ISRCTN14481560 https://doi.org/10.1186/ISRCTN14481560

MRI for early response prediction to anti-TNF therapy

Submission date 19/01/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/04/2017	**Overall study status** Completed	
Last Edited 28/05/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Crohn's disease (CD) is one of the main types of inflammatory bowel disease (IBD), a name given to long-term conditions which causes inflammation (swelling) in the digestive system (gut). Although it can affect any part of the gut, it is most common at the end of the ileum (the last part of the small intestine) or the colon (the large intestine). This can lead to abdominal (belly) pain and diarrhoea, fatigue (extreme tiredness), loss of appetite and weight loss, and feeling generally unwell. People who have severe symptoms of CD are sometimes treated with powerful medicines called anti-TNFs which can be very effective. However, anti-TNFs can occasionally cause life-threatening side effects and are very expensive. Although many patients do improve on these medicines, about half the patients who start treatment will show no improvement after a year, and many continue to be given the medication for long periods of time, with no benefit. It is therefore important to identify a way, at an early stage, to see if the treatment is going to work and, if not, change to a different treatment. This will help patients and may reduce costs to the NHS. The study team has developed a new test using MRI scanning and computer software (mMRI) to monitor the movement of the bowel motility. The more inflamed the bowel is, the less it moves, and initial data suggests that if the motility improves, this might predict a successful response to treatment. The aim of this study is to find out if the changes in motility measuring using MRI (the new test), is better and quicker than current tests (based on blood and stool samples) in predicting if the anti-TNF medicines will still be working after a year.

Who can participate?
Patients aged 16 years and over who have Crohn's disease and are scheduled to commence or recommence eligible biological therapies (including biosimilars).

What does the study involve?
All participants start their biological therapy as planned. At the beginning of their treatment and then 20-28 weeks and one year later, participants provide blood and stool samples and undergo the MRI-scan to assess their bowel motility, which takes around 40 minutes. If any of the procedures are done as part of standard of care, this will not be repeated as part of the study; instead, the standard procedures will be used, to reduce burden for participants.

What are the possible benefits and risks of participating?
There are no direct benefits involved for those taking part in the study, however the study results could help improve understanding of patient response to biological therapy which could help future patients. There are no notable risks involved with participating in this study.

Where is the study run from?
University College Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2016 to December 2023

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Sue Philpott, s.philpott@ucl.ac.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
201079

Protocol serial number
CTU/2014/159

Study information

Scientific Title
MOTILITY: Small bowel motility quantified by cine MRI as a predictor of long term response in patients with Crohn’s disease commencing biological therapy: A prognostic accuracy study

Acronym
MOTILITY

Study objectives
Current study hypothesis as of 07/01/2019:
Early improvements in Small bowel motility measured using mMRI at 20 – 28 weeks after biological therapy initiation better predicts long term response (at 1 year) than current standard clinical tools i.e. measurement of plasma CRP and faecal calprotectin (fC)
Should further information be required, please do let me know.

Previous study hypothesis:
Early improvements in Small Bowel motility measured using mMRI at 20-28 weeks after anti-TNF therapy initiation better predicts long term response (at 1 year) than current standard clinical tools i.e. measurement of plasma CRP and faecal calprotectin (fC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/05/2017, West Midlands - Edgbaston Research Ethics Committee (The Old Chapel, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8115; nrescommittee.westmidlands-edgbaston@nhs.net), ref: 17/WM/0106

Study design
Prospective multi-centre cohort prognostic accuracy study

Primary study design
Observational

Study type(s)
Diagnostic

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

Interventions
Current interventions as of 07/01/2019:
Eligible patients will be recruited consecutively. All patients will undergo all tests at baseline (prior to beginning the standard biological therapy), at 20 – 28 weeks and 1 year after initiation of therapy, unless rendered unnecessary due to clinical non – response to treatment.

