ISRCTN13323475 https://doi.org/10.1186/ISRCTN13323475

Investigating the difference between infliximab treatment injected into a vein and injected under the skin in patients with inflammatory bowel disease and inflammatory arthritis already established on infliximab injected into a vein

Submission date 22/01/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol
Registration date 10/02/2021	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 18/01/2022	**Condition category** Other	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

This study is looking at the effects of switching from intravenous (administered into a vein in the hospital) infliximab to infliximab administered subcutaneously (injection under the skin administered at home). The subcutaneous infliximab (commercially known as Remsima) and intravenous infliximab are highly similar.

This study aims to explore the following:

1. Does the clinical status of inflammatory bowel disease (Crohn's disease or ulcerative colitis) or inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis) patients stay the same after switching the route of infliximab administration?
2. How safe and is it to switch from intravenous infliximab to infliximab self-administered subcutaneously?
3. What are the views and experiences of patients who switch from intravenous infliximab to infliximab self-administered subcutaneously?
4. Does the quality of life change for patients switching the route of infliximab administration?

Who can participate?

Patients aged 18 or over with inflammatory bowel disease (Crohn's disease or ulcerative colitis) or inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis) being treated with intravenous infliximab

What does the study involve?

This study aims to follow the normal standard of care as much as possible. Participants will be required to attend up to 4 hospital visits at University Hospital Southampton NHS Foundation

Trust (UHS) for trial assessments which will, as far as possible, mirror normal clinical care. These would replace their normal visits for infusions. Participants will be trained on how to self-inject the study drug and will administer this themselves at home every 2 weeks. The study will last for 24 weeks, after which participants will return to their normal clinical care.

What are the possible benefits and risks of participating?
It is not known if participants will personally benefit from this research, however, it is hoped that this research will show that it is safe and tolerable to switch to the subcutaneous route. One possible benefit is that participants will have fewer visits to the hospital over the time they are in the study.

Most of the treatments and assessments participants will receive will be standard of care (i.e. participants would have received the treatments and assessments anyway even if they weren't involved in the study). There will be several extra questionnaires to complete as part of the study.

The only additional risk beyond the risks of receiving infliximab via the intravenous route could be discomfort or reactions around the subcutaneous injection site. These can include redness, pain, itching, swelling, hardness, bleeding, bruising, cold sensation, irritation, tingling sensation, ulcer, hives, rash, and scab on the skin of the injection site. Most of these reactions are mild and resolve relatively quickly on their own.

The most common risks of receiving infliximab via either the subcutaneous or intravenous routes include viral infections (such as flu or cold sores), headache, upper-respiratory-tract infection (colds), sinusitis (inflammation of the sinuses), nausea (feeling sick), abdominal pain (stomach ache), and injection site-related reactions and pain.

With any infliximab medication, there is a risk of developing an allergic reaction. If a serious reaction occurs, treatment will be given to alleviate the symptoms and further treatment with infliximab will be reviewed. In previous clinical trials, delayed hypersensitivity reactions (unwanted reactions produced by the normal immune system) have been reported so participants will be advised to seek immediate medical advice if they experience any delayed adverse effects.

Where is the study run from?
University Hospital Southampton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
From July 2020 to May 2022

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

Who is the main contact?
Sohail Rahmany, sohail.rahmany@uhs.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Sohail Rahmany

Contact details
Southampton Centre for Biomedical Research
MP 218
D Level
West Wing
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD
No telephone contact available
sohail.rahmany@uhs.nhs.uk

Additional identifiers

EudraCT/CTIS number
2020-004463-25

IRAS number
286907

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 47620, IRAS 286907

Study information

Scientific Title
SWitching InflixiMab to SUbcut from Intravenous Therapy (SWIMSUIT)

Acronym
SWIMSUIT

Study objectives
To evaluate the clinical outcomes of switching a cohort of inflammatory bowel disease (Crohn's disease, Ulcerative Colitis) and inflammatory arthritis (Rheumatoid arthritis, Psoriatic arthritis, and Ankylosing spondylitis) patients from IV infliximab to S/C CT-P13. The study will also explore:
1. Subject clinical characteristics and disease status over time
2. Infliximab and relevant concomitant medication use over time
3. Immunogenicity to infliximab
4. The presence of inflammatory markers over time
5. Subject experience and treatment satisfaction over time

