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PROFILE - personalised medicine in Crohn's disease

Submission date 30/10/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/11/2017	**Overall study status** Completed	
Last Edited 14/03/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Crohn’s disease is a type of inflammatory bowel disease (IBD) that can affect any part of the intestine. The severity of Crohn’s disease varies a lot between different people, and this means that what might be the best treatment for one person may not be appropriate for someone else. This study will see whether a simple blood test (‘biomarker’) can improve Crohn’s disease outcomes and reduce the number of flares experienced by enabling delivery of ‘personalised therapy’ (that is, treatment tailored to the individual person based on their predicted disease course and severity). All patients enrolled receive established treatments (there are no new drug therapies being trialed – rather, it is the new blood ‘biomarker’ that is being tested). The aim of this study is to see if the biomarker allows us to choose the right strategy for the right patient at diagnosis, and so improve short-term and long-term outcomes.

Who can participate?
Adults aged 16 to 80 who have been diagnosed with Crohn’s disease diagnosed within three months.

What does the study involve?
All participants receive established treatments (there are no new drug therapies being trialed rather, it is the new blood ‘biomarker’ that is being tested). Participants are randomly allocated to one of two groups. Those in the first group are treated with a course of 8 infusions of Infliximab (“Top-Down”) over the first year together with an additional tablet-based treatment (immunomodulator). This is currently the most effective treatment in Crohn’s disease and is usually reserved for patients who have developed severe disease. Those in the second group follow the usual standard of care (“Step-Up”), which may include infliximab if the disease flares recurrently. Participants are assessed to see if the biomarker helps improve their symptoms.

What are the possible benefits and risks of participating?
It is expected that participants willl experience relief in their symptoms or an improvement in their disease, as all participants will be receiving active treatment (there are no placebos / dummy drugs being used). There are no notable risks with participating.

Where is the study run from?
This study is being run by the Cambridge Clinical Trials Unit and takes place in hospitals in the UK.

When is the study starting and how long is it expected to run for?
June 2014 to February 2023

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Mr Francis Dowling
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Study website
http://www.crohnsprofiletrial.com

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
35971

Study information

Scientific Title
PRedicting Outcomes For Crohn’s dIsease using a moLecular biomarkEr (PROFILE) trial

Acronym
PROFILE

Study objectives
This study aims to demonstrate that a new 'biomarker' test will allow patients with Crohn's disease to the receive the most appropriate treatment from the time of diagnosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England – Cambridge South REC, 02/11/2017, ref: 17/EE/0382

Study design
Randomised; Interventional; Design type: Prevention, Other

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Crohn’s disease

Interventions
This trial aims to test the prognostic capabilities of a new biomarker. Participants with Crohn’s disease are stratified using a biomarker, then randomised to receive either ‘Top down’ or ‘Step up’ treatment. All participants are given a course of steroids at their screening visit to ensure no participants is without suitable medication prior to being randomised.

Step up therapy is in line with current standard practice. If patients experience a disease flare following the course of steroids provided at screening, a second course will prescribed. If patients are still not suitably maintained participants continue on to Anti-TNF therapy (Infliximab infusions).

Top down therapy requires participants to start on Anti TNF therapy (Infliximab infusions) two weeks after their baseline/randomisation visit until week 48.

All patients are in the trial and followed up for 48 weeks.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
1. Sustained surgery free remission is measured using questionnaires from steroid induction treatment (screening) through weeks 4, 16, 32 and 48.
2. Steroid free remission is measured using questionnaires from steroid induction treatment (screening) through weeks 4, 16, 32 and 48.

The primary outcomes are measured using the sustained surgery and steroid free remission from completion of steroid induction treatment through to week 48 based upon information we collected at each trial time point.

Secondary outcome measures
1. Mucosal healing is measured using local and central reading of colonoscopy and MRE from baseline to week 48.
2. Quality of life is measured using the IBDQ questionnaire from screening through weeks 16, 32 and 48.
3. Quality of life is measured using the EuroQol questionnaire from screening through weeks 16, 32 and 48.
4. Quality of life is measured using the IBDQ questionnaire from screening through weeks 16, 32 and 48.
5. Health resource usage is measured using the resource usage questionnaire from screening through weeks 16, 32 and 48.

Secondary outcomes are measured using the local and central reading of colonoscopy/MRE over 1 year and the quality of life assessment (IBDQ) provided over the duration of the study and the patient rated resource usage / quality of life assessment (EuroQol) questionnaires provided over the duration of the study.