Test under evaluation: MRI: a medical imaging technique using magnetic fields and radio frequency waves to generate detailed images of internal body structure. Patients drink liquid to distend the bowel and stimulate movement. Rapid MRI imaging allows "cine" imaging of this bowel motion which will be measured and quantified using the software

Primary comparator: CRP; a blood test that measures plasma concentration of a protein produced by the body in response to inflammation

Secondary comparator: Faecal calprotectin; a stool sample that measures the level of a granulocyte protein that is released into the bowel in response to inflammation

Patients will be followed up for 1 year after starting biological therapy. They will attend outpatient clinics and for medication infusions where needed, as per the normal routine for their care. The study interventions (MRI, stool and blood tests) and questionnaires will be times to coincide with routine clinical visists wherever possible.

Previous interventions:
Eligible patients will be recruited consecutively. All patients will undergo all tests at baseline (prior to beginning the standard anti-TNFalpha therapy), at 20-28 weeks and 1 year after initiation of therapy, unless rendered unnecessary due to clinical non-response to treatment.

Test under evaluation: MRI: a medical imaging technique using magnetic fields and radio frequency waves to generate detailed images of internal body structure. Patients drink liquid to distend the bowel and stimulate movement. Rapid MRI imaging allows “cine” imaging of this bowel motion which will be measured and quantified using the software

Primary comparator: CRP; a blood test that measures plasma concentration of a protein produced by the body in response to inflammation

Secondary comparator: Faecal calprotectin; a stool sample that measures the level of a granulocyte protein that is released into the bowel in response to inflammation

Patients will be followed up for 1 year after starting anti-TNF therapy. They will attend outpatient clinics and for medication infusions where needed, as per the normal routine for their care. The study interventions (MRI, stool and blood tests) and questionnaires will be timed to coincide with routine clinical visits wherever possible.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 07/01/2019:
Difference in sensitivity between stable or improved MRI-measured segmental small bowel motility versus normalisation of CRP at 20-28 weeks to predict response or remission (RoR) to anti-TNF or anti-interleukin therapy at 1 year.

Previous primary outcome measure:
Difference in sensitivity between stable or improved segmental small bowel motility versus normalisation of CRP to predict response or remission (RoR) to anti-TNFα therapy at 1 year. Small bowel motility will be measured by MRI and CRP levels via a blood test at 0 and 20-28 weeks.

Key secondary outcome(s))
Current secondary outcome measures as of 07/01/2019:
1. Difference in specificity between stable or improved small bowel motility versus normalisation of C-reactive protein to predict RoR at 1 year. Small bowel motility will be measured by MRI and CRP levels via a blood test at 0 and 20-28 weeks
2. Difference in area under the receiver operating characteristic curve (ROC AUC) in continuous small bowel motility and in C-reactive protein levels to predict RoR at 1 year. Small bowel motility will be measured by MRI and CRP levels via blood test at 0 and 20-28 weeks
3. Difference in prognostic accuracy to predict clinically significant improvements in each quality of life measure at 1 year between continuous small bowel motility MR score versus changes in C-