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/12/2020, East Midlands - Nottingham 2 Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)2071048103;nottingham2.rec@hra.nhs.uk) ref: 20/EM/0285

Study design
Single centre, Phase IV non-randomized interventional study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Ulcerative colitis, crohn's disease, rheumatoid arthritis, psoriatic arthritis, or ankylosis spondylitis

Interventions
This study will aim to recruit participants with inflammatory bowel disease or inflammatory arthritis who are being treated with intravenous (IV) infliximab as part of their routine clinical care. Participants will be switched from IV infliximab to a self-administered subcutaneous injection of 120 mg/ml infliximab biosimilar (CT-P13) every 2 weeks for a duration of 24 weeks. The first subcutaneous injection will be given when the patient is scheduled to receive their next dose of IV infliximab. Training will be provided and the first dose will be administered under supervision. Thereafter subcutaneous CT-P13 will be self-administered every 2 weeks by the subject in their home.

Potential participants will be sent the patient information sheet by post, email, or another contact with the clinical or research team up to 24 h prior to enrolment. The patients will be given adequate time to consider the trial information before being asked to sign the informed consent form. Patients who do not wish to take part in the study will be given the opportunity to take part in the semi-structured qualitative interviews to capture their reasons for not participating.

Participants will be assessed at a screening visit and 3 further visits.

Baseline (screening) visit
At the screening visit, the investigator will go through the inclusion and exclusion criteria and ensure that the patient is eligible to proceed.
The patient will be fully informed of all aspects of the trial, the potential risks, and their

obligations. The aims of the study and all tests to be carried out will be explained. The patient will be given the opportunity to ask any questions that they have and will then have time to consider whether to participate. If they do decide to participate, they will sign and date the consent form and will be given a copy to take away. The original will be kept in the site file and stored as source documentation. These forms will also be signed and dated by the Investigator.

The assessments at the baseline visit will include:
1. Medical history, listing any concomitant medications, establishing a baseline of adverse events, and review of any contraindications
2. Tests for active and inactive tuberculosis, hepatitis B virus, hepatitis C, and varicella, if previous test results are not available
3. Pregnancy tests for women of childbearing potential
4. Laboratory tests including haemoglobin, platelets, albumin, and C-reactive protein (CRP)
5. Completion of disease scores (disease-specific). For Crohn's disease patients, the Modified Harvey-Bradshaw Index (mHBI) and IBD Control (IBD-CTRL) Patient-Reported Outcome Measure (PROM). For ulcerative colitis patients, the Simple Clinical Colitis Activity Index (SCCAI) (UC) and IBD Control (IBD-CTRL) Patient Reported Outcome Measure (PROM). For rheumatoid arthritis and psoriatic arthritis patient's, the Clinical Disease Activity Index/Simplified Disease Activity Index (CDAI/SDAI) and Disease Activity Score from 28 joints (DAS28). For ankylosis spondylitis patients, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).
6. Completion of Health-Related Quality of Life measures. For Crohn's disease and ulcerative colitis patients, the Short Form 36 Health Survey Questionnaire (SF-36) and IBD Control (IBD-CTRL) Patient-Reported Outcome Measure (PROM). For rheumatoid arthritis, psoriatic arthritis and ankylosis spondylitis patients, the SF-36, pain visual analogue score (VAS), and Health Assessment Questionnaire Disability Index (HAQ-DI), and one of the following, as appropriate: Bath Ankylosing Spondylitis Functional Index (BASFI), Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, or Rheumatoid Arthritis Impact of Disease (RAID) questionnaire .
7. Qualitative assessments using semi-structured interviews

If the patient is eligible to continue onto the study, they will be enrolled into the inflammatory bowel disease or inflammatory arthritis cohort. Participants will be allocated a subject study ID number and will receive a participant dosing and questionnaire diary with the relevant research team's contact details. Participants will be trained on injection requirements at this visit. A letter will be sent to the GP for each participant informing them of the clinical study.

