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

Submission date
06/05/2022

Recruitment status
Recruiting

Registration date
23/06/2022

Overall study status
Ongoing

Last Edited
04/07/2022

Condition category
Digestive System

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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

Type(s)
Scientific

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Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
290708

Central Portfolio Management System (CPMS)
52035

Protocol serial number
M2019/2 Powell

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

Primary study design
Observational

Study design
Observational cohort study

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 determine 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 stool frequency (SF) score ≥4 and/or average daily abdominal pain (AP) score ≥2,
- faecal calprotectin ≥250micrograms/gram;
OR

- UC / IBD-U symptom flare as indicated by PRO-2 (UC) of ≥3 including a rectal bleeding score of ≥1,
- faecal calprotectin ≥250micrograms/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
United Kingdom
HA1 3UJ

Study participating centre
St Georges Hospital
Blackshaw Road

London
United Kingdom
SW17 0QT

Study participating centre
Guy's & St Thomas Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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Study participating centre
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NW3 2QG

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E1 1BB

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
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W2 1BL

Study participating centre
Chelsea & Westminster Hospital
369 Fulham Road
London
United Kingdom
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