Overall study start date
01/06/2014

Completion date
01/02/2023

Eligibility

Key inclusion criteria
1. Crohn’s disease diagnosed within 3 months* using standard endoscopic, histologic or radiological criteria
2. Clinical evidence of active Crohn’s disease (corresponding to an HBI > 7)
3. Endoscopic evidence of at least moderately active Crohn’s disease (corresponding to an SES-CD > 6 or > 4 if limited to terminal ileum)
4. CRP > upper limit of normal on local assay OR Calprotectin > 200 µg/g

5. Immunomodulator and anti-TNFα naïve
6. Aged 16-80 years old

* Patients that have glucocorticoids in this period need to have discontinued this medication prior to screening assessments and still have active disease.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Total final enrolment
390

Key exclusion criteria
1. Patients with ulcerative colitis or indeterminate colitis
2. Patients with fistulating peri-anal Crohn's disease or active perianal sepsis
3. Patients with obstructive symptoms AND evidence of a fixed stricture on radiology or colonoscopy, which suggest that the subject is at high risk of requiring surgery over the following year. N.B. patients with modest degrees of stricturing on imaging but no obstructive symptoms may be included according to clinician judgement
4. Patients with contra-indications to study medications including a history of hepatitis B or C, tuberculosis
5. Patients with a history of malignancy
6. Patients who are pregnant or breastfeeding at screening
7. Other serious medical or psychiatric illness currently on going, or experienced in the last 3 months, that could compromise the study
8. Patients unable to comply with protocol requirements (for reasons including alcohol and/or recreational drug abuse)

Date of first enrolment
01/12/2017

Date of final enrolment
15/12/2021

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Barts and Royal London Hospital
The Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Bedford Hospital
Kempston Road
Bedford
United Kingdom
MK42 9DJ

Study participating centre
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
Derriford Hospital, Plymouth
Derriford Road
Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Epsom General Hospital
Dorking Road
Epsom
United Kingdom
KT18 7EG

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
New Victoria Hospital, Glasgow
52 Grange Road
Glasgow
United Kingdom
G42 9LF

Study participating centre
Gloucestershire Royal Hospital
Great Western Road
Gloucestershire
Gloucester
United Kingdom
GL1 3NN

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

Study participating centre

Hull Royal Infirmary
Hull and East Yorkshire Hospitals NHS Trust
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
James Paget Hospital, Great Yarmouth
Lowestoft Road
Gorleston-on-Sea
Great Yarmouth
United Kingdom
NR31 6LA

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Lincoln County Hospital
Greetwell Road
Lincoln
United Kingdom
LN2 5QY

Study participating centre
Luton & Dunstable University Hospital
Lewsey Road
Luton
United Kingdom
LU4 0DZ

Study participating centre
Musgrove Park Hospital, Taunton
Parkfield Drive
Taunton

United Kingdom
TA1 5DA

Study participating centre
New Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Study participating centre
Norfolk and Norwich Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre

Royal Bournemouth Hospital
Castle Lane E
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Royal Devon and Exeter Hospital, Wonford
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Hampshire County Hospital
Romsey Road
Winchester
United Kingdom
SO22 5DG

Study participating centre
Royal Liverpool Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Royal Sussex County Hospital
Barry Building
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
Royal Victoria Infirmary, Newcastle
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Royal Wolverhampton NHS Trust
West Midlands
United Kingdom
WV10 0QP

Study participating centre
Russells Hall Hospital
Pesnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
St George's Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
St Mark's Hospital
Watford Road
Middlesex
Harrow
United Kingdom
HA1 3UJ

Study participating centre
St Mary's Hospital, London
Praed Street

London
United Kingdom
W2 1NY

Study participating centre
The Cumberland Infirmary
Newtown Road
Carlisle
United Kingdom
CA2 7HY

Study participating centre
Torbay Hospital
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre
University College Hospital
235 Euston Road
Bloomsbury
London
United Kingdom
NW1 2BU

Study participating centre
University Hospital of Wales, Cardiff
Heath Park Way
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Watford General Hospital
Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
Western General Hospital
Crewe Rd S
Edinburgh
United Kingdom
EH4 2XU

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Addenbrookes Hospital
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal in 2020.

Intention to publish date
15/06/2023

Individual participant data (IPD) sharing plan
The data sharing plans for the trial are currently unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2	20/10/2017	03/11/2017	No	Yes
Protocol article	protocol	05/12/2018	04/11/2019	Yes	No
HRA research summary			28/06/2023	No	No
Results article		21/02/2024	26/02/2024	Yes	No
Statistical Analysis Plan	version 3	17/08/2023	14/03/2024	No	No