In order to minimise the number of potential visits to the hospital, the baseline visit and study visit 1 may take place on the same day. Visit 1 will involve the first subcutaneous CT-P13 administration as well as the following assessments:
1. Clinical review
2. Routine laboratory tests
3. Anti-Drug Antibody and drug trough level measurements
4. A stool sample will also be collected at this visit for faecal calprotectin for the inflammatory bowel disease cohort
5. Pregnancy test for women of childbearing potential
6. Completion of disease scores (disease-specific) as at the baseline visit
7. Completion of Health-Related Quality of Life measures as at the baseline visit
8. Completion of Treatment Satisfaction questionnaire of Medication (these will be completed every 2 weeks)
9. Completion of VAS pain scores (these will be completed after each administration of injection)
10. Drug accountability/compliance
11. Incidence of adverse events
At this visit, the study team will provide the CT-P13 medication to participants, and re-training

for subcutaneous injections will be provided if necessary. The first dose will be administered under supervision.

Visit 2 will take place after 12 weeks and involve the following assessments:
1. Clinical review
2. Routine laboratory tests
3. Anti-Drug Antibody and drug trough level measurements
4. Pregnancy test for women of childbearing potential
5. Completion of disease scores (disease-specific) as at the baseline visit
6. Completion of Health-Related Quality of Life measures as at the baseline visit
7. Completion of Treatment Satisfaction questionnaire of Medication (these will be completed every 2 weeks)
8. Completion of VAS pain scores (these will be completed after each administration of injection)
9. Drug accountability/compliance (using the dosing diary)
10. Incidence of adverse events
At this visit, the study team will provide further CT-P13 medication to participants.

Between weeks 12 and 24, there is the option of participating in a semi-structured interview exploring the participant's experience of switching from IV Infliximab to subcutaneous Infliximab.

Visit 3, the end of study visit, will take place after 24 weeks and involve the following assessments:
1. Clinical review
2. Routine laboratory tests
3. Anti-Drug Antibody and drug trough level measurements
4. A stool sample will also be collected at this visit for faecal calprotectin for the inflammatory bowel disease cohort
6. Completion of disease scores (disease-specific) as at the baseline visit
7. Completion of Health-Related Quality of Life measures as at the baseline visit
8. Completion of Treatment Satisfaction questionnaire of Medication
9. Completion of VAS pain scores
10. Drug accountability/compliance
11. Incidence of adverse events
At this visit, the study team will collect completed diary dosing cards and questionnaires as well as any unused pens or syringes.

Patient withdrawal:
Subjects may withdraw from the study at any time and are not obliged to give their reasons for doing so. The investigator may withdraw the subjects at their discretion or due to any adverse events. An end of study visit will be completed if a withdrawal occurs.

Semi-structured Interviews with Participants:
The study team will conduct semi-structured interviews on a purposive sample of patients in a setting of their choice, either in person or over the phone. Interviews will take place at times convenient to the interviewees (likely to be at a study visit) and will last no longer than 1 h. An interview guide will be constructed based on key issues identified from the literature and drawing on our combined clinical experience. This guide will be piloted with a small sample of patients and revised if necessary. Subject interviews will also draw on individual subject responses in the outcome measures completed at regular time points throughout the period of the study. Interviews will be audio-recorded using a digital recorder and fully transcribed.

Interview data will be analysed using thematic analysis to identify key themes and issues which characterise the patient and clinical staff experience. Braun and Clarke's (2006) six steps of thematic analysis will be used: data familiarisation, generating initial codes, themes searching, reviewing themes, defining and naming the themes, and producing the report.

In addition, the study team will conduct qualitative interviews with participants who have been approached but declined to participate in the study from the outset. Only a selection of these participants will be approached to take part in the interview only process in order to explore reasons and potential barriers. These will be conducted over the phone. Participants will also be required to verbally consent to take part in the interview only process over the phone. As with the interviews conducted on trial participants, interview data will be analysed using thematic analysis to identify key themes and issues.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
infliximab, CT-P13 SC

