Host microbiota mechanisms in PSC-IBD
Participant information Sheet (Version 1.1 9th Sep 2021)

PART 1

1. **Full study title**

A SYSTEMS BIOLOGY APPROACH FOR IDENTIFICATION OF HOST & MICROBIAL MECHANISMS AND DRUGGABLE TARGETS FOR THE TREATMENT OF PSC-IBD (PSC-Vanc)

2. Invitation paragraph

You are being invited to take part in a research study. Before you decide 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 and discuss it with others if you wish. Ask 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. Thank you for reading this.

3. What is the purpose of the study?

It has only recently been recognised that we are only 10% human. Our human DNA is outnumbered by a factor of 100 by that from the bacteria, fungi and viruses in our bodies. The majority of these bugs live in the colon (large intestine) and this population of organisms is known as the colonic microbiome or "microbiome" for short. Research in patients with primary sclerosing cholangitis (PSC) has identified differences in the gut flora (living microorganisms such as bacteria and viruses that collectively form a community) compared to subjects that don't have PSC. Preliminary research suggests that these differences in the gut flora may play a crucial role in the development of PSC and the colonic inflammation associated with it. Our study endeavours to understand what these differences mean for patients with PSC and uncover potential targets for treatment.

4. Why have I been invited?

You have received this information because you have been diagnosed as having primary sclerosing cholangitis for which you attend the hospital and are due to have a colonoscopy as part of your care.

5. Do I have to take part?

It is up to you to decide whether or not to take part. Your contribution or not, will have no consequence to your management or treatment. 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 without giving a reason and this will not affect your management or the care you are given.

6. What will happen to me if I take part?

The duration of your participation in this study will be up to 8 weeks. If you decide to take part in this study, we may ask your permission to take up to 8 colon biopsies during your standard of care colonoscopy. Following your colonoscopy at this baseline visit (week 0 of the study) we will ask you to take a gut selective oral antibiotic (does not get absorbed) called oral vancomycin for up to 4 weeks. You will then undergo a mini camera test called a flexible sigmoidoscopy to examine your colon at baseline week 0 and take further four biopsies following the completion of your antibiotic treatment at this timepoint (week 4 of the study).

We will also ask you to continue to provide a stool sample at the start (week 0) then at week 2, week 4 and week 8 of the study. We will provide you with equipment to collect this stool samples and will arrange to collect it from you at a convenient time at the hospital or ask you to post it to us using the

prepaid sealed packs accompanying these kits. We will also collect blood at week 4 and week 8 to measure liver enzymes, however this will be done in conjunction with your clinical care.

We may also ask you questions around disease activity at weekly timepoints to ensure your colonic disease is not flaring or getting worse. These again can be done remotely as a virtual consultation for timepoints that don't involve a hospital visit.

7. Access to personal information

Any information relating to you will be held in strictest confidence. We will be collecting demographic data (including age, gender, ethnicity, BMI) and disease characteristics. You will be given a code number that will be used on all your samples so that no one else will know, or be able to work out that the samples are yours. Access to your medical records is restricted to the medical team looking after you and your GP.

8. What is being tested?

With your samples we will evaluate changes in the gut bacteria and other flora, the chemicals it produces, bile acids and genes being expressed within your bowel during treatment with oral vancomycin. This analysis may be done either locally or via external service providers. This will help us identify specific disease pathways that may potentially be implicated in PSC-IBD. We will ask your permission to store any remaining samples for use in future ethically approved studies.

9. What are the possible disadvantages and risks of taking part?

You will be undergoing a repeat camera test (flexible sigmoidoscopy) for the purposes of research. You will only require an enema prep (for clearing stool from the large bowel) and not full bowel prep. Flexible sigmoidoscopy is a very low risk procedure with risk of complications stated to be under 0.1%. Risks of a flexible sigmoidoscopy are specifically discomfort, bleeding (often minimal from biopsies) and damage to the bowel (perforation of the bowel which occurs roughly once for every 2500 sigmoidoscopies performed). There is also no significant additional risk with regards to obtaining further biopsies from your colon for research. In the event of unexpected findings from the biopsies the clinical team overseeing the patient's care will be informed. The participant will be free to withdraw from the study whenever they feel necessary.

