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EValuating the efficacy Of upadacitinib and combination upadacitinib pLus risankizumab for the treatment of fistulising perianal Crohn's Disease – an open-label Phase IV a randomisEd controlled trial

Submission date 28/07/2026	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 25/09/2026	**Overall study status** Ongoing	
Last Edited 25/09/2026	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims

A perianal fistula is an abnormal tunnel that forms between the back passage and the skin around the bottom. Fistulas can happen for different reasons. When this happens in people with Crohn’s disease (CD), it is called fistulising perianal Crohn's disease (fpCD). fpCD can cause pain around the bottom, leakage and difficulty controlling bowel movements. It is usually treated with medicine to calm down the inflammation and surgery.

It is unclear which treatments work best for people with fpCD. A recent priority-setting partnership brought patients, clinicians, and researchers together to set the top 10 research priorities for fpCD. The highest priority was finding the best treatment strategy for fpCD. This study aims to address this.

Recent research suggests that a newer treatment, licensed for CD, called upadacitinib (Upa), might be helpful in treating fpCD. We aim to research how helpful this drug is in treating fpCD in a clinical trial.

Another drug (Risa) may also be helpful in treating fpCD. Risa works on a different part of the immune system to Upa. We aim to see if combining risa with upa will help more people with fpCD than taking upa alone.

Who can participate?

Patients aged 18 years and over with active fpCD

What does the study involve?

Everyone will be given the Upa medicine. Half of people taking part in this study will also receive Risa on top of Upa. This study will look at how well the study drugs can heal fistulas and whether the fistula has stopped draining and whether the inflammation has settled on an MRI scan. We will also look at other areas that are important to people living with fpCD, such as improvement in controlling their bowel movements, depression, and quality of life. Participants will be

followed up for a year after entering the study. With consent, we will also ask for sample donations from people taking part, including blood, stool, tissue and swabs.

What are the possible benefits and risks of participating?
Upadacitinib is a licensed medication in the UK that is given to people with a number of different health conditions, including Crohn's disease. Eligibility will be assessed prior to informed consent, including an assessment of any previous reactions and treatments with JAK inhibitors. In some cases, side effects may occur. The most common reported side effect is an infection in the nose and throat. Most cases are mild and can be dealt with using over-the-counter medication. Other less common side effects include fever, flu, headaches, acne, shingles, an increase in a type of fat in your blood, tiredness and weight gain.
Risankizumab is a licensed medication in the UK that is given to people with a number of different health conditions, including Crohn's disease.
The most common reported side effects include the common cold, infections of the nose and throat, pain and redness where the needle went in, tiredness, itching and fungal skin infections. Where risankizumab is occurring at home, the site nurse will check in each time the participant has administered the dose. The participant will be fully trained on how to do the dose, as well as advised on good hygiene when administering the dose at home.
Participant safety will be monitored closely throughout, and a DMEC oversight committee will review presented safety data at frequent periods throughout the trial.
The type of MRI scan uses a dye called contrast to get more detailed images. A contrast dye is a chemical that is injected into the body through a vein in the arm or groin. Sometimes people can have a reaction to this. This happens in fewer than 1 in 100 people (6 in 1000). This will be explained at the informed consent stage and a check will be made by the site team at eligibility to ensure the participant can have an MRI scan safely.
The risks of a blood test are small but in some cases can include pain, a bruise at the point where the blood is taken, redness and swelling of the vein, infection, and sometimes fainting. This will be explained at each procedure and the participant will be monitored in clinic at each blood draw.
Pregnancy will be assessed at screening. Patients on JAK-inhibitor medication are advised not to become pregnant because of the potential for harm to the unborn baby. Pregnancy tests will be taken throughout the 52 weeks (if applicable). Likewise, these women must use an effective contraceptive during the course of this study.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
September 2026 to December 2029

Who is funding the study?
AbbVie (USA)

Who is the main contact?
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Scientific, Public

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Additional identifiers

Integrated Research Application System (IRAS)
1012946

Sponsor's protocol code number
176584

Study information

Scientific Title
EValuating the efficacy Of upadacitinib and combination upadacitinib pLus risankizumab for the treatment of fistulising perianal Crohn's Disease – an open-label Phase IV a randomisEd controlled trial

Acronym
U-EVOLVE

Study objectives
Primary objective:
The primary objective is to compare the efficacy of upadacitinib monotherapy with upadacitinib plus risankizumab combination therapy for the induction of clinical and radiological perianal fistula response in fistulising perianal Crohn’s disease (fpCD).

