

Exploring detailed patient-specific biological analyses to personalise treatment in inflammatory bowel disease

Submission date 06/05/2022	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 23/06/2022	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 04/07/2022	Condition category Digestive System	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Inflammatory bowel disease (IBD) is a term mainly used to describe 2 conditions: ulcerative colitis and Crohn's disease. Ulcerative colitis and Crohn's disease are long-term conditions that involve inflammation of the gut. Ulcerative colitis only affects the colon (large intestine). Crohn's disease can affect any part of the digestive system, from the mouth to the bottom (anus). Nationally, over 300,000 people suffer from inflammatory bowel disease (IBD). Biologic medications target different chemicals involved in inflammation. However, we currently cannot tell which biologic will be most effective for which patient. Therefore, patients often cycle through ineffective medications before finding the best one, allowing disease progression and exposure to unnecessary side-effects, notwithstanding cost implications. We aim to collect a range of samples and information from adult patients with active IBD who are likely to start new advanced medication.

Who can participate?

Healthy subjects and inflammatory bowel disease patients, including ulcerative colitis, Crohn's disease and IBD-unclassified.

What does the study involve?

Once their normal clinician has started the new treatment, we will monitor participants' progress at specific time-points to understand if the drug is effective or not. With the large cohort of over 400 patients that we are aiming for over a 4-5-year period (June 2022 to December 2026).

What are the possible benefits and risks of participating?

Positive findings from this study could herald a novel, personalised approach to treating IBD. The risks of taking part are minimal. There is negligible risk from taking colonic biopsies during lower gastrointestinal endoscopy if a patient is already undergoing endoscopy for clinical reasons, and several biopsies would normally be taken for diagnostic purposes anyway. The rest of the study involves providing samples and completing questionnaires, with all clinical decisions made by the patient's normal clinical team. There may be some inconvenience with providing

samples, but this is only 2-3 monthly for 6 months, and these visits will be aligned with normal clinical visits in most cases.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
March 2021 to December 2027

Who is funding the study?
Crohn's and Colitis UK

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

290708

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

CPMS 52035, M2019/2 Powell, IRAS 290708

Study information

Scientific Title

Therapy Personalisation using Multiomic Analyses in Inflammatory Bowel Disease – THAMES-IBD

Acronym

THAMES-IBD

Study objectives

Despite recent advances, treatments for inflammatory bowel disease remain ineffective for a large proportion of patients. This study hopes to understand the reasons for this and develop biomarkers that can predict response to specific medications.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 21/04/2022, Yorkshire and The Humber – Sheffield (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 207 104 8388; Sheffield.rec@hra.nhs.uk), ref: 22/YH/0043

Study design

Observational cohort study

Primary study design

Observational

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Inflammatory Bowel Disease

Interventions

This will be a prospective, multi-site observational cohort study, in order to gain 'real world' evidence that is then applicable to standard practice across a range of institutions. All patients who are beginning work-up (including endoscopy) to start a new biologic because of active IBD, both biologic-naïve and biologic-experienced patients, will be considered.

Regarding endoscopic biopsies, the non-IBD patients will be those undergoing endoscopy for other indications, e.g. polyp surveillance, lower gastrointestinal symptoms, anaemia, bowel cancer screening (noting that some trusts do not permit research biopsies to be taken during cancer screening). Minimally invasive biological samples will also be taken from participants with /without active IBD, such as blood, urine and stool, as control samples, with appropriate consent. After this, no further participation from control patients will be required. Their samples will be processed in the laboratory and analysed in the same way as the IBD patients' samples, and used to compare with the IBD samples.

Patients with active IBD will be recruited, along with those with quiescent IBD and non-IBD patients, who will act as controls.

A participant with active IBD will be required to provide different samples. Most of the procedures are part of standard clinical care, but extra material will be taken for research purposes. Depending on the scheduling of these tests, the order may be different for each patient. Local clinical and research teams will coordinate sample collection. Patients can still be enrolled and continue within the study if they cannot provide all of the samples, because of individual

preference, logistical reasons at specific research sites, or because it would involve an invasive procedure that is not clinically indicated. For some patients, longitudinal samples will be required, as described in the protocol. These include:

Biopsies from the small and/or large bowel during lower gastrointestinal endoscopy - during the procedure, standard clinical assessment will be made by the endoscopist. Extra biopsies, normally 2-4, but up to 12-14, will be taken for research purposes.

Blood tests – patients will undergo blood tests routinely as part of active disease assessment. Further blood will be taken for research purposes for laboratory analyses.

Stool sample – patients are also likely to be asked to provide a stool sample as part of routine care to measure the amount of inflammation. Further samples, in different containers, will be requested for research purposes. With two stool collections at baseline, two at weeks 4-8, two at weeks 10-14 and two at weeks 28-32, this equates to 8 samples, in total, 4 of which are part of routine care.

