ISRCTN80103507 https://doi.org/10.1186/ISRCTN80103507

A clinical trial to see if a mesenchymal stem cells treatment called ORBCEL-C™ can help to treat primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis and Crohn’s disease

Submission date
30/11/2021

Recruitment status
No longer recruiting

Registration date
01/04/2022

Overall study status
Ongoing

Last Edited
07/02/2025

Condition category
Other

[_] 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
The aim of this study is to find out whether patients with primary sclerosing cholangitis (PSC), rheumatoid arthritis (RA), lupus nephritis (LN) or Crohn's disease (CD) can potentially be treated safely with a cell therapy called ORBCEL-C™. Primary sclerosing cholangitis (PSC) is a rare disease that attacks the bile ducts. Rheumatoid arthritis causes pain, swelling and stiffness in the joints. Lupus nephritis is inflammation of the kidney. Crohn's Disease is a condition that causes inflammation of the digestive system. Specifically, the aim of this study is to see if ORBCEL-C™ can restore the balance between certain immune cell types in the blood. Although patients may not directly benefit from taking part in this study, they will help to see if ORBCEL-C™ can be used in the future as a new or alternative treatment. ORBCEL-C™ is made from mesenchymal stromal cells (MSCs). MSCs are thought to play a role in the repair and renewal of tissue as well as reducing inflammation. MSCs have been safely used in over 100 clinical trials and when used as a cell therapy in patients with inflammatory diseases they have been shown to reduce damage and inflammation to tissue. Tests have shown ORBCEL-C™ to be safe. This is the first time this form and dose of ORBCEL-C™ has been used in a clinical trial.

Who can participate?
Patients aged 18 years and over with either primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis or recurrent Crohn’s disease, who are able to fulfil entry requirements. (Updated 07/02/2025: Please note the lupus nephritis and Crohn's disease cohorts are currently closed to recruitment).

What does the study involve?
Patients will be involved in the trial for approximately 25 months and will be required to attend up to 13 extra hospital appointments in addition to their normal treatment visits (depending on their disease). There will also be two booked telephone calls to see how they are.
At two of the visits, patients with primary sclerosing cholangitis, rheumatoid arthritis and lupus nephritis will receive a dose of ORBCEL-C™ into their arm using a drip and needle, otherwise

known as an intravenous infusion. This will take up to 15 minutes. Patients will have to stay in hospital for 4 hours after having ORBCEL-C™, so that doctors can monitor their vital signs.
At two of the visits, patients with Crohn's disease will receive an injection of ORBCEL-C™ into their digestive tract tissue using a needle during a colonoscopy. The injection of MSCs will take up to 15 minutes. Patients will have to stay in hospital for 4 hours after the injection, so that doctors can monitor their vital signs.
Study visits will last between 2 and 8 hours and include the collection of health history, heart rhythm scan (electrocardiogram [ECG]), body systems exam, disease-specific measures, blood tests, pregnancy tests (if applicable), medication reviews, patient questionnaires and possible symptoms and side-effects reviews. In addition, patients with rheumatoid arthritis or Crohn's disease will have two biopsy (tissue) samples collected. Patients will have the option to complete patient questionnaires either electronically or in a paper booklet.

What are the possible benefits and risks of participating?
Participants will help the researchers to understand whether ORBCEL-C™ is safe and potentially effective in reducing inflammation and damage in patients with primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis and Crohn's disease. It is important to understand that participants may not directly benefit from taking part in this study, as the benefit of ORBCEL-C™ in patients with these diseases is not yet proven. However, participants will be helping to see if ORBCEL-C™ could be used in the future as an alternative treatment for people with these diseases. ORBCEL-C™ has been used in one clinical trial and MSCs have been used in many other clinical trials. Participants will be monitored for any symptoms or possible side effects.
Previously, some patients who have received MSCs (reported in 1 in 100 patients) have had a few mild and common possible side-effects, all resolving within 3 to 4 hours: pain or itch at the injection site, high temperature, headache, and a foul/metallic taste in the mouth. In some cases, paracetamol was given to treat the headache or high temperature. A few mild and uncommon symptoms and possible side-effects (reported in 1 in 1000 patients) have been felt, all resolving within 3 to 4 hours: tiredness and bad breath. A serious and uncommon sign and symptom (reported in 1 in 893 patients) was an allergic reaction. This can cause redness, itchiness and swelling of the face/lips/tongue, otherwise called anaphylaxis. If this does happen, it tends to occur in the half an hour after an injection. The trial team will recognise and treat this quickly. In rare cases, the immune system may make anti-HLA antibodies in response to having ORBCEL-C™. Once the body has made these, they are likely to remain in the body. Although they are not harmful, they may mean participants are at an increased risk of rejecting a transplant (i.e. kidney, bone marrow) in the future.
For patients with rheumatoid arthritis, ultrasound-guided biopsy procedures of joints are performed under local anaesthetic. Once the local anaesthetic wears off there may be mild, transient pain and discomfort in around a third of patients; temporary swelling of the joint can also occasionally occur. The procedure will leave a tiny 2-3 mm scar (less than 1/8th of an inch). The risk of significant complications, such as infection or a thrombosis (clot) in the veins of the knee, occurring as a result of the procedure is less than 1 in 500. For patients with Crohn's disease, a colonoscopy is usually safe but in rare cases it can cause harm to the bowel. About 1 person in every 400 has bleeding after their colonoscopy but it is usually easy to stop. Bleeding is more common if a polyp is removed, but rare if biopsies are taken. Rarely, the bleeding is more difficult to stop and means that the person needs to be admitted to hospital. This happens to about 1 in every 2000 people having a colonoscopy. Even more rarely, colonoscopy can cause a small tear (perforation) in the bowel. This happens to about 1 in every 2500 people having a colonoscopy. If a patient received sedation for colonoscopy, hypoxia (lack of oxygen reaching the tissues) may occur rarely, but patients are constantly under monitoring. The sedation used during a colonoscopy is usually safe but the effects of sedation can last up to 24 hours, during which participants may be forgetful and sleepy. At the pre-colonoscopy discussion with the doctor or nurse, participants will be given full information about the sedative they will be using

and be given an NHS leaflet with further information. No adverse reports in pregnancy or breastfeeding have been reported in patients who have received MSCs. However, the researchers are still taking precautions to avoid harm to any potential children. Both men and women who take part in this study must use a contraception method considered to be highly effective.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
March 2018 to May 2027