reactive protein levels . Quality of life will be measured by EQ-5D-5L, CUCQ-8 and IBD-Control 8 questionnaires at 20-28 weeks and 1 year. Small bowel motility will be measured by MRI and CRP levels via blood test at 0 and 20-28 weeks
4. Difference in both sensitivity, specificity and ROC AUC between stable or improved small bowel motility versus normalisation of Faecal Calprotectin predict RoR at 1 year. Small bowel motility will be measured by MRI and calprotectin levels via a stool test at 0 and 20-28 weeks
5. Difference in prognostic accuracy to predict clinically significant improvements in each quality of life measure at 1 year between continuous small bowel motility MR score versus changes in faecal calprotectin levels. Quality of life will be measured by EQ-5D-5L, CUCQ-8 and IBD-Control 8 questionnaires at 0, 20-28 and 52 weeks. Small bowel motility will be measured by MRI and calprotectin levels via a stool test at 0, 20-28 weeks and 52 weeks
6. Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models including MRI-measured small bowel motility versus those including (i) C-reactive protein and (ii) faecal calprotectin for response to anti-TNFα or anti-interleukin therapy at one year.
7. Interobserver variability of radiologists without prior mMRI experience and experts in MRI imaging . Radiologists will interpret MRI images of small bowel motility at two time points
8. Difference in plasma levels of gut peptides and inflammatory cytokines and small bowel motility variance between patients with and without RoR at 1 year. Small bowel motility will be measured by MRI and gut peptides and inflammatory cytokines will be measured by blood tests at 0, 20-28 and 52 weeks.
9. Difference in small bowel motility variance between patients with normal and elevated levels of gut peptides inflammatory cytokines and between patients with and without abdominal symptoms. Small bowel motility will be measured by MRI, gut peptides and inflammatory cytokines will be measured by blood tests and abdominal symptoms will be measured by CUCQ-8 and IBD-Control 8 questionnaires, all at 0, 20-28 weeks and 52 weeks .
10. Difference in response rates to anti-TNFα or anti-interleukin therapy at one year for (a) patients with and without skeletal muscle myopenia and (b) patients with and without low skeletal muscle:fat ratios.
11. Sensitivity and specificity of (a) >10% increase in ADC and (b) >25% reduction in Clermont score between weeks 0 and 20-28 for RoR to biologic therapy at one year.
12. Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models including change in ADC value derived from DW-MRI between baseline and week 20-28 versus those including (i) C-reactive protein and (ii) faecal calprotectin for response to biologic therapy at one year.
13. Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models including the Clermont score derived from DW-MRI versus those including (i) C-reactive protein and (ii) faecal calprotectin for response to biologic therapy at one year.
14. Difference in prognostic accuracy between changes in the Clermont score versus changes in (i) C-reactive protein and (ii) faecal calprotectin levels at week 20-28 to predict clinically significant improvements from baseline to one year in each quality of life measure.
15. Incremental prognostic value of DW-MRI parameters in conjunction with motility MRI scores for response to biologic therapy at one year.
16. Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models including the small bowel ultrasound (SBUS)-derived activity score (SSS) between baseline and week 20-28 versus those including (i) C-reactive protein and (ii) faecal calprotectin for response to biologic therapy at one year.
17. Difference in prognostic accuracy between multivariate prognostic models including the small bowel ultrasound (SBUS)-derived activity score (SSS) between baseline and week 20-28 versus those including (i) motility MRI alone, (ii) DW-MRI alone, and (iii) combined motility+DW-MRI features for response to biologic therapy at one year.

Previous secondary outcome measures:
1. Difference in specificity between stable or improved small bowel motility versus normalisation of C-reactive protein to predict RoR at 1 year. Small bowel motility will be measured by MRI and CRP levels via a blood test at 0 and 20-28 weeks
2. Difference in area under the receiver operating characteristic curve (ROC AUC) in continuous small bowel motility and in C-reactive protein levels to predict RoR at 1 year. Small bowel motility will be measured by MRI and CRP levels via blood test at 0 and 20-28 weeks
3. Difference in prognostic accuracy to predict clinically significant improvements in each quality of life measure at 1 year between continuous small bowel motility MR score versus changes in C-reactive protein levels . Quality of life will be measured by EQ-5D-5L, CUCQ-8 and IBD-Control 8 questionnaires at 20-28 weeks and 1 year. Small bowel motility will be measured by MRI and CRP levels via blood test at 0 and 20-28 weeks
4. Difference in both sensitivity, specificity and ROC AUC between stable or improved small bowel motility versus normalisation of Faecal Calprotectin predict RoR at 1 year. Small bowel motility will be measured by MRI and calprotectin levels via a stool test at 0 and 20-28 weeks
5. Difference in prognostic accuracy to predict clinically significant improvements in each quality of life measure at 1 year between continuous small bowel motility MR score versus changes in faecal calprotectin levels. Quality of life will be measured by EQ-5D-5L, CUCQ-8 and IBD-Control 8 questionnaires at 0, 20-28 and 52 weeks. Small bowel motility will be measured by MRI and calprotectin levels via a stool test at 0, 20-28 weeks and 52 weeks
6. Difference in prognostic accuracy and incremental prognostic value of multivariate prognostic models for response to anti-TNFα therapy at 1 year between changes in small bowel motility, C-reactive protein and faecal calprotectin. Small bowel motility will be measured by MRI, CRP levels via blood test and calprotectin levels via a stool test at 0 and 20-28 weeks.
7. Interobserver variability of radiologists without prior mMRI experience and experts in MRI imaging . Radiologists will interpret MRI images of small bowel motility at two time points
8. Difference in plasma levels of gut peptides and inflammatory cytokines and small bowel motility variance between patients with and without RoR at 1 year. Small bowel motility will be measured by MRI and gut peptides and inflammatory cytokines will be measured by blood tests at 0, 20-28 and 52 weeks.
9. Difference in small bowel motility variance between patients with normal and elevated levels of gut peptides inflammatory cytokines and between patients with and without abdominal symptoms. Small bowel motility will be measured by MRI, gut peptides and inflammatory cytokines will be measured by blood tests and abdominal symptoms will be measured by CUCQ-8 and IBD-Control 8 questionnaires, all at 0, 20-28 weeks and 52 weeks .
10. Difference in response rates to anti-TNFα therapy at one year for patients with and without skeletal muscle myopenia and patients with and without low skeletal muscle:fat ratios. Skeletal myopenia and muscle fat ratios will be measured using analysis of MRI images at weeks 0, 20-28 and 52.

