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Additional treatment for improving severe colitis

Submission date 08/08/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 30/10/2024	**Overall study status** Ongoing	
Last Edited 15/04/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Ulcerative colitis (UC) is a condition in which the large intestine, also known as the colon, becomes inflamed. In most patients, UC involves some periods when well but also periods where the symptoms become more severe (called flares).
Sometimes, the intensity of UC symptoms means patients need to be admitted to hospital. If this happens, patients will be given drugs called corticosteroids (commonly known as steroids) to control and reduce the inflammation. If steroids on their own work, patients can be discharged from hospital, usually after just a few days. However, if the steroids are not making the symptoms better, other medicines can be given to try to help. This would normally be either a drug called Infliximab or Ciclosporin. Either drug can be used and both are equally effective but the improvements with these drugs only occurs in some patients. If these additional treatments do not work, then is some cases, surgery to remove the colon would be considered. This is called a colectomy.
Currently, we know that only half of patients given steroids alone will get better, whilst the other half will need one of the other medications and some patients will still need to have surgery.
This study will test whether giving patients another medicine, Upadacitinib which is approved for use in UC, in addition to the standard initial treatment with steroids, will reduce the number of patients who go on to receive further medical treatments or need surgery.

Who can participate?
This randomised controlled trial will recruit 300 adults who have been admitted to UK NHS hospitals with an Acute Severe flare of UC (ASUC) .

What does the study involve?
The study has a double blind active/placebo medication period when the patient and clinical team wont know which additional treatment but after 10 days all participants will know what they have been taking. Depending on the response to study medication/placebo, participants may be in the study for up to 8 weeks.

What are the possible benefits and risks of participating?
Benefits:

Not provided at time of registration
Risks:
There are potential risks from the side effects from the study medication but the risk : benefit ratio is considered to be positive in the setting of active ulcerative colitis. In addition, the study medication is licensed for use in the study population and for the indicated disease and has a well known risk profile. The risk include a small increase in risk of venous thrombosis. The risk of this is minimal and mitigated already as these patients will be given venous thromboprophylaxis as per standard care and anyone with previous history of venous thromboembolism are excluded. In the study protocol patients will be monitored daily by the clinical and research team for any adverse effects . Participants will be acutely unwell at study entry and for this reason, non response to treatment with worsening of Ulcerative Colitis and related symptoms (in the clinical opinion of the local PI will be exempt from reporting as SAEs. However, they will still be recorded in the study database and safety reporting will be conducted throughout the study and a review of safety event trends will be undertaken by the DMEC at designated time points during the study and in the event of escalation and SUSAR.
In addition there is planned interim analysis for futility and safety within protocol so that if the intervention do not meet the thresholds of efficacy the study will be terminated at the interim analysis.
Participants will be given a Subject ID Card on which their local research team contact details in the event of an emergency. All participants will be unblinded at Day 10, but should the need arise, they can be unblinded earlier to support emergency clinical care decisions.
Non responders have the option to join a sub-study if they are unblinded at Day 10 have been on Placebo. They do not have to enrol in a sub study if they choose not to.

Pregnant or lactating women will not be eligible and all women of child bearing potential will be asked to follow contraception guidance.
All procedures that the study will collect data on, will be routine standard of care procedures reducing the burden of study interventions on participants. No additional interventions will be included in the study design, other than the collection of biobank blood samples which we will try and do at the same time as routine blood samples are taken. Participant can withdraw at any time during the study and clinicians can choose to withdraw the participant if it is in the patients best interest. No routine standard of care procedure will be withheld.
Patients are required to fill some questionnaires but as described in the PPI section the questionnaire burden has minimised and is at 3 time points across the 12 month duration.

Where is the study run from?
Hull University Teaching Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
August 2024 to February 2029

Who is funding the study?
AbbVie (UK)

Who is the main contact?
aceso@hyms.ac.uk

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1010109

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 1010109

Study information

Scientific Title
ACESO trial: Upadacitinib Co-therapy with Corticosteroids in Early Acute Severe Ulcerative Colitis (A Phase III randomised placebo controlled double blinded trial)

Acronym
ACESO

Study objectives

The overall study objective is to evaluate the clinical efficacy of Upadacitinib as combined treatment with intravenous steroids in patients with ASUC

Secondary objectives:
1. To evaluate the impact of combination therapy (Upadacitinib + steroids) on the need for rescue medical or surgical therapy
2. Evaluate the safety of use of combination therapy (Upadacitinib + steroids) in the setting of ASUC
3. Evaluate the efficacy and safety of the combination (Upadacitinib + steroids) in a subgroup of patients with prior exposure to advanced therapies
4. Determine the impact of combination therapy (Upadacitinib + steroids) on a range of other indices of treatment response including duration of hospital stay, time to treatment response, quality of life using CUCQ-32, patient preference using DISCUSS tool and 2 Validated psychometric tools (Decision Conflict Scale & Decision Regret Scale)
5. Collect biobanking samples to develop and refine high risk immunophenotype in ASUC who will benefit from combination (Upadacitinib + steroids) therapy