Who is funding the study?
Innovate UK

Who is the main contact?
Prof. Philip Newsome

Contact information

Type(s)
Scientific

Contact name
Miss Camilla Bathurst

Contact details
POLARISE Trial Office
Inflammation - Advanced and Cellular Therapy (I-ACT) Team
Cancer Research UK Clinical Trials Unit (CRCTU)
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 371 8467
polarise@trials.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2019-003404-13

Integrated Research Application System (IRAS)
272535

Protocol serial number
CPMS 49716, IRAS 272535

Study information

Scientific Title
A single-arm, multi-centre, Phase II basket trial investigating the safety and activity of the use of ORBCEL-C™ in the treatment of patients with primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis and Crohn's disease

Acronym
POLARISE

Study objectives
The aims of the POLARISE trial are:
1. To provide insights into the mechanisms of action of ORBCEL-C™ in the treatment of immune-mediated diseases such as primary sclerosing cholangitis (PSC), rheumatoid arthritis (RA), lupus nephritis (LN) and Crohn's disease (CD)
2. To determine the short-term safety and activity of ORBCEL-C™ in patients with PSC, RA, LN and CD
3. To assess the feasibility of the use of the PROmics electronic Patient Reported Outcome (ePRO) system
The primary objective for all patients is to investigate whether the administration of ORBCEL-C™ elicits a change in the peripheral blood ratio of M1- and M2-like monocyte/macrophage cells in patients with PSC, RA, LN and CD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/08/2021, London - West London & GTAC Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048 007; westlondon.rec@hra.nhs.uk), REC ref: 21/LO/0475

Study design
Non-randomized; Interventional; Design type: Treatment, Cellular, Other

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis, Crohn's disease

Interventions
Mesenchymal stromal cells (MSC) have been safely used in over 100 clinical trials, and have been shown to be effective at potentially treating a number of inflammatory conditions. The aim of this study is to see if patients with primary sclerosing cholangitis, Crohn's disease, rheumatoid arthritis or lupus nephritis can potentially be treated safely with two doses of MSC (ORBCEL C™), and whether ORBCEL C could be used in the future as an alternative treatment for patients with one of these conditions. The researchers are hoping to find 15 patients from each disease group to take part in this trial, 60 patients in total.

Updated 07/02/2025: Following the closure of two cohorts (lupus nephritis and Crohn's disease), the total recruitment target is 30 patients (15 PSC and 15 RA).

All patients who consent to take part in the POLARISE trial will be involved for just over 25 months and will be required to attend up to 13 extra clinic visits (depending on disease group) in addition to their normal treatment appointments. The appointments are made up of screening visits (one or two visits), two treatment visits and eight or nine follow-up visits. There are also two follow-up telephone appointments that the patient does not attend clinic for.

ORBCEL C™ is made from Mesenchymal Stromal Cells (MSC). MSCs are cells that can be found in every part of the body and are thought to play a role in the repair and renewal of tissue as well as reducing inflammation.

When MSCs have been used as a cell therapy in patients with inflammatory diseases, they have been shown to reduce damage and inflammation to tissue. In this trial, the MSCs come from several screened human umbilical cords donated within the UK only. The MSCs are cleaned, mixed together and grown so that they can be injected into the body. The umbilical cords have been ethically collected from mothers who have agreed to donate their cords after childbirth.

Consenting patients will receive two doses of ORBCEL C™, containing a total of 200 million cells. This will be the first time this form of ORBCEL C™ has been used in a clinical trial. However, a different form of ORBCEL C™, using a different cleaning and growing process, has been used in patients on clinical trials before, with a very good safety profile. Tests within our laboratory have shown this form of ORBCEL C™ to be safe.

It is also important to understand how ORBCEL C™ affects how the patients feel. The researchers are asking all consenting trial patients to let them know about their symptoms or possible side effects during the trial by completing questionnaires.

Instead of asking patients to fill out paper questionnaires, the PROmics sub-study is asking patients to fill out questionnaires using the PROmics system, via an application (app) on the patient's own smartphone or tablet. This is a new way for patients in clinical trials to share how a treatment is making them feel.

Using the PROmics system, patients will be asked to fill in questionnaires about how they feel and will also be asked to fill in an extra questionnaire that asks about any symptoms or possible side effects. If the patients report symptoms or possible side-effects on this questionnaire, the PROmics system will let their trial team know and they can use this information to decide what to do next.