Secondary objective:
To characterise the molecular landscape of fpCD and treatment response through multiomic profiling in a translational sub-study.

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control

Active

Assignment
Parallel

Purpose
Treatment, Safety

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Fistulising perianal Crohn's disease (fpCD)

Interventions
Participants will be randomised in a 1:1 ratio using the Sealed Envelope randomisation system to one of two parallel treatment arms:

Arm 1: Upadacitinib monotherapy
Participants will receive upadacitinib orally at a dose of 45 mg once daily from baseline to Week 12, followed by 30 mg once daily from Week 12 to Week 48.

Arm 2: Upadacitinib and risankizumab combination therapy
Participants will receive upadacitinib orally at a dose of 45 mg once daily from baseline to Week 12, followed by 30 mg once daily from Week 12 to Week 48. Participants will also receive risankizumab 600 mg by intravenous infusion at Weeks 0, 4 and 8, followed by risankizumab 360 mg by subcutaneous injection every 8 weeks from Week 12 to Week 44.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Updacitinib, risankizumab

Primary outcome(s)
The proportion of participants achieving combined clinical and radiological fistula response, where clinical fistula response is defined as a reduction of 50% or more in the number of fistula tracts that were draining at baseline assessed by clinical examination, and radiological fistula response is defined as a reduction of 4 points or more from baseline in the Magnetic Resonance Novel Index for Fistula Imaging in Crohn’s Disease (MAGNIFI-CD) score, assessed by blinded central review of pelvic magnetic resonance imaging (MRI) performed for fistula assessment, at Week 24.

Key secondary outcome(s)
1. The proportion of participants achieving complete closure of all treated external fistula openings without development of a new fistula, abscess or significant fluid collection at Week 24, defined as clinical closure of all treated external fistula openings, with no development of a new fistula or abscess and no fluid collection measuring more than 1 cm in at least two of three

dimensions on pelvic MRI performed for fistula assessment, assessed by blinded central review at Week 24.
2. The proportion of participants achieving combined clinically assessed fistula remission and radiological fistula response at Week 48, where clinically assessed fistula remission is defined as cessation of drainage from all fistula tracts that were draining at baseline and radiological fistula response is defined as a reduction of 4 points or more from baseline in the MAGNIFI-CD score, assessed by blinded central review of pelvic MRI performed for fistula assessment at Week 48.
3. The proportion of participants achieving radiological fistula response, defined as a reduction of 4 points or more from baseline in the MAGNIFI-CD score, assessed by blinded central review of pelvic MRI performed for fistula assessment at Weeks 24 and 48.
4. The proportion of participants achieving combined clinically assessed and radiological fistula remission at Week 48, where clinically assessed fistula remission is defined as cessation of drainage from all fistula tracts that were draining at baseline and radiological fistula remission is defined as a MAGNIFI-CD score of 0, assessed by clinical examination and blinded central review of pelvic MRI performed for fistula assessment at Week 48.
5. The proportion of participants achieving clinically assessed fistula response at Week 48, defined as a reduction of 50% or more in the number of fistulas that were draining at baseline, assessed by clinical examination at Week 48.
6. Change from baseline in the MAGNIFI-CD score, assessed by blinded central review of pelvic MRI performed for fistula assessment at Weeks 24 and 48.
7. The proportion of participants with Class 2b fpCD at baseline who downstage to Class 2a, determined according to the TOpClass classification for fpCD by a central Downstaging Committee using prespecified clinical, radiological and treatment-related criteria at Weeks 24 and 48. A participant will be considered to have achieved this outcome if they are re-classified to Class 2a at either Week 24 or Week 48.
8. The number and proportion of participants experiencing adverse events, serious adverse events and prespecified adverse events of special interest, recorded and classified in accordance with the study protocol, including assessment of seriousness, severity and relationship to study treatment, from the first administration of study treatment through Week 52. Prespecified adverse events of special interest include serious infections, including tuberculosis, herpes zoster and opportunistic infections; malignancies; gastrointestinal perforation; major adverse cardiovascular events, including myocardial infarction and cardiovascular death; thromboembolic events, including deep-vein thrombosis and pulmonary embolism; and drug-induced liver injury.