Primary outcome measure
Clinical status at 24 weeks measured using the following at baseline, 12, and 24 weeks:
1. For Crohn's disease patients: Modified Harvey-Bradshaw Index (mHBI) and IBD Control (IBD-CTRL) Patient Reported Outcome Measure (PROM). An increase in mHBI score of ≥3 and/or a decline in IBD-CTRL score of ≥4 points at any time during the respective study period will be classified as failure to maintain baseline clinical status.
2. For ulcerative colitis patients: Simple Clinical Colitis Activity Index (SCCAI) (UC) and IBD Control (IBD-CTRL) Patient Reported Outcome Measure (PROM). An increase in SCCAI ≥3 score and/or a decline in IBD-CTRL score of ≥4 points at any time during the respective study period will be classified as failure to maintain baseline clinical status.
3. For rheumatoid arthritis and psoriatic arthritis patient's: Clinical Disease Activity Index /Simplified Disease Activity Index (CDAI/SDAI) and Disease Activity Score from 28 joints (DAS28) where an increase of >0.6 or a score of >5.1 deemed to be a failure
4. For ankylosis spondylitis patients: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) where a >50% worsening of BASDAI score will be deemed a failure

Secondary outcome measures
1.Safety and tolerability measured using the incidence of Adverse Events (AE), Serious Adverse Events (SAE), and Adverse Events of Special Interest (AESI) causally related to Infliximab between baseline and 24 weeks
2. Pharmacokinetics measured using blood samples to determine drug trough levels at baseline, 12, and 24 weeks
3. Immunogenicity measured using the presence of anti-drug antibodies in blood samples baseline, 12, and 24 weeks
4. Quality of life measured using the following at baseline, 12, and 24 weeks:
4.1. For Crohn's disease and ulcerative colitis patients: Short Form 36 Health Survey Questionnaire (SF-36) and IBD Control (IBD-CTRL) Patient-Reported Outcome Measure (PROM)
4.2. For rheumatoid arthritis, psoriatic arthritis and ankylosis spondylitis patients: SF-36, pain visual analogue score (VAS), and Health Assessment Questionnaire Disability Index (HAQ-DI),

and one of the following, as appropriate: Bath Ankylosing Spondylitis Functional Index (BASFI), Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, or Rheumatoid Arthritis Impact of Disease (RAID) questionnaire
5. Levels of laboratory inflammatory markers measured using the following at baseline, 12, and 24 weeks:
5.1. For all participants: Full Blood Count (FBC), C-reactive protein (CRP), and serum albumin from blood samples
5.2. For Crohn's disease and ulcerative colitis patients: faecal calprotectin from stool samples
5.3. For rheumatoid arthritis, psoriatic arthritis and ankylosis spondylitis patients: Erythrocyte sedimentation rate (ESR) from blood samples
6. Patient experience measured using semi-structured interviews analysed using thematic analysis, IBD control Patient-Reported Outcome Measure (PROM), patient Treatment Satisfaction Questionnaire for Medicine (TSQM), Disease-specific PROM for rheumatology patients (HAQ-DI and pain VAS), and injection site discomfort VAS at 24 weeks

Overall study start date
31/07/2020

Completion date
02/05/2022

Eligibility

Key inclusion criteria
1. Confirmed diagnosis of Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, and/or ankylosis spondylitis
2. Established on IV infliximab (>4 doses) prior to study enrolment
3. Anticipated to remain on infliximab for the duration of the study
4. Last dose of IV infliximab received <8 weeks ago
5. Able to comply with study requirements
6. Able to provide informed consent
7. Aged ≥18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
200 (150 with inflammatory bowel disease and 50 inflammatory arthritis)

Key exclusion criteria

1. Allergic to any of the known excipients of infliximab
2. Scheduled for a surgical procedure or planned hospitalisation within 6 months of enrolment
3. Not anticipated to remain on infliximab for >6 months after enrolment
4. Pregnant or lactating

Date of first enrolment
25/02/2021

Date of final enrolment
25/10/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospital Southampton NHS Foundation Trust
Gastroenterology and Hepatology
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

Sponsor details
R&D Department
University Hospital Southampton NHS Trust
Tremona Road
Southampton
England
United Kingdom
SO16 6YD
+442381205664
sponsor@uhs.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.uhs.nhs.uk/home.aspx

ROR
https://ror.org/0485axj58

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
Planned publication in October 2022.

Intention to publish date
31/10/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Sohail Rahmany (Sohail.rahmany@uhs.nhs.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No