The PROmics project is being led by the Centre for Patient-Reported Outcomes Research (CPROR) at the University of Birmingham. CPROR is working with the POLARISE Trial Office at the University of Birmingham, and a UK software company called Aparito Ltd (Aparito). The development of the PROmics system is part of a bigger research project funded by Innovate UK.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

ORBCEL C™

Primary outcome(s)

Current primary outcome measure as of 02/07/2024:
The relative proportion of M1- and M2-like monocyte/macrophage cells in peripheral blood, determined from cell counts quantified using flow cytometry, after ORBCEL-C™ administration:
PSC patients: at Visits 2, 3, 4, 5, 6 & 7
RA patients: at Visits 2, 3, 4, 5, 6 & 7
LN patients: at Visits 2, 3, 4, 5, 6, 7 & 8
CD patients: at Visits 2, 3, 4, 5, 6, 7 & 8

Previous primary outcome measure:
The relative proportion of M1- and M2-like monocyte/macrophage cells in peripheral blood, determined from cell counts quantified using flow cytometry, after ORBCEL-C™ administration:
PSC patients: at Visits 2, 3, 4, 5, 6 & 7
RA patients: at Visits 2, 3, 4, 5, 6 & 7
LN patients: at Visits 2, 3, 4, 5, 6, 7 & 8
CD patients: at Visits 2, 3, 4, 5, 6, 7 & 8a

Key secondary outcome(s))

Current secondary outcome measures as of 02/07/2024:
Secondary outcome measures for all patients:
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Quality of life measured by Euroqol 5D-5L (EQ-5D-5L), Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) & Fatigue Severity Scale (FSS):
1.1. PSC patients: at Visits 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
1.2. RA patients: at Visits 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
1.3. LN patients: at Visits 2, 4, 6, 7, 7a, 8, 9, Month 18 and Month 24
1.4. CD patients: at Visits 2, 4, 6, 7, 8, 9, Month 18 and Month 24
2. Inflammatory markers measured by C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR):
2.1. PSC patients: at Visits 1a, 1b, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2.2. RA patients: at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2.3. LN patients: at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
2.4. CD patients: at Visits 1, 2, 3, 4, 5, 6, 7, 8, 9, Month 18 and Month 24
3. Adverse events (AEs) measured by Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 throughout the trial, commencing from the date of consent until Month 24
4. Patient-reported AEs measured by PRO-CTCAE™ Version 1.0 (where applicable) at Visit 2 and thereafter every 7 days. After Visit 7, it will be measured:
4.1. PSC patients: at Visit 7a, 8, Month 18 and Month 24
4.2. RA patients: at Visit 7a, 8, Month 18 and Month 24
4.3. LN patients: at Visit 7a, 8, 9, Month 18 and Month 24
4.4. CD patients: at Visit 8, 9, Month 18 and Month 24
Where necessary, patients can also complete ad hoc questionnaires.
5. Patient-reported global tolerability of treatment measured by FACT-G GP5 Version 4.0 (where applicable) at Visit 2 and thereafter every 7 days. After Visit 7, it will be measured:
5.1. PSC patients: at Visit 7a, 8, Month 18 and Month 24
5.2. RA patients: at Visit 7a, 8, Month 18 and Month 24
5.3. LN patients: at Visit 7a, 8, 9, Month 18 and Month 24
5.4. CD patients: at Visit 8, 9, Month 18 and Month 24
Where necessary, patients can also complete ad hoc questionnaires

Secondary outcome measures for patients with primary sclerosing cholangitis:
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. ALP, aspartate aminotransferase (AST), ALT, Alb and Br at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2. Composite risk scores (Mayo PSC risk score and Model For End-Stage Liver Disease [MELD]) at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 8
3. Enhanced liver fibrosis (ELF) measured using transient elastography (FibroScan®) at Visit 1a and 7
4. Quality of life measured by Primary Sclerosing Cholangitis-Patient Reported Outcomes (PSC-PRO) at Visit 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
5. Severity of inflammatory bowel disease (IBD) measured by the Partial Mayo Ulcerative Colitis Score or Harvey Bradshaw Index for CD at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 8

Secondary outcome measures for patients with rheumatoid arthritis:
After ORBCEL-C™ administration:
1. Any change in M1- and M2-like monocyte/macrophage cell counts and ratio in synovial tissue (if available) measured by synovial biopsy at Visits 2 and 6
2. Any response as measured by the European League Against Rheumatism (EULAR) response criteria, Disease Activity Score 28 C-Reactive Protein (DAS28 CRP) and Disease Activity Score 28 Erythrocyte Sedimentation Rate (DAS28 ESR) at Visits 1, 2, 3, 4, 5, 6, 7 and 8
3. Any response as measured by the American College of Rheumatology (ACR) response criteria at Visits 2, 3, 4, 5, 6, 7 and 8
4. Any change in patient-reported physical function as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI) at Visits 2, 3, 4, 5, 6, 7 and 8

Secondary outcome measures for patients with lupus nephritis (updated 07/02/2025: please note this cohort is closed to recruitment):
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Incidence of relapse and urinary markers of renal injury measured using urine albumin-creatinine ratio (uACR) at Visits 1, 2, 3, 4, 5, 6, 7, 8, 9
2. Serum markers of renal injury measured using estimated glomerular filtration rate (eGFR) at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
3. Disease activity measured using Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at Visit 1, 2, 3, 4, 5, 6, 7, 8, 9
4. Serum markers of renal injury measured using creatinine and eGFR at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
5. Urinary markers of renal injury measured using uACR at Visits 1, 2, 3, 4, 5, 6, 7, 8, 9
6. Incidence of relapse measured via clinician assessment based on the patients symptoms, blood tests (such as immunology, creatinine and GFR) and renal function (such as uACR), reviewed with the patient at all protocol scheduled visits and any unscheduled visits

Secondary outcome measures for patients with Crohn’s disease (updated 07/02/2025: please note this cohort is closed to recruitment):
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Disease activity as measured by anastomotic ulceration score (Rutgeerts score) (at Visit 2 and 8) and Crohn's Disease Activity Index (CDAI) (at Visit 2, 3, 4, 5, 6, 7, 8, and 9)