10. What are the side effects of any treatment received when taking part?

We will ask you to take oral vancomycin for a period of 4 weeks as part of the study. Oral vancomycin has very low absorption and is therefore only effective for treating intestinal conditions such as Clostridiodes difficile infections. Oral vancomycin has previously been explored in clinical studies for the treatment of colitis in patients with PSC-IBD and is used as part of off-label standard of care practice in many countries. However, we will not include you in this study if you are having a severe flare of your colitis. Moreover, in order to minimise the risk to you, you will undergo weekly monitoring during the course of the study. During this monitoring period if it appears that your disease has become increasingly active then we will withdraw you from the study so that you can receive other forms of treatment for your colitis. A further potential risk of oral vancomycin treatment is the development of antibiotic resistance genes. However, to date there is currently no evidence to state that extended treatment with oral vancomycin is independently associated with an increase in the acquisition of antimicrobial resistance genes.

11. What are the possible benefits of taking part?

Although this study is unlikely to be of direct benefit to you, the results may contribute to the development of novel treatments for PSC and other chronic inflammatory diseases to benefit future patients. You will not be paid for taking part in the study. Please note that by consenting to this study you agree to not have any ownership of your data generated from this study, your biological samples collected for this study and will not be entitled to any subsequent financial proceeds that might be generated from the research.

12. What happens when the research study stops?

Your participation in this project will stop as soon as you have completed the 8-week duration of the study and have provided the relevant samples. You will continue to receive normal care for your PSC and PSC-IBD.

This completes Part 1 of the information sheet.

If the information in Part 1 has interested you and you are considering taking part, please read the additional information in Part 2 before making a decision.

PART 2

1. What if relevant new information becomes available or changes to the study are made?

If this happens we will tell you. If changes to the study have to be made you may be asked to sign another consent form.

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

You are free to withdraw at any time without giving a reason. If you withdraw from the study, we will destroy all your identifiable samples, but we will need to use the data collected up to your withdrawal. Samples collected will need to be kept until the study has been completed following which the samples will be destroyed.

3. What if there is a problem?

If you are harmed by taking part in this research project, this study will be covered by NHS insurance in the same way as any treatment in the hospital. If you are harmed due to someone's negligence, then you may have grounds for a legal action. You may however need to pay for your own legal costs. As this study is being undertaken at University Hospitals Birmingham NHS Foundation Trust you will be able to address any complaints through the normal National Health Service complaints mechanisms available to you.

4. What will happen to the results of the research study?

Results gained from this study are likely to be presented to and published within the scientific community. They will also be used to inform our future studies designed to test new treatments. If any findings of clinical significance are found in the course of this study the research team will inform you and your GP. None of the published data will contain any information or data that would be identifiable to you.

5. How will we use information about you?

We will need to use information from you and from your medical records for this research project. This information will include your initials, NHS number, name, contact details, demographics and disease characteristics and will be held on site by University Hospitals Birmingham. 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. 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. Your data will be kept in a secure archive in University Hospitals Birmingham NHS Foundation Trust for up to 12 months years after the study has been completed and will then be destroyed. Any data that needs to be archived during this period of time will be sent off site to an external archiving facility. Any samples remaining after testing will be kept for future studies which will be subject to future ethics applications. Your pseudo-anonymised samples and data may be shared with institutes nationally and internationally. Further details of the University Hospitals Birmingham's Privacy Notice can be found on https://www.uhb.nhs.uk/privacy-notice/research.

6. 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 central NHS records and your hospital. 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.

7. 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/

by asking one of the research team, by sending an email to R&D@uhb.nhs.uk, or

by ringing us on 0121 371 2000.

8. Involvement of your GP

Your GP will be informed of your participation in this study with your permission. We would also inform your usual secondary care physician.

9. Who has funded this study?

The European Crohns and Colitis Organisation have funded this study

10. Who is sponsoring this study?

University Hospitals Birmingham NHS Foundation Trust is sponsoring this study.

11. Who has reviewed the study?

The West Midlands - South Birmingham Research Ethics Committee has reviewed and approved this study.

12. Contact for Further Information

If you have any concerns or further questions about the study, you should contact the investigator Dr M Nabil Quraishi on 0121 371 2020 or you may contact the University Hospital Birmingham Patient Advice and Liaison Service (PALS) on 0121 424 0808.

You will be provided with a copy of this form for your records.

Study Number: Patient Identification Number for this trial: