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Investigating the need to continue taking immunomodulator tablets for patients with inflammatory bowel disease, when switching from treatment with intravenous infliximab infusions (infliximab given directly into a vein) to subcutaneous infliximab (infliximab given by an injection under the skin).

Submission date
20/09/2022

Recruitment status
No longer recruiting

Registration date
13/10/2022

Overall study status
Completed

Last Edited
22/10/2024

Condition category
Digestive System

[X] 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
Infliximab is a well-established treatment for inflammatory bowel disease (IBD). Traditionally infliximab is given to patients as an intravenous infusion, which is an injection directly into a vein. Although treatment with infliximab infusions is effective, patients can develop antibodies against this drug over time. Antibodies are proteins produced by our body when the immune system detects something that could be harmful, such as a virus, bacteria or a chemical. These antibodies can inactivate infliximab, making it less effective and causing IBD flare-ups. To reduce this risk, the infusions are often combined with another drug, a tablet, called an immunomodulator. Unfortunately, immunomodulator drugs are not well tolerated by some patients. They can also cause serious side effects, including a small increase in the risk of developing certain cancers. Recently, infliximab became available as a subcutaneous injection. Subcutaneous means that the injection goes under the skin, as opposed to into a vein. This newer form of treatment has been shown to work just as well as the infusions and has the advantage that they can be done at home by patients themselves. Additionally, it is possible that the injections may not need to be combined with the immunomodulator tablets, which could reduce the side effects and risks of treatment. We designed a study to find out if patients need to continue taking immunomodulator tablets when switching from intravenous to subcutaneous infliximab.

Who can participate?
Adults with IBD, such as Crohn's disease and ulcerative colitis

What does the study involve?
We plan to enrol 102 patients across 3 NHS hospitals in the UK, who were previously on infliximab infusions and are about to start infliximab injections as part of their routine care. Patients will attend 5 research visits over a period of 6 months, where blood samples will be taken. The study will be running for 32 months in total.

What are the possible benefits and risks of participating?
Participating in this trial may not have any direct benefits. We hope that this trial will provide information that will help us to improve the care of patients with IBD in the future.
The risk of stopping immunomodulator tablets is a risk of increased disease activity. Participants will be assessed for signs and symptoms of worsening disease activity at each study visit (by means of physical examination and HBI/SCCAI indexes). Blood tests will be performed which will be reviewed for evidence of worsening inflammation (CRP and calprotectin measurements).
For participants randomised to continuing immunomodulators, the risks of side effects from the medication are no different from before (participants would have been on combination therapy for at least 22 weeks prior to randomisation).
For all participants, there may be bruising and discomfort at the site of the blood tests, as with any blood test. Where possible, the blood taken for research purposes will be collected at the same time as your routine blood tests to minimise discomfort.

Where is the study run from?
Guy's and St Thomas' NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
July 2022 to July 2025

Who is funding the study?
Celltrion Healthcare (South Korea)

Who is the main contact?
Alima Rahman (Clinical Trial Manager) (UK)
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
2021-006803-13

IRAS number
1005499

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
3632-MINIMISE, IRAS 1005499, CPMS 53185

Study information

Scientific Title
Subcutaneous CT-P13 monotherapy versus combination with immunomodulation when switching from intravenous infliximab in inflammatory bowel disease – A multicentre, randomised withdrawal trial

Acronym
MINIMISE

Study objectives
To determine whether discontinuing immunomodulation after switching from IV infliximab to SC CT-P13 is non-inferior to continuing combination therapy with a thiopurine in terms of occurrence of free antibody positivity at week 24

1. To assess if discontinuing immunomodulators after switching from IV infliximab to SC CT-P13 results in lower infliximab levels at weeks 8, 16 and 24
2. To assess if discontinuing immunomodulators after switching from IV infliximab to SC CT-P13 results in increased anti-drug antibodies at weeks 8, 16 and 24; and by Week 24
3. To assess the efficacy and tolerability of therapy in participants continuing and discontinuing immunomodulators after switching from IV infliximab to SC CT-P13
4. To assess acceptability of switching from IV to SC treatment at Week 24/ Early termination, regardless of randomisation allocation
5. To assess quality of life in patients switching from IV to SC treatment at Week 24/ Early termination, regardless of randomisation allocation
6. To understand how baseline TGN levels and DQA1*05 positivity affect infliximab drug levels and anti-drug antibody production, regardless of randomisation allocation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/09/2022, ref: 22/EE/0166

Study design
Randomized controlled open-label multicentre withdrawal study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Crohn's disease and ulcerative colitis

Interventions
The intervention is the withdrawal of immunomodulators (azathioprine or mercaptopurine) in IBD patients switching from IV infliximab to subcutaneous infliximab (SC CT-P13). Participants

will be randomised 1:1 to either continue or discontinue immunomodulators (IMP) when switching from IV infliximab to subcutaneous infliximab (SC CT-P13) (NIMP). We will stratify the treatment allocation by HLA-DQA1*05 status.

For participants randomised to continuing the immunomodulators, the IMP will continue to be prescribed to participants as part of their standard of care and at the same stable dose and frequency that they were taking for the 4 weeks prior to commencement of SC CT-P13 (NIMP). If changes in dose or frequency are deemed necessary during the trial, these changes are allowed at the discretion of the treating investigator. Immunomodulator drugs are taken by mouth, usually once a day, with or just after food, at a dosage that depends on age, body weight and severity of disease activity.

Participants will continue/stop taking immunomodulators as part of this trial from the Baseline Visit up to the Week 24 Visit. The maximum trial treatment duration is 25 weeks which includes the trial follow-up activity and study visits every 8 weeks from the Baseline up until Week 24. Therefore, study visits at Week 8, Week 16 and Week 24 with a ±1 week window for each visit.