Previous secondary outcome measures:
Secondary outcome measures for all patients:
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Quality of life measured by Euroqol 5D-5L (EQ-5D-5L), Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) & Fatigue Severity Scale (FSS):

1.1. PSC patients: at Visits 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
1.2. RA patients: at Visits 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
1.3. LN patients: at Visits 2, 4, 6, 7, 7a, 8, 9, Month 18 and Month 24
1.4. CD patients: at Visits 2, 4, 6, 7, 8, 8a, 9, Month 18 and Month 24
2. Inflammatory markers measured by C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR):
2.1. PSC patients: at Visits 1a, 1b, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2.2. RA patients: at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2.3. LN patients: at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
2.4. CD patients: at Visits 1, 2, 3, 4, 5, 6, 7, 8, 8a, 9, Month 18 and Month 24
3. Adverse events (AEs) measured by Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 throughout the trial, commencing from the date of consent until Month 24
4. Patient-reported AEs measured by PRO-CTCAE™ Version 1.0 (where applicable) at Visit 2 and thereafter every 7 days. After Visit 7, it will be measured:
4.1. PSC patients: at Visit 7a, 8, Month 18 and Month 24
4.2. RA patients: at Visit 7a, 8, Month 18 and Month 24
4.3. LN patients: at Visit 7a, 8, 9, Month 18 and Month 24
4.4. CD patients: at Visit 8, 8a, 9, Month 18 and Month 24
Where necessary, patients can also complete ad hoc questionnaires.
5. Patient-reported global tolerability of treatment measured by FACT-G GP5 Version 4.0 (where applicable) at Visit 2 and thereafter every 7 days. After Visit 7, it will be measured:
5.1. PSC patients: at Visit 7a, 8, Month 18 and Month 24
5.2. RA patients: at Visit 7a, 8, Month 18 and Month 24
5.3. LN patients: at Visit 7a, 8, 9, Month 18 and Month 24
5.4. CD patients: at Visit 8, 8a, 9, Month 18 and Month 24
Where necessary, patients can also complete ad hoc questionnaires

Secondary outcome measures for patients with primary sclerosing cholangitis:
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. ALP, aspartate aminotransferase (AST), ALT, Alb and Br at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 7a, 8, Month 18 and Month 24
2. Composite risk scores (Mayo PSC risk score and Model For End-Stage Liver Disease [MELD]) at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 8
3. Enhanced liver fibrosis (ELF) measured using transient elastography (FibroScan®) at Visit 1a and 7
4. Quality of life measured by Primary Sclerosing Cholangitis-Patient Reported Outcomes (PSC-PRO) at Visit 2, 4, 6, 7, 7a, 8, Month 18 and Month 24
5. Severity of inflammatory bowel disease (IBD) measured by the Partial Mayo Ulcerative Colitis Score or Harvey Bradshaw Index for CD at Visit 1a, 1b, 2, 3, 4, 5, 6, 7, 8

Secondary outcome measures for patients with rheumatoid arthritis:
After ORBCEL-C™ administration:
1. Any change in M1- and M2-like monocyte/macrophage cell counts and ratio in synovial tissue (if available) measured by synovial biopsy at Visits 2 and 6
2. Any response as measured by the European League Against Rheumatism (EULAR) response criteria, Disease Activity Score 28 C-Reactive Protein (DAS28 CRP) and Disease Activity Score 28 Erythrocyte Sedimentation Rate (DAS28 ESR) at Visits 1, 2, 3, 4, 5, 6, 7 and 8
3. Any response as measured by the American College of Rheumatology (ACR) response criteria at Visits 2, 3, 4, 5, 6, 7 and 8
4. Any change in patient-reported physical function as measured by Health Assessment Questionnaire Disability Index (HAQ-DI) at Visits 2, 3, 4, 5, 6, 7 and 8

Secondary outcome measures for patients with lupus nephritis:
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Incidence of relapse and urinary markers of renal injury measured using urine albumin-creatinine ratio (uACR) at Visits 1, 2, 3, 4, 5, 6, 7, 8, 9
2. Serum markers of renal injury measured using estimated glomerular filtration rate (eGFR) at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
3. Disease activity measured using Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at Visit 1, 2, 3, 4, 5, 6, 7, 8, 9
4. Serum markers of renal injury measured using creatinine and eGFR at Visits 1, 2, 3, 4, 5, 6, 7, 7a, 8, 9, Month 18 and Month 24
5. Urinary markers of renal injury measured using uACR at Visits 1, 2, 3, 4, 5, 6, 7, 8, 9
6. Incidence of relapse measured via clinician assessment based on the patients symptoms, blood tests (such as immunology, creatinine and GFR) and renal function (such as uACR), reviewed with the patient at all protocol scheduled visits and any unscheduled visits

Secondary outcome measures for patients with Crohn’s disease:
Please note this cohort is not open to recruitment at this time.
Any change in the secondary outcome measures after ORBCEL-C™ administration:
1. Disease activity as measured by anastomotic ulceration score (Rutgeerts score) (at Visit 2 and 8a) and Crohn's Disease Activity Index (CDAI) (at Visit 2, 3, 4, 5, 6, 7, 8a, and 9)

Completion date
01/05/2027

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 02/07/2024:
Inclusion criteria for ALL patients:
1. Age ≥18 years at Visit 1/1a (screening)
2. In this clinical trial, for all cohorts, only participants with severe active disease and refractory to the standard of care treatment (and biologic-refractory for Rheumatoid Arthritis and Crohn’s Disease cohort) can be included (where a standard of care therapy is available*)
3. Active, uncontrolled, or partially controlled inflammatory disease despite receiving standard-of-care therapy (where a standard-of-care therapy is available*)
4. On an approved therapy if indicated and available, unless the patient is intolerant of, or has refused, the standard of care therapy

*For patients with PSC, no ‘standard of care treatment’ or standard definition for ‘uncontrolled /partially controlled disease’ is available. Patients must have severe active disease to be included.