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/10/2024, West of Scotland REC 1 (West of Scotland Research Ethics Service, Ward 11, Dykebar Hospital, Grahamston Road, Paisley , PA2 7DE, United Kingdom; -; ggc.wosrec1@nhs.scot), ref: 24/WS/0123

Study design
Interventional double blind randomized placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Acute severe ulcerative colitis

Interventions
Double blind placebo controlled
Investigation arm: Upadacitinib 45mg orally + Standard care
Comparator arm : Placebo orally + Standard care
Stratification: Prior steroid use, Prior Infliximab use
Duration of treatment : 2 months

Intervention Type
Drug

Pharmaceutical study type(s)
Therapy

Phase
Phase III

Drug/device/biological/vaccine name(s)
Upadacitinib

Primary outcome measure
Need for medical or surgical rescue therapy within 10 days following commencement of IV corticosteroids therapy

Secondary outcome measures
1. Percentage of patients who achieve clinical response at Day 10 from baseline (MTWSI reduction ≥3 points and MTWSI < 10)
2. Time to clinical response (MTWSI reduction ≥3 points + MTWSI <10)
3. Time to rescue therapy (medical or surgical) (MTWSI)
4. Percentage of patients who meet Oxford Travis rescue criteria for rescue therapy on or beyond Day 3 of hospitalisation
5. Percentage of patients who achieve clinical remission at 10 days and 8 weeks (Mayo stool frequency sub-score of 0 or 1, and rectal bleeding sub-score of 0)
6. Percentage of patients who achieve biomarker remission at 10 days and 8 weeks (CRP ≤ 5mg /L, calprotectin ≤ 250µg/g where available)
7. Percentage of patients who achieve endoscopic remission at 8 weeks where data available (endoscopic Mayo sub-score 0-1)
8. Incidence of colectomy within 8 weeks following commencement of IV corticosteroid therapy
9. Incidence of Adverse Events (AE) and Serious Adverse Events (SAE)
10. Total duration of hospital stay

Overall study start date
06/08/2024

Completion date
26/02/2029

Eligibility

Key inclusion criteria
1. Patients aged 18 – 65 years inclusive
2. Have given written informed consent to participate
3. Hospitalised patients with clinically confirmed or suspected ASUC
4. Modified Truelove and Witts severity index (MTWSI) score ≥ 11
5. Requirement for treatment with IV corticosteroids in the judgement of the treating clinician and the possibility to receive the IMP within 36 hours of admission

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
300

Key exclusion criteria
1. Patients with any absolute contraindication to Upadacitinib
2. Proven infective colitis within 4 weeks of baseline assessment (Stool Cultures or C Diff Toxin assay positive, Cytomegalovirus (CMV) on biopsies)
3. Pregnant patients or patients breast feeding
4. Patients with toxic megacolon (TMC) at baseline assessment prior to randomisation
5. Use of strong CYP3A4 inhibitor medications (azoles, clarithromycin) and co-administration of food and drink containing grapefruit
6. Use of strong CYP3A4 inducer medications (including Rifampicin and Phenytoin)
7. Recent history of incompletely treated malignancy within 12-months (patients with a solid organ malignancy that remains under active treatment or where oncologists have not confirmed complete eradication)
8. Neutropenia with baseline ANC <1 x 10^9 cells/L
9. Absolute Lymphocyte Count <1 x 10^9 cells/L
10. Hb <80 g/L
11. Moderate or Severe renal impairment (estimated glomerular filtration rate [eGFR] <40ml/min /1.73m²)
12. Severe hepatic impairment (Child-Pugh C)
13. ALT or AST >2.5 the upper limit of normal
14. Patients with personal history of confirmed Venous Thromboembolism (VTE)/Pulmonary Embolism (PE) who are not on effective anticoagulation (e.g. history of previous Deep Vein Thrombosis ((DVT) or PE)) but no longer requiring anticoagulation, history of previous DVT or PE requiring anticoagulation where anticoagulation was not tolerated or withdrawn because of side-effects)
15. Evidence (from blood cultures etc) or clinical suspicion of systemic infection
16. English not adequate in absence of local translation service (i.e. patient unable to comprehend trial patient information sheet)
17. Currently taking part in another Clinical Trial of an Investigational Medicinal Product [CTIMP]
18. Treatment with other Janus kinase (JAK) inhibitors (e.g. Tofacitinib or Filgotinib) within 4 weeks of the time of screening
19. Patients previously exposed to Upadacitinib as per local label
20. Patients with risk factors for MACE/malignancy unless no suitable treatment alternatives available
21. A history of untreated pulmonary Tuberculosis (TB) infection

22. Any absolute contraindication to corticosteroid
23. Patients with administered live vaccines of replication potential within 30 days prior to screening

Date of first enrolment
30/04/2025

Date of final enrolment
30/11/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Hull University Teaching Hospitals NHS Trust

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Industry

Funder Name
AbbVie

Alternative Name(s)
AbbVie Inc., AbbVie U.S., AbbVie US, Allergan

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities

Intention to publish date
26/02/2030

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

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