Randomisation will only be performed once screening has been completed, blood test results reviewed and eligibility re-confirmed at baseline. A secure computerised web-based programme provided by MedSciNet will be used to generate the treatment allocation. Appropriately delegated members of the research team will randomise participants by completing an on-screen form via their personal MedSciNet account. All parties will be aware of the participants' allocation as this is an open-label trial.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Azathioprine and mercaptopurine (IMPs), subcutaneous infliximab (CT-P13) (NIMP)

Primary outcome measure
Free antibody positivity (i.e. ≥10 ng/mL) measured using blood sample analysis at week 24 in patients continuing and discontinuing thiopurines after switching from IV infliximab to SC CT-P13

Secondary outcome measures
1. Infliximab drug levels measured using blood sample analysis at weeks 8, 16 and 24 in participants continuing and discontinuing immunomodulators after switching from IV infliximab to SC CT-P13
2. Total anti-drug antibodies measured using blood sample analysis at weeks 8, 16 and 24 and free anti-drug antibodies at weeks 8 and 16 in participants continuing or discontinuing immunomodulators after switching from IV infliximab to SC CT-P13
3. Anti-drug antibody positivity (free and total) measured using blood sample analysis by week 24 in participants continuing or discontinuing immunomodulators after switching from IV infliximab to SC CT-P13
4. Efficacy of therapy by week 24/ Early termination measured using the proportion of participants developing clinically active disease (HBI> 4 or SCCAI>2), biochemically active disease (CRP >5 mg/l and/or faecal calprotectin >250mcg/g), and both clinically and biochemically active disease, in participants continuing or discontinuing immunomodulators after switching from IV

infliximab to SC CT-P13
5. Tolerability of treatment through to week 24/ Early termination measured as the rate of AE and SAEs in participants continuing or discontinuing immunomodulators after switching from IV infliximab to SC CT-P13
6. Quality of life in participants switching from IV to SC treatment at Week 24/ Early Termination, regardless of randomisation allocation, measured using the IBD-Control Questionnaire.
7. Proportion of participants having to revert back to IV in each randomisation arm measured using data collected at each visit
8. Acceptability of switching from IV to SC treatment measured using a treatment acceptability questionnaire at week 24/ Early termination
9. Infliximab drug levels and anti-drug antibodies positivity measured using blood sample analysis at weeks 8, 16, and 24 in participants with positive and negative HLA DQA1*05, regardless of randomisation allocation
10. Infliximab drug levels and anti-drug antibodies positivity measured using blood sample analysis at weeks 8, 16, and 24 in participants with baseline TGN concentrations greater/ equal to versus less than 125 pmol/8x10^8 RBC and greater/ equal to versus less than 235 pmol /8x10^8 RBC, regardless of randomisation allocation.

Week 8, 16 and/or 24 (or early termination)

Overall study start date
07/07/2022

Completion date
31/07/2025

Eligibility

Key inclusion criteria
1. Aged 18 years and over
2. Diagnosis of Crohn's disease, ulcerative colitis or IBD-U for at least 6 months at the time of commencement of SC CT-P13
3. A clinical decision has been made to switch from intravenous infliximab to SC CT-P13
4. On stable IV infliximab at 5mg/kg Q8W for at least 22 weeks at the time of commencement of SC CT-P13
5. On azathioprine or mercaptopurine for at least 3 months, at a stable dose for at least 4 weeks at the time of commencement of SC CT-P13
6. Clinical remission defined by HBI ≤4 or SCCAI ≤2 at screening
7. Infliximab levels above or equal to the lower therapeutic level (as per local lab) at the time of the final or penultimate IFX infusion
8. Written informed consent to participate
9. Sufficient English to understand the study and sign informed consent, or available local interpreting service

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
All

Target number of participants
102

Total final enrolment
102

Key exclusion criteria
1. Not willing or able to switch to subcutaneous (SC) treatment
2. Evidence of clinically active severe infections such as, bacterial sepsis, active viral infection and opportunistic infections. Severity as judged by the investigator
3. Any clinically significant test results that in the opinion of the investigator should exclude the participant
4. In the opinion of the investigator, patient in whom withdrawal of the thiopurine would not be appropriate
5. Known allergy/ hypersensitivity/ intolerance to the active substance or excipients, or patients taking any medications which are contraindicated as per the IMPs SmPCs
6. Participation in an investigational trial that involves ongoing treatment with an investigational medicinal product at baseline
7. Pregnant women and women of child bearing potential who are planning to get pregnant during the trial

Date of first enrolment
19/10/2022

Date of final enrolment
17/10/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre

University College Hospital
235 Euston Rd
London
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NW1 2BU

Sponsor information

Organisation
Kings Health Partners

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Sponsor type
Hospital/treatment centre

Website
http://www.guysandstthomas.nhs.uk/Home.aspx

ROR
https://ror.org/01xcsye48

Funder(s)

Funder type
Industry

Funder Name
Celltrion Healthcare

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location
Korea, South

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

Data collected for this trial (an extract from the database) may be shared with external collaborators for the purpose of validating the results or supporting future research. This is explicitly mentioned in the PIS. Data will be shared with the funder, under a non-exclusive, non-transferable, non-sub-licensable, royalty-free licence to use the results for non-commercial research purposes. Appropriate data sharing agreements will be put in place before sharing data with external collaborators.

Intention to publish date
31/07/2026

Individual participant data (IPD) sharing plan
The 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?
HRA research summary			28/06/2023	No	No
Protocol file	version 1.0	07/06/2022	23/10/2023	No	No