Inclusion criteria specific to patients with primary sclerosing cholangitis (PSC):
1. Diagnosis of PSC at Visit 1a (screening) as evidenced clinically by Radiological AND/OR histological evidence. Individuals with small duct PSC may be included, only if they have concomitant inflammatory bowel disease
2. Serum ALP ≥ 1.5 x ULN at Visit 1a and 1b (screening)
3. Serum ALP value at Visit 1b within ± 40% of ALP value at Visit 1a as per the formula below:
3.1. ((ALPVisit 1b - ALPVisit 1a) / ALPVisit 1a) x 100 ≤ 40%
4. At Visit 1b, it should be confirmed that a patient does not meet any of the exclusion criteria

Inclusion criteria specific to patients with rheumatoid arthritis (RA):
1. Patients fulfilling 2010 ACR/EULAR criteria or 1987 ACR criteria for a diagnosis of RA for ≥ 6 months
2. Previous failure (inefficacy according to investigator judgement) to at least one biologic therapy or targeted synthetic Disease-Modifying Anti-Rheumatic Drug (tsDMARD)
3. DAS28 ESR ≥ 3.2 with at least three swollen joints
4. Willing to have a synovial biopsy

Inclusion criteria specific to patients with lupus nephritis (LN) (updated 07/02/2025: please note this cohort is closed to recruitment):
1. Has received induction of remission therapy for new diagnosis OR relapse of LN within 36 months of Visit 1 (screening) with corticosteroids AND mycophenolate mofetil OR azathioprine OR cyclophosphamide OR rituximab
2. Renal biopsy with evidence of active LN within 36 months of Visit 1 (screening). Biopsy-proven active LN for the purposes of eligibility is defined as LN class III, IV or V with evidence of activity. Concurrent evidence of chronic damage is permitted (Priority will be given to the recruitment of patients with biopsy-proven evidence of active LN within 36 months of the screening date. Patients that have had a renal biopsy with evidence of active lupus nephritis prior to 36 months of Visit 1 [screening] may be recruited following discussion with the coordinating centre as long as they have received induction of remission therapy within 36 months of Visit 1 [screening], as per inclusion criterion 1)
3. Ongoing proteinuria with uACR ≥ 50 mg/mmol
4. If the patient is on mycophenolate mofetil or azathioprine, stable or reducing dose of the drug for the last three months prior to Visit 1 (screening)

Main inclusion criteria specific to patients with Crohn's disease (CD) (updated 07/02/2025: please note this cohort is closed to recruitment):
1. Confirmed diagnosis of CD as per standard clinical criteria
2. Colonoscopic detection of post-operative disease recurrence as scored as Rutgeerts > i2a (i2b, i3 or i4) OR Active Crohn's disease with SES-CD ≥ 7 with at least one area of stricturing < 5cm in length (by endoscopic or radiological assessment) that is endoscopically accessible, within 90 days prior to consent to the POLARISE Trial
3. Evidence of failure or contra-indications to conventional therapy, i.e. refractory to at least one biologic therapy, or requiring escalation in medical management

Previous participant inclusion criteria:
Inclusion criteria for ALL patients:
1. Age ≥18 years at Visit 1/1a (screening)
2. In this clinical trial, for all cohorts, only participants with severe active disease and refractory to the standard of care treatment (and biologic-refractory for rheumatoid arthritis and Crohn's disease cohort) can be included.
3. Active, uncontrolled, or partially controlled inflammatory disease despite receiving standard of care therapy
4. On an approved therapy if indicated and available, unless the patient is intolerant of, or has refused, standard of care therapy

Inclusion criteria specific to patients with primary sclerosing cholangitis (PSC):
1. Diagnosis of PSC at Visit 1a (screening) as evidenced clinically by:
1.1. Chronic biochemical cholestasis (elevated ALP above the Upper Limit of Normal (ULN) and /or GGT above the ULN) ≥6 months duration AND
1.2. Radiological AND/OR histological evidence of clinically documented PSC
2. Serum ALP ≥1.5 x ULN at Visit 1a and 1b (screening)

3. Serum ALP value at Visit 1b within ± 40% of ALP value at Visit 1a as per the formula below: ((ALPVisit 1b - ALPVisit 1a) / ALPVisit 1a) x 100 ≤ 40%
4. At Visit 1b, it should be confirmed that a patient does not meet any of the exclusion criteria

Inclusion criteria specific to patients with rheumatoid arthritis (RA):
1. Patients fulfilling 2010 ACR/EULAR criteria or 1987 ACR criteria for a diagnosis of RA for ≥6 months
2. Previous failure (inefficacy according to investigator judgement) to at least one biologic therapy or targeted synthetic Disease-Modifying Anti-Rheumatic Drug (tsDMARD)
3. DAS28 ESR ≥ 3.2 with at least three swollen joints
4. Willing to have synovial biopsy

