twenty) of patients. Other minor post-operative complications such as nausea, shoulder pain or sluggish bladder function can also occur for the first few hours after surgery and in our similar study looking at the feasibility of undertaking appendicectomy in UC patients across the UK, such transient issues occurred in 4

out of 24 patients (16.7%). More serious risks are possible but far rarer, and include the development of an abscess within the abdomen, damage to the neighbouring small or large bowel during surgery, pneumonia and deep vein thrombosis. The exact risk of any of these major complications occurring is unknown, but felt to be less than 1% (one in a hundred) in the group of patients eligible to enter **ACCURE-UK 2.** No patient experienced a major complication such as these in our feasibility study.

After the operation you would be able to return to work and resume normal activities as soon as you feel able to. This will depend on the type of work that you do (physical work or non-physical work). It is usually generally recommend that you take one to two weeks off, but you may wish to go back to work sooner if you are in a non-physical job. If your job involves heavy lifting or manual labour, we recommend that you may need longer off, or to return with adjusted activities for up to four weeks.

Your hospital can provide you with separate information sheet(s) about the operation that will explain more about an appendicectomy (what will happen before, during and after) and the general anaesthetic.

## What will happen if I agree to take part in ACCURE-UK 2?

Before agreeing to enter the trial, you should have discussed it with both your gastroenterologist and a specialist colorectal surgeon. The surgical team will be undertaking your appendicectomy operation if you are allocated to this arm of the trial, and we feel that it is important for you to talk through all possibilities with both teams of doctors.

If you do decide to enter the trial, you will undergo tests to confirm that your UC is currently inactive. This may involve a camera examination (endoscopy) of the lower bowel to look at either all of your large bowel (colonoscopy), the left side only (sigmoidoscopy) and/or testing your stool (faeces) for signs of inflammation (faecal calprotectin test). This will depend on the hospital and your personal medical history. You will have undergone these tests previously at least once for your UC at some stage and your hospital can provide you with separate information sheet(s) or leaflet(s) about the procedures that will explain more about an endoscopy (what will happen before, during and after). If your previous camera examination was less than 3 months prior to entry into the study you will not need to have another before you can enter. You will also be asked to complete some baseline questionnaires about your symptoms and disease activity at entry into the study. At this stage, you will then be 'randomised' using a secure online computer system hosted by the Academic Medical Centre, University of Amsterdam in the Netherlands. This system will allocate you, at random, to either:

**a) the appendicectomy group**, in which case an appendicectomy operation (as above) will be arranged to take place at some stage in the following nine weeks, and you will also continue standard tablet medication, or

**b) the 'control' or comparison group**, in which case you will simply continue with standard tablet medication for your UC.

After this stage, follow-up will involve regular reviews where your doctor and/or the research team will discuss your current symptoms and complete further questionnaires. These reviews are scheduled to take place at around 6 weeks (appendicectomy group only for standard post-operative checks), 3, 6, 9 and 12 months after your entry to the trial and will take place in hospital at outpatient clinics. However, the reviews at 3, 6 and 9 month mays be done remotely via a video consultation or over the telephone. At the end of the trial we will undertake final tests to access your UC status at 12 months. This will involve camera examination of your bowel and/or testing your stool, but only if you have not had a confirmed UC flare. After this point, your involvement in the **ACCURE-UK 2** trial will be complete.

After you have entered the study, if you feel that you are developing symptoms of a flare of your UC outside of the review points, regardless of which group of the trial you are in, we would like you to contact the local research team (contact details are on the last page) who will arrange an urgent clinic appointment for clinical review, and possibly blood tests and a camera examination of your bowel.

At each stage, we will collect information to determine your Mayo score, which is a grading system of UC activity. The score is made up of 4 separate parts;

1. How often you pass stools
2. If there is blood in your stool
3. What the doctors see during the camera examination of your bowel
4. An assessment of your overall disease activity by your doctors or specialist nurse

A full Mayo score is collected when you have a camera examination of your bowel, such as when you enter the trial and after 12 months. Otherwise a partial Mayo score is collected, such as at 3, 6 and 9 months.

## What are the alternatives for my UC treatment?

If you choose not to go into this trial, you are likely to simply continue your tablet medication for UC into the future to try to prevent further relapses (flare-ups) of your disease activity.

