ACCURE-UK Trial: The feasibility of undertaking Appendicectomy to impact upon the Clinical Course of Ulcerative Colitis

Patient Information Sheet
Version 3.0; 10-Dec-14

Summary of an Invitation to take part in a research study called ACCURE-UK.

- 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 national study called ACCURE-UK, 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 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, 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 study. More details are provided below and your medical team will be happy to answer any questions.
Patient Information Sheet

Version 3.0 10-Dec-15

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

We would like to invite you to take part in a research study called ACCURE-UK. Before you decide whether or not you wish to take part in ACCURE-UK, 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.

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 study?

ACCURE stands for: the feasibility of undertaking Appendicectomy to impact upon the Clinical Course of Ulcerative Colitis. This is the UK arm of a group of studies that are being run here and in the Netherlands.

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.

This first phase of the research is called a feasibility study as it aims to explore whether this is an attractive treatment to offer to UC sufferers, both from the patients’ and the doctors’ point of view.

If we can successfully recruit patients to this trial, and review them regularly throughout the one
year period afterwards, we plan to undertake a follow-on trial in the future to establish exactly how beneficial this treatment is in a larger group of UC patients.

**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 be able to 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?**

Your medical team have identified you as being potentially eligible to enter the ACCURE-UK trial because you have proven ulcerative colitis and have experienced a flare-up (or 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 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 is a good option to help find out if
the new treatment might work to help patients suffering from UC. This initial feasibility phase of the research aims to recruit 48 patients like you from hospitals throughout the UK.

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, then you don’t have to give any reason. 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.

What does removal of the appendix (an appendicectomy operation) involve?
To remove a patient’s appendix requires a minor operation. In this trial this would be undertaken by a consultant specialist colorectal surgeon, using a laparoscopic (keyhole) technique. This would normally be a day-case operation, but an overnight stay in hospital may be required in some cases. The surgeon will make three small cuts on the tummy (1-3cm 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 lasts 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. 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.

What will happen if I agree to take part in ACCURE-UK?
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 a camera examination (endoscopy) of the lower bowel to confirm that your UC is currently inactive (and your previous camera examination was more than 3 months prior to entry into the trial). You will have undergone this test previously at least once for your UC at some stage. You will also be asked to complete some baseline questionnaires about your symptoms and disease activity at entry to the trial. At this stage, you will then be ‘randomised’ using a secure online computer system hosted by the University of Birmingham. 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 six 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, regardless of which group you were in, the follow-up will be the same. This will involve regular reviews in outpatient clinic, where your doctor and/or the research team will discuss your current symptoms and complete further questionnaires. These reviews are scheduled to take place around 6 weeks (operational arm only), 3, 6, 9 and 12 months after your entry to the trial. If you experience a definite flare-up of your UC outside of these review points, regardless of which group of the trial you were in, we would like to collect further information from you on the phone or in person if you re-attend the hospital. Similarly, any patient’s medication can be changed or increased during the trial period if felt necessary by the medical team. We plan to document all medication use during the trial period, and additionally make note of any other effects of disease activity you may suffer, such as time off work or days where patients are unable to function as they would like to, due to their UC.

At the end of the trial we will undertake one final camera examination of your bowel. After this point, your involvement in the ACCURE-UK trial will be complete.

As part of the ACCURE-UK trial you may also be asked to take part in a discussion (research interview) with a researcher from the ACCURE-UK team. These discussions will help the team understand what it is like for patients like you to take part in the study, and will be help us to make sure that these perspectives influence the design of any follow on trial.
Additional research

Patients entering the trial at some centres will be asked to consider being involved in additional research exploring the relationship between the appendix and the bowel in UC in more detail. If you are at a participating centre, and consent to this sub-study, we would take an extra blood sample and biopsy from the lining of the bowel (at the time of the camera test) at the start of your involvement in the trial, and again 12 months later when your involvement would be complete. These samples, as well as the actual appendix specimens (in those allocated to receive this treatment) will be centralised to the research laboratories at the University of Birmingham and will be used to evaluate if 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 specimens, and if those who respond display different immune cells within the bowel wall and appendix.

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 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.

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) could 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.

**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 medical treatment and 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 (like a lottery). You have an equal chance of being allocated to the standard treatment or standard treatment plus appendectomy 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.

**Will I be reimbursed for my travel expenses when taking part in the trial?**
Yes. Patients will be reimbursed for any additional travel costs incurred from trial related visits to the hospital (outside of standard medical care). To claim, please contact your local researcher:

Name.................................................................................................................................

Job title............................................................................................................................

Contact Details..............................................................................................................

**Part 2**

**What if relevant new information becomes available?**

Sometimes we get new information about the treatment being studied. If this happens, your surgeon will discuss how this affects your care and your participation in ACCURE-UK. Your research 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. 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 complaints mechanisms; this is usually the Patient Advisory and Liaison Service (PALS). Taking part in the study would not affect your legal rights.

Will my taking part be kept confidential?

If you decide to take part in ACCURE-UK, 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 treatment and follow-up will be sent by your doctors to the ACCURE-UK study office at the University of Birmingham Clinical Trials Unit (BCTU), on paper and electronically, where it will be securely stored under the provisions of the 1998 Data Protection Act. This will include a signed copy of your consent form, including your full name. Your GP and the other doctors involved in your clinical care will be notified of your participation in the ACCURE-UK trial and kept informed of your progress. We may use national records to track your progress, but otherwise all information about you and your treatment will remain confidential.

As we may also contact you by post or telephone to ask you to complete questionnaires asking about your progress, we will ask you to give us your permission to do so. With your permission, your relevant medical notes may be inspected by authorised individuals from the BCTU. They may also be looked at by regulatory authorities. The purpose of this is to check that the study is being carried out correctly.

If you consent, the research staff involved in the ACCURE-UK trial may, in the future, access electronic data from your central NHS records, for example through the Health and Social Care Information Centre (HSCIC). 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.
What will happen to the results of the study?

Once ACCURE-UK 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 No individual patients will be identified in any publications. A copy of the published results of the study will be sent to all patients who have participated in ACCURE-UK upon request in line with clinical trial guidelines, at the end of the study, personal data will be securely stored for up to 5 years while research data will need to be securely archived for 20 years. Arrangements for confidential destruction will then be made. Should you withdraw consent for your data to be used, it will then be confidentially destroyed.

Who is organising and funding the research?

The ACCURE-UK 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 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 Tyne and Wear South 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 surgeon or the local trial investigator.

details of local trial investigator/person to contact:
Name......................................................................................................................
Job title....................................................................................................................

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Contact Details...................................................................................

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