Completion date
31/12/2023

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 07/01/2019:
1. Patients aged 16 years or more with active luminal small bowel Crohn’s disease, with or without colonic disease
2. Disease distribution and activity documented by ileocolonoscopy or (for patients with

endoscopically-inaccessible disease) magnetic resonance enterography (MRE), enteric ultrasound (US), computed tomography (CT), barium fluoroscopic follow – through (BaFT) or video capsule endoscopy (VCE) performed as part of usual clinical care within the previous 3 months of starting eligible biological therapy
3. Scheduled to commence or recommence eligible biological treatment (including biosimilars); specifically anti-TNF and anti-interleukin agents.
4. The primary target of therapy, in the opinion of the treating physician, is small bowel disease (with or without treatment of concomitant colonic disease).

Previous participant inclusion criteria:
1. Patients aged 16 years or more with active luminal small bowel Crohn's disease, with or without colonic disease
2. Disease distribution and activity documented by ileocolonoscopy or (for patients with endoscopically-inaccessible disease) magnetic resonance enterography (MRE) performed as part of usual clinical care within the previous 3 months
3. Scheduled to commence anti-TNFα treatment (including biosimilars) for the first time
4. The primary target of therapy, in the opinion of the treating physician, is small bowel disease (with or without treatment of concomitant colonic disease)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Sex
All

Total final enrolment
219

Key exclusion criteria
Current participant exclusion criteria as of 07/01/2019:
1. Biological therapies other than anti-TNF and anti-interleukin agents, such as anti – integrin therapy (e.g. vedolizumab)
2. Primary target of therapy is limited to colonic or perianal fistulising disease
3. mMRI contraindicated (e.g. MRI-incompatible cardiac pacemaker, unable to lie flat, pregnancy)
4. Any psychiatric or other disorder precluding informed consent
5. Small bowel surgery within the preceding 3 months
6. Small bowel stricture causing upstream dilatation on imaging or endoscopy (defined as a >50% increase in diameter in comparison to the adjacent small bowel segment)

Previous participant exclusion criteria:
1. Primary target of therapy is limited to colonic or perianal fistulising disease
2. mMRI contraindicated (e.g. MRI-incompatible cardiac pacemaker, unable to lie flat, pregnancy)

3. Any psychiatric or other disorder precluding informed consent
4. Small bowel surgery within the preceding 3 months
5. Small bowel stricture causing upstream dilatation on imaging or endoscopy (defined as a >50% increase in diameter in comparison to the adjacent small bowel segment)

Date of first enrolment
01/05/2017

Date of final enrolment
30/04/2022

Locations

Countries of recruitment
United Kingdom

England

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

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are 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?
Basic results			29/01/2025	No	No
Other publications	Prespecified substudy of body composition for prediction of therapeutic response	19/03/2025	25/03/2025	Yes	No
Other publications	Inter- and intra-observer variability of software quantified bowel motility measurements	27/05/2025	28/05/2025	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 6.0	28/04/2022	28/06/2022	No	No