Your gastroenterologist may recommend increasing your treatment by adding in new or different medications in the future, as they would normally. There may be other new treatments developed for UC in the future, and this trial is not designed to interfere with any of these in any way.

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

If you enter the trial and are allocated to undergo appendicectomy, this operation would be an additional treatment compared to the routine care of patients with UC. The procedure is outlined above, and like any surgery there is always the possibility of complications. We have done our best to reduce the chances of these by ensuring that only experienced and specialised colorectal consultant surgeons undertake operations during the trial. All adverse events relating to the operations within **ACCURE-UK 2** will be carefully recorded as this is important information to know if we are to propose that this operation be offered more widely to UC sufferers.

We know from research that patients with chronic inflammatory bowel disease (IBD) such as UC, have an increased risk of developing bowel cancer. IBD patients routinely have surveillance colonoscopies to look for early changes in the large bowel (colon) before cancer develops. These examinations usually begin 8-10 years after diagnosis and then every 3 or 5 years or, less commonly, yearly. The frequency will depend on what was seen during the previous colonoscopy and any other risk factors you may have, and you should talk to your gastroenterologist if you have any questions about your routine surveillance. Generally, this risk of cancer increases the longer a patient has had the disease. Previous research has suggested that patients with UC are less likely to have their colon removed after having an appendicectomy. Consequently, preserving the colon does mean that the risk of colon cancer probably remains. Therefore, it is important that you continue to have regular surveillance colonoscopies after your participation in the study is complete.

For patients who enter the control arm there will be no disadvantages from a medical point of view as they will receive standard treatment with tablet medications as they would anyway if they were not involved in the trial. Additionally, the reviews planned every 3 months throughout the trial (with the exception of the final 12 month review) can be completed over the phone if you do not already need to visit the outpatient clinic. The only additional burdens are the camera tests at the beginning and end of the trial.

## Will my taking part in ACCURE-UK 2 increase my chances of catching SARS-CoV-2 / Coronavirus / Covid-19?

There is a small increased risk of catching the SARS-CoV-2 virus (also called 'Coronavirus', which can sometimes develop into Covid-19 disease) from participating in the **ACCURE-UK 2** because you will need to make visits to the hospital and/or undergo assessments or interventions that you may have not done if you were not taking part. Wherever possible, activities with be combined with your normal hospital visits to keep these risks to a minimum and study activities will be undertaken remotely via a video consultation or on the telephone where possible.

If you enter the trial and are allocated to undergo the appendicectomy operation, your hospital will have routine pre-operative preparation pathways, including self-isolation or SARS-CoV-2 swabbing policies which all patients need to adhere to prior to surgery to reduce risks. Your hospital may also have separate areas or sites, sometimes referred to as "cold sites" or "green sites", where planned surgery can be undertaken away from any patients affected by Covid-19. You will have a review around 6 weeks after the operation and if you are not able to return to hospital in person for this, for example due to current hospital policies to try and limit movement on hospital sites, this review will be undertaken remotely via a video consultation or on the telephone.

## What are the possible benefits of taking part?

If allocated to the appendicectomy group and the operation does prove to have an impact on the disease activity in UC, there may be a potential benefit to an individual patient in taking part in terms of reducing

the number or severity of disease relapses. This may in turn impact upon the future use of medication, number of hospital admissions and the need for major bowel surgery.

If allocated to the control group, there is unlikely to be any personal benefit from taking part in the trial, although patients will undergo a period of careful disease and medical treatment monitoring. Some patients will draw satisfaction from the knowledge that their involvement, in either group, will help determine if this new proposed treatment has the potential to benefit all patients affected by UC.

### Can I pick which group to go in (i.e. whether to have an appendicectomy or not)?

No. So that we can find out which treatment is best, each person is put in a treatment group randomly. You have an equal chance of being allocated to the appendicectomy group or comparison group. Neither you nor your surgeon can choose which treatment you receive. This is essential so that a fair comparison can be made between the two groups. Dividing people into treatment groups in this way is what is called a 'randomised clinical trial' and is the standard and most reliable way of comparing different treatment options.

