Participant Information Sheet

MARVEL Study

Mitochondrial Anti-oxidant therapy to Resolve Inflammation in Ulcerative Colitis (MARVEL): A randomised placebo-controlled trial on oral MitoQ in Ulcerative Colitis

You are invited to take part in a research study. To help you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

Ulcerative Colitis (UC) is a condition that causes inflammation and ulceration of the inner lining of the rectum and colon (the large bowel). In UC, ulcers develop on the surface of the lining and these may bleed and produce mucus. Individuals with UC can become very unwell with disabling bloody diarrhoea, uncontrollable bowel habit and profound tiredness. And in some rare cases UC can lead to other serious problems.

The MARVEL study investigates whether a new treatment using a tablet medication, MitoQ can be beneficial for UC.

Our recent studies have shown that the inflamed UC gut lining releases ‘danger signals’ arising from the mitochondria.

These ‘danger signals’ attract inflammatory cells to the gut lining as one of the reasons for a flare-up of UC.

Mitochondria are ‘batteries’ that are present in all living cells, and they have an important function to make energy to allow these cells to be healthy.

In the gut lining of individuals with UC, we think that the mitochondria become damaged (‘faulty batteries’), and they leak these danger signals that make gut inflammation worse.

MitoQ works by protecting the mitochondria by reducing this danger signal. In effect, MitoQ has an anti-inflammatory (a soothing) effect on the inflamed UC gut lining.

We want to test if MitoQ will improve UC and allow the bowels to heal properly following a disease flare up.

In the MARVEL study, participants with an active flare up of UC who need oral steroid medication will be given either MitoQ or placebo as a daily tablet for 24 weeks.

We will carry out an assessment after 12 and 24 weeks to find out if MitoQ will result in higher rates of improvement in the participants’ symptoms and gut lining inflammation.

Furthermore, we will investigate if their UC will be better controlled and that they are less likely to need further steroids or more potent forms of drugs.

MitoQ has been shown to be safe in two large human clinical studies in Parkinson's disease and Hepatitis C, but the MARVEL study will be the first study in UC. At low doses, MitoQ is used as a nutritional supplement that has an anti-oxidant effect on the mitochondria.

Currently, many drug treatments in UC are very strong, expensive and aimed at suppressing the immune system.

If MARVEL study provides supportive data, MitoQ can be a safe and cost-effective new treatment that works at blocking the specific inflammatory signal found in the gut lining of individuals with UC.

We are looking to recruit 206 patients across the UK. 103 patients will receive MitoQ and103 patients will receive placebo.

Why have I been invited to take part?

You have been asked to take part as you have been diagnosed with Ulcerative Colitis and are experiencing a flare.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?

You can take as long as you like to decide if you want to take part in the study. A doctor will explain the study to you and give you the opportunity to ask any questions. If you decide to take part in the study, the doctor will ask you to sign a consent form.

The first part of the study is called the screening period. We will carry out different tests to make sure it is safe for you to go into the study and that you fit the eligibility criteria. You will need to come to the hospital for a visit. As part of the screening period, we will ask you about your medical history, smoking status and any medications you take. The doctor will do a physical exam, including making routine checks of your general well-being such as taking your temperature, blood pressure, breathing and pulse rate; and oxygen levels in your blood.

We will also take three tubes of blood for tests (approximately 6 teaspoons). We will also ask you to give us a stool (poo) sample to make sure you do not have an infective reason for your UC flare, such as c.difficile infection. This stool test is commonly carried out routinely in usual clinical practice. Participants will be provided a stool sample collection document that explains the process of how to do this. An additional 2 stool samples will be required throughout the study at weeks 12 and 24. After these tests have been completed, the doctor will confirm if you can join the study.

If you join the study you need to have a flexible sigmoidoscopy or a colonoscopy (internal camera test) to look at the inflammation in your bowel. This test is carried out to assess how severe the bowel inflammation is and will be used again to check if it the trial treatment has made any difference to this. These procedures involve the use of a specialised camera via a flexible tube to examine the large bowel. This camera test will performed by specialised trained staff. Full details of this procedure including a separate consent form and will be further explained to you before this procedure takes place.

Once we have done all the tests, you will be allocated either the drug or placebo. What treatment you get is decided by chance (50:50, like a toss of a coin). The randomization through a computer system. Regardless of treatment allocation you will receive standard care treatment with oral steroids for ulcerative colitis.