Inclusion criteria specific to patients with lupus nephritis (LN):
1. Has received induction of remission therapy for new diagnosis OR relapse of LN within 36 months of Visit 1 (screening) with corticosteroids AND mycophenolate mofetil OR azathioprine OR cyclophosphamide OR rituximab
2. Renal biopsy with evidence of active LN within 36 months of Visit 1 (screening). Biopsy proven active LN for the purposes of eligibility is defined as LN class III, IV or V with evidence of activity. Concurrent evidence of chronic damage is permitted (Priority will be given to recruitment of patients with biopsy-proven evidence of active LN within 36 months of screening date. Patients that have had a renal biopsy with evidence of active lupus nephritis prior to 36 months of Visit 1 [screening] may be recruited following discussion with the coordinating centre as long as they have received induction of remission therapy within 36 months of Visit 1 [screening], as per inclusion criterion 1)
3. Ongoing proteinuria with uACR ≥50 mg/mmol
4. If the patient is on mycophenolate mofetil or azathioprine, stable or reducing dose of the drug for the last three months prior to Visit 1 (screening)

Main inclusion criteria specific to patients with Crohn’s disease (CD):
Please note this cohort is not open to recruitment at this time.
1. Confirmed diagnosis of CD who have undergone ileocolonic resection with ileocolonic anastomosis
2. Ileocolonic anastomosis performed 6 to 24 months prior to Visit 1
3. Colonoscopic detection of recurrent anastomotic or peri-anastomotic ulceration scored as Rutgeerts i2, i2a, i2b, i3 or i4 within 3 months prior to consent to the POLARISE Trial AND/OR faecal calprotectin > 250 mcg/gm in the absence of colonoscopic evidence

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

Current participant exclusion criteria as of 02/07/2024:
Exclusion criteria for ALL patients
1. Refusal or lacks the capacity to give informed consent to participate in the POLARISE Trial
2. Patient who is unable to participate in follow-up assessment
3. Participation actively or within five half-lives of Investigational Medicinal Product (IMP) and/or Advanced Therapy Investigational Medicinal Product (ATIMP) in another clinical trial
4. Known hypersensitivity to the ATIMP
5. Evidence of active malignancy (within three years of Visit 1/1a [screening]), other than non-melanoma skin cancer and cervical dysplasia in situ
6. Major surgical procedure within 30 days of Visit 1/1a (screening)
7. Prior organ transplantation (with the exception of a corneal transplant ≥ three months prior to Visit 1/1a [screening])
8. Active harmful alcohol consumption as evaluated and documented by the Investigator (as defined by NICE [3])
9. Any active treatment on biologic therapy (monoclonal antibodies), or within the washout period for previous biologic therapy at the time of screening (Visit 1/1a); Updated 07/02/2025: 9. Any active treatment on biologic therapy (monoclonal antibodies) or targeted synthetic DMARDs, or within the washout period (two half-lives for previous biologic therapy and 4 weeks for previous targeted synthetic DMARDs) at time of screening (Visit 1/1a)
10. Received oral corticosteroids > 10 mg (prednisolone or equivalent) in the four weeks prior to Visit 2 (first ORBCEL-C™ administration)
11. Clinically severe cardiovascular disease as evaluated by the Investigator
12. Pregnancy or breast-feeding
13. Women of childbearing potential (see Appendix 1 for definition) who are unwilling to practise effective contraception (see Appendix 2 for further detail) for the duration of the trial and up to 90 days after the last trial drug is administered. If using hormonal agents the same method must have been used for at least one month before the trial dosing and patients must use a barrier method during that time period
14. Non-vasectomised men, sexually active with women of childbearing potential, who are not willing to practise effective contraception (i.e. condom with spermicide) for the duration of the trial and up to 90 days after the last trial drug is administered
15. Any evidence of current (surface antigen positive) hepatitis B infection
16. Patients with active hepatitis C infection (Polymerase Chain Reaction (PCR) positive)
17. Known positivity for antibody to HIV
18. Presence of an acute/chronic infection or illness that, at the discretion of the Investigator, might compromise the patient's health and safety in the trial
19. Receipt of live vaccination within six weeks prior to Visit 1/1a (screening)
20. Any symptoms indicative of COVID-19
21. Renal impairment defined as an eGFR < 30ml/min at Visit 1/1a (screening).
22. Confirmed or clinically suspected liver cirrhosis

Exclusion criteria specific to patients with primary sclerosing cholangitis:
1. Documented alternative aetiology for sclerosing cholangitis (i.e. secondary sclerosing cholangitis)
2. A dominant (as determined by the Investigator) alternative chronic or active liver injury other than PSC at the time of Visit 1a (screening)
3. Ursodeoxycholic Acid (UDCA) dose modification within the last 90 days
4. ALP > 10 x ULN at Visit 1a (screening)
5. Evidence of cholangitis within 90 days of Visit 1a (screening), i.e. documented evidence of cholangitis by a doctor

6. Need for any systemic antibiotics (oral or intravenous) within 90 days of Visit 1a (screening)
7. Any patient taking new prophylactic antibiotics for recurrent cholangitis started or dosage changed in the last 90 days
8. Presence of percutaneous biliary drain or internal biliary stent
9. Diagnosed hepatocellular carcinoma or cholangiocarcinoma or high clinical suspicion thereof
10. Dominant stricture clinically suspicious of cholangiocarcinoma (as determined by the Investigator)
11. AST or ALT > 10 x ULN at Visit 1a (screening)
12. Total Br > 50 µmol/L at Visit 1a (screening)
13. International Normalised Ratio (INR) > 1.3 (in the absence of concomitant use of Warfarin or equivalent anticoagulant therapy) at Visit 1a (screening)
14. Alb < 35 g/L at Visit 1a (screening)
15. Platelets < 50 x 109/L at Visit 1a (screening)
16. Past or present evidence of decompensated chronic liver disease:
16.1. Radiological or clinical evidence of ascites
16.2. Hepatic encephalopathy
16.3. History of portal hypertensive bleeding