## PART 2

### What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your research doctor/surgeon will discuss how this affects your care and your participation in **ACCURE-UK 2.** Your doctor might consider whether you should continue in the study or withdraw. Either way, he/she will explain the reasons and arrange for your care to continue. If you decide to continue in the study he may ask you to sign an updated consent form. If the study is stopped for any other reason, your doctor would, again, tell you and arrange your continuing care.

### What will happen if I don't want to carry on with the study?

You can decide not to continue with study follow-up at any time but, if you do, we would still like your data to remain on file and be included in the final study analysis unless you specifically ask to be excluded.

### What if something goes wrong?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If the harm is due to someone's negligence, then you may have grounds for a legal action but you may have to pay for this. Taking part in the study would not affect your legal rights. Whether or not you take part in the study, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, you should ask to speak to the researchers involved in the study who will do their best to answer your questions (contact details are at the bottom of this form).

If you remain unhappy and wish to complain formally, you can do this through the normal National Health Service (NHS) complaints mechanisms; this is usually the Patient Advisory and Liaison Service (PALS).

## Will my taking part be kept confidential?

If you decide to take part in **ACCURE-UK 2**, we will need to collect information about you and some of this information will be your personal data; name, date of birth, NHS number, postal address, health information and medical history. Under data protection law, we have to provide you with very specific information about what we do with your data and about your rights. All information collected about you during the course of the study will be kept strictly confidential in the same way as all of your other medical records.

Information about your condition, treatment and follow-up will be sent by your doctors to the **ACCURE-UK 2** study office at University of Birmingham, on paper and electronically, where it will be securely stored under the provisions of the Data Protection Act 2018. Your pseudo-anonymised data will be shared with the Academic Medical Centre (AMC), University of Amsterdam in the Netherlands to combine with the other ACCURE study group data. This data will not identify you but will include the trial number you are assigned on entering **ACCURE-UK 2**.

The University of Birmingham is the sponsor for this study based in the United Kingdom. The University will use information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that the University is responsible for looking after your information and using it properly. We consider the processing of your information to be necessary for the purpose of:

- carrying out research, which is a task performed by the University in the public interest;
- scientific or historical research purposes, statistical purposes or archiving purposes in the public interest;
- for compliance with a legal obligation to which the University is subject, for example, retention of records in accordance with good (clinical) practice, inspection or audit.

Your hospital and the University of Birmingham will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. The University takes great care to ensure that personal data is handled, stored and disposed of confidentially and securely. Staff receive regular data protection training and the University has put in place organisational and technical measures so that personal data is processed in accordance with the data protection principles set out in data protection law. Any physical paperwork containing identifiable data will be kept in an access-controlled and secured room inside a locked filing cabinet. In relation to this project, electronic data will be kept on secure, encrypted IT servers within the University of Birmingham. More information on how the University processes personal

data can be found on the University's website on the page 'Data Protection – How the University Uses Your Data' (http://www.birmingham.ac.uk/privacy/index.aspx).

Your Hospital will collect information from you and your medical records for this research study in accordance with our instructions. Your Hospital will use your name, NHS number and contact details to contact you about **ACCURE-UK 2**, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Your hospital will pass these details to the University of Birmingham along with the information collected from you and your medical records. Individuals from the University of Birmingham and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people at the University of Birmingham who will have access to information that identifies you will be people who need to contact you to complete questionnaires or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

With your permission, your GP and the other doctors involved in your clinical care will be notified of your participation in the **ACCURE-UK 2** trial and kept informed of your progress. Also, the research staff involved in the study may, in the future, access electronic data from your central NHS records, for example through NHS Digital. This will provide researchers with information that is routinely gathered and stored during your visits to primary care and hospital, and will allow researchers to find out about your health after the trial has ended and the long-term effects of the treatments. By using routinely collected data we will be able to do this without needing to contact you further. In order to do this, we would need to send your name, gender, date of birth and NHS number with any request for information.

## How will we use information about you?

We will need to use information from you and from your medical record for this research project. This information will include your name, date of birth, gender and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Some of

your information will be sent to the Netherlands. They must follow our rules about keeping your information safe.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

## What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital and from central NHS records. If you do not want this to happen, tell us and we will stop. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. More information on this is provided in **Part 3**.

## Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from http://www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- at www.birmingham.ac.uk/research/bctu/data-sharing-and-protection-policy
- at www.birmingham.ac.uk/privacy/, or
- by contacting the University of Birmingham's Data Protection Officer via this email address: dataprotection@contacts.bham.ac.uk

## What will happen to the results of the study?

Once **ACCURE-UK 2** has finished we will publish the results in a medical journal so that others can benefit. We will also publicise the results on the study's website; www.brimingham.ac.uk/ACCURE-UK2. No individual patients will be identified in any publications. A copy of the published results of the study will be sent upon request to patients who have participated in **ACCURE-UK 2** in line with clinical trial guidelines, at the end of the study.

## Who is organising and funding the research?

The **ACCURE-UK 2** study was developed by a group of doctors from across several hospitals and universities, including Birmingham, Leicester and Amsterdam. The study is coordinated by the **ACCURE-UK 2** office at

University of Birmingham Clinical Trials Unit and is sponsored by the University of Birmingham. The research has been approved and reviewed by all of these organisations.

## Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people called the Research Ethics Committee to ensure your safety, rights, wellbeing and dignity. This study has been reviewed by the East Midlands - Leicester South Research Ethics Committee.

## Where can I get further information?

If you have any further questions about your operation or this clinical trial, please discuss them with your doctor/surgeon or the local trial investigator.

Details of local trial investigator/ person to contact:

| | |
|---|---|
| Name | |
| Job title | |
| Contact Details | |

Support can also be found through the NHS Patient Advisory and Liaison Service (PALS):

| | |
|---|---|
| Local PALS contact number(s) | |
| Local PALS email address | |

The **ACCURE-UK 2** study office is located at the University of Birmingham Clinical Trials Unit, Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, B15 2TT.
Web address: www.birmingham.ac.uk/ACCURE; e-mail: Accure@trials.bham.ac.uk

# PART 3

## Additional research

Patients entering the trial at some hospitals will be asked to consider being involved in additional research exploring the relationship between the appendix and the bowel in UC in more detail using tissue samples.

The samples will then be used to investigate whether the environment within the bowel and bloodstream changes before and after appendicectomy in UC patients and what may cause this. We hope to also determine if the level of response to the operation (in terms of decreased flare-ups of disease over the following twelve months) can be predicted using the same samples, and if those who respond display different immune cells within the bowel wall and appendix.

In the future we hope that studying these samples will enable us to give patients more information about their condition and which treatments are likely to work best for them.

If you are at one of these hospitals and are willing to take part you will be asked to complete a separate consent form.

## What tissue samples will I be asked to donate?

If your hospital is taking part in this additional research we are asking you to donate samples. The samples we will collect are:

- Blood – a 10ml sample (about 2 teaspoons) will be taken at the start of your involvement in the trial, again after 3 months and finally after 12 month, when your involvement would be complete.

- Biopsies from the lining of the bowel – the samples will be collected at the time of the camera test at the start of your involvement in the trial (if you have one), and again 12 months later when your involvement would be complete.

- Appendix (appendicectomy group only) – this will be collected when removed during the operation.

If you do not wish to take part in this additional research, you do not have to as it is optional and you can still be involved in the main **ACCURE UK-2** trial.

## What will happen to the samples I give?

All samples will initially be stored in the laboratory at the hospital in which you have been seen. The samples will then be sent to the Human Biomaterials Resource Centre (HBRC), which is a Human Tissue Authority (HTA) licensed human sample biorepository operated by and located at the University of Birmingham. The custodian of the samples will be the ACCURE-UK 2 Trial Management Group.

All samples will be labelled with a code number (not your name), with your initials and these will be stored anonymously at the University of Birmingham and not linked directly to any of your identifiable information. They will be used in a future research project(s) that must be reviewed and approved by a research ethics committee, just as was needed for the ACCURE-UK 2 trial. Access to your samples is limited to the HBRC staff or individuals involved with future, research ethics committee approved projects.

## How are samples transferred?

Blood samples and biological tissue samples will be securely packaged and sent to the University of Birmingham through either Royal Mail or by courier. They will not be transferred outside of the UK unless as part of a research ethics committee approved project.