This is a double-blind study. That means that you will not be told if you get the study drug or placebo. In addition to this, the doctors and nurses looking after you will not know either. This type of approach is undertaken to reduce any chance of bias and is generally regarded as the best of way to carry out a trial to test if a treatment works or not.

You will take the drug or placebo for 24 weeks. Every 4 weeks, we will ask you to complete a short online questionnaire to see how you are feeling. After 12 weeks on the study you need to have a second internal camera test of your large bowel so we can accurately check if there have been any changes to the gut wall inflammation after trial treatment.

At weeks 4, 8, 16 and 20 you will be asked to complete a brief online questionnaire.

Throughout the study you will be asked by the research team about any side effects or sickness that you have had since taking the drug. If you experience any side effects or develop any kind of illness then please notify the study team directly. It is important that we record all the side effects and potential risks of taking this drug even if it is not directly related. We ask participants to be as detailed as possible. If you are admitted to hospital as a result of illness please inform the hospital that you are taking this drug.

What will happen and when?

Screening Visit	Randomisation Visit (Week 0)
- You will be asked to fill in a Quality of Life questionnaire - The study doctor will do a physical exam and ask you about any medications you take - Routine measurements of your well-being (vital signs) including respiratory rate, oxygen level, heart rate, blood pressure and temperature will be taken. - Blood tests taken including 3 research samples - Pregnancy test (if applicable) - Stool sample will be collected for microbiology - Any recent changes in health will be recorded - You will have a flexible sigmoidoscopy or colonoscopy, an internal camera test of your large bowel carried out (this will not be on the same day as the other tests)	- You will be randomised to either MitoQ or placebo - Bring stool samples with you - Be given the trial medication (MitoQ or placebo)

Weeks 4, 8, 16, 20 (From home)	Weeks 12 and 24 (Visit to the hospital)
- You will be asked to complete a Quality of Life questionnaire via the MARVEL database	- Quality of Life questionnaire - You will be asked about any side effects that you may have experienced - The study doctor will carry out a physical examination - Routine measurements of your well-being (vital signs) including respiratory rate, oxygen level, heart rate, blood pressure and temperature will be taken - Blood tests including 3 research samples - Bring stool (poo) samples with you to the visit - Bring your study drug bottles back - **(Week 12 only)** A second internal camera test of the large bowel will be carried out.

Is there anything I need to do or avoid?

Before you have an internal bowel camera test, you will need to carry out an overnight fast and use a bowel cleansing laxatives beforehand. You will be given a separate information booklet detailing this. There are some risks associated with this test such as bleeding, infection and perforation of the bowel. The leaflet explaining the fasting and laxative will describe these in further details. Please speak with your doctor or nurse if you have any questions about this.

Do not take any products containing Mitoquinol mesylate (Coenzyme Q10) or any products containing Coenzyme derivatives such as Coenzyme A (CoA, SCoA, CoASH) for the duration of the study.

You should not take part in this study if you are pregnant, or if you (or your partner) are planning on getting pregnant during the 24 weeks the study last. If you are breast feeding you should not take part in this study. The study doctor or nurse will discuss this with you during the visit and explain suitable methods of contraception. If you (or your partner) become pregnant when you are on the study you should tell the research team.

What are the possible benefits of taking part?

You may/may not get a benefit from taking part in this study.

The results of this study may be used for the future treatments or tests. Your participation in this study will not entitle you to benefit financially from the commercial development of the product, treatment or test.

What are the possible disadvantages of taking part?

You may experience some side effects from the MitoQ medication. The most common side effects are constipation, diarrhoea, nausea and vomiting.

Taking part in this study involves internal camera tests being performed to examine your large bowel, which carries risks associated with the procedure. In usual clinical setting however, most individuals with a flare of UC will require a camera examination. Taking part in this study will required a second examination 12 weeks after the start of trial treatment.

The internal camera examination may potentially uncover other findings and we have a requirement to inform your GP and/or directly act on these findings to help your overall well-being.

There are potential risks with having a blood sample taken. The most common side effect is pain at the puncture site and bruising. Other risks from this include haematoma or thrombus, extensive bleeding, nerve damage, vasovagal reactions (fainting) and infection.