Exclusion criteria specific to patients with primary sclerosing cholangitis and inflammatory bowel disease:
1. Unstable disease as evidenced by:
1.1. Documented clinically significant flare of Inflammatory Bowel Disease requiring any commencement of steroid, thiopurine, 5-aminosalicylate, oral
prednisolone or biologics therapy (this is an exclusion criterion), within 90 days of Visit 1a (screening)
1.2. Requirement for daily prednisolone > 10 mg
1.3. Clinical assessment of active disease that requires up-titration of treatment
2. Any evidence of clinically significant dysplasia at the last colonoscopy or flexible sigmoidoscopy
3. Patients who have not had their routine colonoscopy within 24 months prior to planned ORBCEL-C™ administration and/or are unwilling to have their surveillance colonoscopic examination as per standard of care prior to trial Visit 2 (treatment)

Exclusion criteria specific to patients with rheumatoid arthritis:
1. In patients with a joint amenable to synovial biopsy, any pre-existing condition predisposing to bleeding or anticoagulant therapy contraindicating synovial biopsy. Oral antiplatelet agents are permitted
2. History of current primary inflammatory joint disease or primary rheumatological autoimmune disease other than RA (if secondary to RA, then the patient is still eligible)
3. Septic arthritis of a native joint within the last 12 months
4. Septic arthritis of a prosthetic joint within 12 months or indefinitely if the joint remains in situ
5. Liver impairment defined as AST or ALT > 3 x ULN and/or total bilirubin > 1.5 x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤ x 3 ULN and direct bilirubin is < 1.5 x ULN

Exclusion criteria specific to patients with lupus nephritis (updated 07/02/2025: please note this cohort is closed to recruitment):
1. Cyclophosphamide treatment within six months of Visit 1 (screening)
2. Biologic treatment with rituximab or belimumab within six months of Visit 1 (screening)
3. Clinical intention to intensify treatment within the next six months
4. Organ or life-threatening major lupus flare within six months of Visit 1 (screening)
5. Positive screening for alloreactive anti-HLA antibodies with a Mean Fluorescence Intensity

(MFI) > 2000
6. Other concomitant diseases or conditions that in the opinion of the investigator are likely to pose a risk to the patient and/or would render the patient unsuitable for participation such as active malignancy or an irreversible disease or condition for which six-month mortality is estimated to be greater than 50%
7. Liver impairment defined as AST or ALT > 3 x ULN and/or total bilirubin > 1.5 x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤ x 3 ULN and direct bilirubin is < 1.5 x ULN.

Exclusion criteria specific to patients with Crohn's disease (updated 07/02/2025: please note this cohort is closed to recruitment):
1. Active intra-abdominal abscess or patients with isolated perianal disease
2. Existence of non-passable strictures (as judged by colonoscopist)
3. Liver impairment defined as AST or ALT > 3 x ULN and/or total bilirubin > 1.5 x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤ x 3 ULN and direct bilirubin is < 1.5 x ULN

4. The patient is within the washout period for the following medications/therapies at Visit 2:
4.1. TNF-antagonist therapy (e.g., infliximab, etanercept, certolizumab, adalimumab, golimumab), vedolizumab, ustekinumab, taken within 4 weeks of Visit 2
4.2. Cyclosporine, tacrolimus, or sirolimus, taken within 4 weeks of Visit 2
c.6-thioguanine (6-TGN i.e. azathioprine or mercaptopurine) or methotrexate, taken within 4 weeks of Visit 2

Exclusion criteria specific to PROmics System:
1. Patients who are unable to read, understand and complete questionnaires presented in English
2. Patients who decline the optional consent for the use of the PROmics system

Previous participant exclusion criteria:
Exclusion criteria for ALL patients
1. Refusal or lacks the capacity to give informed consent to participate in the POLARISE trial
2. Patient who is unable to participate in follow-up assessment
3. Participation actively or within five half-lives of Investigational Medicinal Product (IMP) or ATIMP in another clinical trial
4. Know hypersensitivity to the ATIMP
5. Evidence of active malignancy (within 3 years of Visit 1 [screening]), other than non-melanoma skin cancer and cervical dysplasia in situ
6. Major surgical procedure within 30 days of Visit 1/1a (screening)
7. Prior organ transplantation (with the exception of a corneal transplant ≥3 months prior to Visit 1/1a [screening])
8. Active harmful alcohol consumption as evaluated and documented by the Investigator (as defined by NICE)
9. Any active treatment on biologic therapy (monoclonal antibodies), or within washout period for previous biologic therapy at time of screening (Visit 1/1a)
10. Received oral corticosteroid >7.5 mg for ≥4 weeks within 3 months of Visit 2 (first ORBCEL-C™ administration)
11. Clinically severe cardiovascular disease as evaluated by the Investigator
12. Pregnancy or breastfeeding
13. Women of childbearing potential who are unwilling to practise effective contraception for the duration of the trial and up to 90 days after the trial drug is administered. If using hormonal agents the same method must have been used for at least one month before the trial dosing

and patients must use a barrier method during that time period
14. Non-vasectomised men, sexually active with women of childbearing potential, who are not willing to practise effective contraception (i.e. condom with spermicide) for the duration of the trial and up to 90 days after the trial drug is administered
15. Any evidence of current (surface antigen positive) hepatitis B infection
16. Patients with active hepatitis C infection (Polymerase Chain Reaction (PCR) positive)
17. Known positivity for antibody to HIV
18. Presence of an acute/chronic infection or illness that, at the discretion of the Investigator, might compromise the patient's health and safety in the trial
19. Receipt of live vaccination within six weeks prior to Visit 1/1a (screening)
20. Any symptoms indicative of COVID-19; including fever, chronic/ persistent cough, loss of sense of taste or smell in the preceding 2 weeks
21. Renal impairment defined as an eGFR <30 ml/min at Visit 1/1a (screening)
22. Confirmed or clinically suspected liver cirrhosis