Completion date
31/12/2029

Eligibility

Key inclusion criteria
1. Adults aged 18-63 years
2. Diagnosis of Crohn's disease (CD) with a minimum duration of at least 3 months
3. At least one active draining perianal fistula as a complication of CD, confirmed by magnetic resonance imaging (MRI)
4. Able to provide written informed consent

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 Years

Upper age limit
63 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Patients with any absolute or relative contraindication to upadacitinib
2. Patients with any absolute or relative contraindication to risankizumab
3. Currently taking part in another Clinical Trial of an Investigational Medicinal Product (CTIMP)
4. Patients unwilling or unable to provide informed consent
5. Patients with contraindications to MRI scans

Pregnancy/breastfeeding exclusions:
6. Female patients who are currently/planning to become pregnant, breastfeeding, or currently /planning to donate eggs during the study period
7. Female patients who are able to become pregnant and are not willing and unable to use a highly reliable form of contraception during treatment and for 4 weeks following the final dose of upadacitinib. Acceptable forms of contraception include the following:
7.1. Established use of oral, injected or implanted hormonal methods of contraception.
7.2. Placement of an intrauterine device or intrauterine system
7.3. Male sterilisation if the vasectomised partner is the sole partner for the participant
7.4. Bilateral tubal occlusion
7.5. True abstinence (defined as refraining from any sexual relationship in which the participant may become pregnant), when this is in line with the preferred and usual lifestyle of the participant. Note periodic abstinence and withdrawal are not acceptable methods of contraception.

IBD exclusions:
8. Participants previously exposed to, or treated with, upadacitinib for any indication
9. Participants previously exposed to, or treated with, risankizumab for any indication
10. Patients who have had inadequate response or loss of response to JAK inhibitors
11. Patients who have had inadequate or loss of response to p19 inhibitors
12. History of, or concurrent rectovaginal, anovaginal, or entero-vesical fistulae
13. Ulcerative colitis (UC), indeterminate colitis, ischemic colitis, fulminant colitis, or toxic mega-colon
14. Total proctocolectomy, total colectomy or likely requirement for luminal disease surgery during the study
15. Current stoma or reversal of stoma within the past 3 months

Infection exclusions:
16. Any active, chronic or recurrent infection that, based on the Investigator's clinical assessment, makes the patient an unsuitable candidate for the study, including:

16.1. Tuberculosis (TB) (active TB, untreated latent TB)
16.2. Active HBV, HCV or HIV infection
16.3. Clinical, radiological or laboratory evidence or suspicion (e.g., positive blood cultures) of systemic bacterial or fungal infection
17. History of one or more prior episodes of disseminated herpes simplex (including eczema herpeticum); history of two or more prior episodes of herpes zoster, or one or more episodes of disseminated herpes zoster
18. In receipt of live vaccines in the 28 days prior to initiating upadacitinib

Oncology exclusions:
19. Active malignancy
20. Significant risk factors for malignancy e.g. malignancy within the past 5 years, prior lymphoma, genetic syndromes (e.g., Lynch syndrome, FAP), unless there are no suitable treatment alternatives available

21. Current organ transplant

Cardiovascular exclusions:
23. History of confirmed venous thromboembolism (VTE) or pulmonary embolism (PE) in individuals who are not on effective anticoagulation, including:
23.1. Those with a history of deep vein thrombosis (DVT) or PE who no longer require anticoagulation
23.2. Those with a history of DVT or PE requiring anticoagulation, who discontinued anticoagulation therapy due to intolerance or side effects
24. Cardiovascular disease including symptomatic ischemic heart disease, cerebrovascular disease, peripheral vascular disease and history of uncontrolled hypercholesterolaemia or lipidaemia, unless there are no suitable treatment alternatives available

Metabolic exclusions:
25. Use of strong CYP3A4 inhibitor medications (azoles, clarithromycin) and co-administration of food and drink containing grapefruit
26. Use of strong CYP3A4 inducer medications (including rifampicin and phenytoin)
27. History of clinically significant (per Investigator’s judgement) illicit drug or alcohol abuse within the last 6 months
28. Screening laboratory values that meet the following criteria at the most recent testing prior to the first dose of study drug:
28.1. Neutropenia (baseline ANC <1 x 10^9 cells/l)
28.2. Absolute Lymphocyte Count <0.75 x 10^9 cells/l
28.3. Hb <80 g/l
28.4. Moderate or Severe renal impairment (estimated glomerular filtration rate [eGFR] <30 ml /min/1.73 m^2)
28.5. Severe hepatic impairment (Child-Pugh C)

Date of first enrolment
14/09/2026

Date of final enrolment
15/08/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Not provided at time of registration
-
-
England
-

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type

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

Individual participant data (IPD) sharing plan

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