We acknowledge the extra contribution of your personal time to attend study visits and clinical procedures. In total, this study will involve 5 visits to the research hospital where each of these visits may take at least two hours. We also acknowledge the extra time required for the two camera tests as part of this study. We will endeavour to make every appointment as convenient as possible for you and reimburse any travel costs to the hospital.

What if there are any problems?

If you have a concern about any aspect of this study please contact The MARVEL Trial Team at MARVEL.Trial@ed.ac.uk who will do their best to answer your questions.

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against NHS [HOSPITAL TRUST NAME] but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

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

You are free to withdraw from the study at any point. In addition to this, you may also be withdrawn by the Investigator. If withdrawal occurs, the primary reason for withdrawal will be documented. If you decide to withdraw your consent, no more information will be collected. All information you gave us before you left the trial will still be used for the trial. We would strongly recommend that you attend the exit check-up so that we can gather all the safety data related to the study drug. Participants are able to ask that any information collected at an exit check-up be included or excluded from the study.

If you decide not to carry on with the study, the quality of care that you receive will not be affected in any way. You will still receive standard care treatment with oral steroids.

What happens when the study is finished?

When the study is over, you will return to routine standard care as normal at your hospital.

Since the drug is not licenced for use in ulcerative colitis in the UK you will not be able to continue using the MitoQ drug after the study finishes.

The data collected in this study will be analysed and used to inform whether MitoQ is a good treatment for ulcerative colitis. Anonymised personal and clinical data obtained from the MARVEL study will be stored securely for a minimum of 5 years at the NHS data warehouse. Your biological samples (stool and blood) will be stored securely at the Wellcome Trust Clinical Research Facility, Western General Hospital, Edinburgh.

Anonymised data and samples may be used for drug concentration analyses and drug biomarker research relating to the Marvel study (for example, to understand if there are groups of patients who have responded better with treatment).

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws, which safeguard your privacy at every stage. For details on what data will be held about you and who will hold and store this information please refer to the Data Protection Information Sheet. The MitoQ drug manufacturer will be sent anonymised information relating to the safety and efficacy of the drug.

What will happen to the results of the study?

The results of the study will be published in scientific journals and presented at conferences. We will not use your name in any reports or presentations of the study findings or reveal

that you were interviewed. Once the study has been published, a summary of the findings will be available on the Edinburgh Clinical Trials website (http://www.ed.ac.uk/edinburgh-clinical-trials). A summary can also be requested through a member of the research team.

Who is organising and funding the research?

This study has been organised by the Edinburgh Clinical Trials Unit and sponsored by The University of Edinburgh and NHS Lothian

The Chief Investigator is Dr Gwo-tzer Ho.

The study is funded by The J P Moulton Charitable Foundation.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from Scotland B REC NHS Management Approval has also been given.

Researcher Contact Details

If you have any further questions about the study please contact Dr Gwo-Tzer Ho on +44 (0)131 242 6683 or email on: gwo-tzer.ho@nhslothian.scot.nhs.uk

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact Dr Alan Shand, Consultant Gastroenterologist, Western General Hospital on 0131 537 1755

Complaints

If you wish to make a complaint about the study please contact:

[Insert local trust/board details here]

Participant ID:

CONSENT FORM
MARVEL STUDY

Please **initial** box

1. I confirm that I have read and understand the information sheet (v 7.0 28 Apr 2023) and the Data Protection Information Sheet (v1.0 10 Feb 2020) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care and/or legal rights being affected. ☐
3. I give permission for the research team to access my medical records for the purposes of this research study. ☐
4. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and NHS Lothian), from regulatory authorities or from the NHS organisation where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data and/or medical records. ☐
5. I give permission for my personal information (including name, address, date of birth, telephone number and consent form) to be passed to the University of Edinburgh and/or Trials Unit Centre ECTU for administration of the study. ☐
6. I agree to my General Practitioner being informed of my participation in the study. ☐
7. I understand that data collected about me during the study may be converted to anonymised data. ☐
8. I understand that anonymised data generated during the study will be sent to the MitoQ drug manufacturer in New Zealand. ☐
9. I agree to my anonymised data and/or tissue being used in future studies. Yes ☐ No ☐
10. I agree to take part in the above study. ☐

Name of Person Giving Consent	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record