Exclusion criteria specific to patients with primary sclerosing cholangitis:
1. Documented alternative aetiology for sclerosing cholangitis (i.e. secondary sclerosing cholangitis)
2. A dominant (as determined by the Investigator) alternative chronic or active liver injury other than PSC at the time of Visit 1a (screening)
3. Ursodeoxycholic Acid (UDCA) dose modification within the last 90 days
4. ALP >10 x ULN
5. Evidence of cholangitis within 90 days of Visit 1a (screening)
5.1. Documented evidence of cholangitis by a doctor
5.2. Need for any antibiotics for presumed cholangitis
6. Any patient taking prophylactic antibiotics for recurrent cholangitis
7. Presence of percutaneous biliary drain or internal biliary stent
8. Diagnosed hepatocellular carcinoma or cholangiocarcinoma or high clinical suspicion thereof
9. Dominant stricture clinically suspicious of cholangiocarcinoma (as determined by the Investigator)
10. AST or ALT >10 x ULN
11. Total Br >2 x ULN
12. INR >1.3 (in the absence of concomitant use of Warfarin or equivalent anticoagulant therapy)
13. Alb <35 g/L
14. Platelets <50 x 10e9/L
15. Past or present evidence of decompensated chronic liver disease:
15.1. Radiological or clinical evidence of ascites
15.2. Hepatic encephalopathy
15.3. History of portal hypertensive bleeding
16. Decompensated chronic liver disease

Exclusion criteria specific to patients with primary sclerosing cholangitis and inflammatory bowel disease:
1. Unstable disease as evidenced by:
1.1. Documented clinically significant flare of Inflammatory Bowel Disease within 90 days of Visit 1a (screening) requiring any commencement of steroid, thiopurine, 5-aminosalicylate, oral prednisolone or biologics therapy (this is an exclusion criteria)
1.2. Requirement for daily prednisolone >10 mg
1.3. Clinical assessment of active disease that requires up-titration of treatment
2. Any colonoscopic evidence of clinically significant dysplasia at last colonoscopy

3. Patients who have not had their routine colonoscopy within 24 months prior to planned ORBCEL-C™ administration and are unwilling to have their annual colonoscopy examination as per standard of care prior to trial Visit 2 (treatment)

Exclusion criteria specific to patients with rheumatoid arthritis:
1. In patients with a joint amenable to synovial biopsy, any pre-existing condition predisposing to bleeding or anticoagulant therapy contraindicating synovial biopsy. Oral antiplatelet agents are permitted
2. History of current primary inflammatory joint disease or primary rheumatological autoimmune disease other than RA (if secondary to RA, then the patient is still eligible)
3. Septic arthritis of a native joint within the last 12 months
4. Septic arthritis of a prosthetic joint within 12 months or indefinitely if the joint remains in situ
5. Liver impairment defined as AST or ALT >3x ULN and/or total bilirubin >1.5x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤x 3 ULN and direct bilirubin is <1.5 x ULN

Exclusion criteria specific to patients with lupus nephritis:
1. Cyclophosphamide treatment within 6 months of Visit 1 (screening)
2. Biologic treatment with rituximab or belimumab within 6 months of Visit 1 (screening)
3. eGFR <30 ml/min
4. Clinical intention to intensify treatment within the next 6 months
5. Organ or life-threatening major lupus flare within 6 months of Visit 1 (screening)
6. Positive screening for clinically significant anti-HLA antibodies (MFI >1500)
7. Other concomitant disease or conditions that in the opinion of the investigator are likely to pose risk to the patient and/or would render the patient unsuitable for participation such as, active malignancy or an irreversible disease or condition for which 6-month mortality is estimated to be greater than 50%
8. Liver impairment defined as AST or ALT >3x ULN and/or total bilirubin >1.5x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤x 3 ULN and direct bilirubin is <1.5 x ULN

Exclusion criteria specific to patients with Crohn's disease:
Please note this cohort is not open to recruitment at this time.
1. Abscess in right iliac fossa
2. Existence of ileal anastomotic strictures (as judged by colonoscopist)
3. CDAI >450
4. Known active CD outside of anastomotic/peri-anastomotic in the gastrointestinal tract
5. Liver impairment defined as AST or ALT >3x ULN and/or total bilirubin >1.5x ULN at screening. If the investigator decides to include patients with Gilbert Syndrome, this will be only possible if total bilirubin is ≤x 3 ULN and direct bilirubin is <1.5 x ULN

Exclusion criteria specific to PROmics System:
1. Patients who are unable to read, understand and complete questionnaires presented in English
2. Patients who decline the optional consent for the use of the PROmics system

Date of first enrolment
21/01/2022

Date of final enrolment
01/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Queen's Medical Centre
Nottingham University Hospital
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Newcastle upon Tyne Hospitals NHS Foundation Trust
Royal Victoria Infirmary
Queen Victoria Road
Newcastle Upon Tyne
United Kingdom
NE1 4LP

Study participating centre
University Hospital Southampton
Southampton University Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Innovate UK; Grant Codes: 104232

Alternative Name(s)
Technology Strategy Board

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Protocol article		06/09/2022	24/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Development and usability testing of an electronic patient-reported outcome (ePRO) solution	09/10/2023	10/10/2023	Yes	No