Urine – urine sample analysis is not a routine part of IBD assessment. One sample will be collected at baseline, weeks 4-8, weeks 10-14 and weeks 28-32.

Nutritional and body composition measurements - in sites where the equipment is available, patients will undergo handgrip strength testing and bioimpedance assessment, a non-invasive way of measuring body muscle and fat composition. These will be checked at baseline and at weeks 10-14 (twice in total).

Participants will be asked to complete questionnaires relating to their quality of life and psychological aspects of IBD. Patient Health Questionnaire-8 (PHQ-8) (depression), Generalised Anxiety Disorder-7, Fatigue in IBD (<http://www.fatigueinibd.co.uk/questionnaire/>), Standardised Assessment of Personality (personality), 3-item UCLA Loneliness Scale (loneliness), Birmingham Irritable Bowel Syndrome-Specific Questionnaire, Arizona Sexual Experience Scale, Pittsburgh Sleep Quality Index, IBD-Control, Brief Resilience Scale and Altman Self-Rating Mania Scale

questionnaires

Patients will also need to complete a dietary questionnaire to improve the accuracy of metabolomic analyses, matched in time to their urine sample collection.

We also plan to review patients' previous and future clinical history and investigations, including endoscopy images and reports, radiological images and reports, histological samples that are no longer needed for diagnostic purposes, and blood and stool samples, to explore other factors that may influence response to biologic medication.

Paraffin-embedded biopsy samples will undergo transcriptomic analysis. This will apply to patients prospectively recruited and to patients who are identified retrospectively.

Patients who have started a new biologic are routinely followed up between 10-14 weeks after commencement as part of standard care, to assess response to the treatment. Further follow-up will take place after approximately 30 weeks of starting the new medication. If a patient switches to a new medication within the study period, ongoing participation will be discussed with them and they will be asked to provide repeat samples, as listed above.

Intervention Type

Other

Primary outcome(s)

Response to medication will be determined by a combination of faecal calprotectin level and patient reported outcome (PRO)-2 score (for either Crohn's disease or ulcerative colitis) at weeks 10-14 and weeks 28-32, compared to pre-treatment levels.

Key secondary outcome(s)

1. Prevalence of psychiatric comorbidity and quality of life disruption in patients with active IBD measured using validated questionnaires at baseline
2. Changes in psychiatric comorbidity and quality of life related to new IBD medications using longitudinal completion of questionnaires at weeks 10-14 and weeks 28-32
3. Prevalence and treatment-induced changes in nutritional status in patients with active IBD measured using hand grip strength and bioimpedance at baseline, weeks 10-14 and weeks 28-32.

Completion date

01/12/2027

Eligibility

Key inclusion criteria

1. Healthy control patients:
 - 1.1. ≥ 18 years-old
 - 1.2. Willing to consent to sample collection
 - 1.3. No prior diagnosis or current clinical suspicion of IBD
2. Inflammatory bowel disease patients, including ulcerative colitis, Crohn's disease and IBD-unclassified
 - 2.1. Active disease as determined by standard clinical parameters measured within the 2 months prior to recruitment:
 - Crohn's symptom flare as indicated by Harvey-Bradshaw score >5 or unweighted PRO-2 (CD) of average daily stool frequency (SF) score ≥ 4 and/or average daily abdominal pain (AP) score ≥ 2 ,

- faecal calprotectin ≥ 250 micrograms/gram;

OR

- UC / IBD-U symptom flare as indicated by PRO-2 (UC) of ≥ 3 including a rectal bleeding score of ≥ 1 ,

- faecal calprotectin ≥ 250 micrograms/gram.

3. Able to consent to the study (with interpreter, if required)

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

Unable or unwilling to provide informed consent

Date of first enrolment

01/06/2022

Date of final enrolment

31/12/2026

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

St Marks Hospital

Watford Road

Harrow

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Study participating centre

St Georges Hospital

Blackshaw Road
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Study participating centre

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Study participating centre

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Study participating centre

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Study participating centre
Chelsea & Westminster Hospital
369 Fulham Road
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SW10 9NH

Sponsor information

Organisation
Imperial College London

ROR
<https://ror.org/041kmwe10>

Funder(s)

Funder type
Charity

Funder Name
Crohn's and Colitis UK

Alternative Name(s)
Crohn's & Colitis UK, CrohnsandColitisUK, NACC

Funding Body Type
Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be stored in a publicly available repository (like Gene Expression Omnibus). The patient-level data will include demographic details to allow future researchers to contextualise the sample information, along with clinical information about patients' IBD and other medical conditions. It will also include details about their response to treatments. Each participant's data will be stored under an alphanumeric ID code, so no identifiable data will be included. Participants will consent to this sharing procedure, which is standard practice following such research

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 0.15	04/04/2022	16/05/2022	No	No