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A clinical trial of Baricitinib in Juvenile Dermatomyositis (BAR-JDM): comparing baricitinib and steroids to methotrexate and steroids over 52 weeks

Submission date
05/02/2025

Recruitment status
Recruiting

Registration date
03/06/2025

Overall study status
Ongoing

Last Edited
03/07/2026

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Juvenile dermatomyositis (JDM) is a rare inflammatory disease affecting muscles, skin, and blood vessels, with an annual incidence of about 3 per 100,000 children. Standard treatment uses high dose steroids (glucocorticoids) and immunosuppressants (like methotrexate (MTX)) which dampens the body's immune system. This treatment only works in some people to control the disease, so doctors are looking at other medicines that could be more effective and have less side effects.

Baricitinib is used in adults with rheumatoid arthritis and children with arthritis. It works by targeting an intracellular signalling pathway called "JAK-STAT", which may provide a more targeted way of reducing inflammation.

The aim of this trial is to find out if baricitinib and steroids is better and safer compared to MTX and steroids in the treatment of children with newly diagnosed JDM. Participating NHS hospital sites across the UK will recruit 30 participants aged 2 years to less than 17 years.

Who can participate?
Patients aged 2 to 17 years with newly diagnosed juvenile dermatomyositis (JDM) who have not had any treatment for it.

What does the study involve?
There will be two groups: one group will receive baricitinib tablets and one group will receive MTX injections which they will take for 52 weeks. Participants will randomly be put into the group; they don't get to choose. Participants in the baricitinib group may have their dose increased. All participants will take steroids, with doses gradually reduced. There will be twice as many people taking baricitinib than MTX as more information is known about the standard treatment. Rescue treatment can be given at any time in the trial following local practices.

After attending a Screening visit, participants eligibility will be confirmed at a Baseline and Randomisation visit. Progress will be checked at participants local research hospital at Week 12, 24, 39, and 52, where questionnaires, assessments, and blood/urine tests are completed. There is an end of trial visit which may be a call or clinic visit.

What are the possible benefits and risks of participating?
Risk mitigation measures added to the protocol to address the important potential risks include appropriate inclusion and exclusion criteria, safety monitoring, study drug interruption, and permanent discontinuation criteria.

Infections are common side effects of the medication studied. The non-serious infections noted in a rheumatoid arthritis (RA) program (upper respiratory tract infections, herpes zoster, herpes simplex) are readily diagnosed, manageable, and typically resolve without long-term sequelae. Prior to receiving baricitinib, the vaccination status of patients must be up to date with all immunisations and follow the local requirements for vaccination guidelines for immunosuppressed patients. Exclusion criteria have been added to the protocol to limit enrolment of patients who are at increased risk of infection.

Hepatotoxicity has not been identified with baricitinib use, but increases in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin have occurred in RA patients treated with baricitinib. Most increases improved with continued use or temporary discontinuation of baricitinib with no long-term effects. In addition to criteria to exclude patients with liver failure or increased liver analytes, appropriate monitoring of hepatic analytes and discontinuation criteria have been included in the protocol.

Effects of baricitinib on human foetal development are not known. The study protocol excludes pregnant and breastfeeding participants. Contraceptive use is required for participants who may become pregnant or cause pregnancy, i.e. women of childbearing potential and fertile men.

Venous thromboembolic events (VTEs) including deep vein thrombosis (DVT) or pulmonary embolism (PE) have been determined to be an important potential risk for baricitinib. There was a numerical imbalance in reports of VTEs in a 24-week placebo-controlled period of the Phase 3 studies of adult patients with RA. Available evidence does not establish a causal association. The exposure-adjusted incidence rate of VTE for baricitinib-treated RA patients over long-term exposures was similar to the background rates published in the literature for the target population. There was no pattern of increased or decreased risk during long-term exposures, and cases observed with baricitinib were confounded by one or more recognised risk factors for VTE. VTE risk can be managed through risk-mitigation strategies. Exclusion and discontinuation criteria have been added to the protocol to limit participation of patients who are at increased risk of VTE.

Baricitinib is being used to treat paediatric patients participating in an expanded access program (see protocol) with over 30 patients aged 2 months to <18 years were enrolled in the program. Safety information has not identified new safety signals for baricitinib beyond those known. As children generally have fewer age-related comorbidities, such as diabetes and heart disease, they are expected to be at a lower risk for some AEs related to comorbidities observed in RA studies and are not anticipated to be at any higher risk of AEs potentially associated with baricitinib.

Therefore, based on the efficacy of baricitinib demonstrated in the Phase 3 RA program and the observed safety profile, the probability of a positive benefit/risk warrants this study to be conducted, given the unmet need in patients with JDM.

More information about the known and expected benefits, risks, SAEs and reasonably anticipated AEs of baricitinib is found in the Summary of Product Characteristics (SmPC).

Children with JDM do not respond satisfactorily after treatment with glucocorticoids in combination with methotrexate, or do not tolerate these drugs. Attempts with other immunosuppressive agents in these group of patients have been disappointing, and these patients may continue to deteriorate with progressive muscle weakness and impaired function in daily activities. There is no guarantee that baricitinib treatment will be efficacious, but no other alternatives are licensed. Thus, there will be considerable benefits for patients with JDM, if they could improve with baricitinib treatment.

The benefits of treatment far outweigh both the risk of adverse events, which may also occur with other combinations of immunosuppressive drugs, and the risk that the drug is not effective. The knowledge gained from this study may also be of help to other participants in the future.

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

When is the study starting and how long is it expected to run for?
The grant started in June 2024 and recruitment is expected to open in March 2024. The trial will end in June 2029.

Who is funding the study?
Versus Arthritis (UK)

Who is the main contact?
cctu.bar-jdm@ucl.ac.uk

Contact information

Type(s)
Public

Contact name
Miss Rachel McComish

Contact details
Comprehensive Clinical Trials Unit at UCL
90 High Holborn
London
United Kingdom
WC1V 6LJ
-
cctu.bar-jdm@ucl.ac.uk

Type(s)
Principal investigator

Contact name
Prof Paul Brogan

Contact details
UCL Great Ormond Street Institute of Child Health, 30 Guilford St
London
United Kingdom
WC1N 1EH
-
p.brogan@ucl.ac.uk

Type(s)
Scientific

Contact name
Dr Charalampia Papadoupoulou

Contact details
Great Ormond Street Hospital, Great Ormond Street
London
United Kingdom
WC1N 3JH
-
charalampia.papadopoulou@gosh.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
1011391

Central Portfolio Management System (CPMS)
67281

Protocol serial number
CTU/2023/432

Study information

Scientific Title
Baricitinib in Juvenile Dermatomyositis (BAR-JDM): A multi-centre, open label, randomised, controlled, superiority, Bayesian, phase 3a trial comparing baricitinib and glucocorticoids to methotrexate and glucocorticoids over 52 weeks

Acronym
BAR-JDM

Study objectives
The main objective is to determine efficacy and safety of baricitinib in combination with steroids (glucocorticoids) compared with methotrexate and glucocorticoids in children with newly diagnosed juvenile dermatomyositis.

Efficacy is determined by meeting the primary endpoint: Proportion of participants achieving clinically inactive disease which is assessed using a criteria known as the modified PRINTO criteria, at the end of the trial (Week 52) AND off steroids (glucocorticoids) from Week 40.

Safety is measured by how many side effects, also called adverse events, are reported by the participants.

Secondary objectives of this trial are related to:
- how many people in the baricitinb group had their medication dose increased
- how many participants achieved clinically inactive disease as determined by clinicians
- information on steroid (glugocorticoids) taken by participants, including the total dose of steroids taken
- how many people had rescue treatment (medications to help them get better) throughout the trial
- Participants disease state as determined by clinician assessments
- Side effects reported
- How many patients have disease flares
- Health-related quality of life, functional ability and disease activity as reported by the participant/their parent/legal representative
- Healthcare resource use and health-related quality of life for health economics analysis

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/05/2025, West Midlands - Edgbaston Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048155; edgbaston.rec@hra.nhs.uk), ref: 25/WM/0037

Primary study design
Interventional

Study design
Interventional open-label randomized parallel-group controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Juvenile dermatomyositis (JDM)

Interventions
a. Trial arms:
i. Experimental arm: Baricitinib and glucocorticoids
i. Control arm: Methotrexate and glucocorticoids (standard of care)

b. Baricitinib:
i. Dose range: Minimum 2mg to maximum 10mg. All participants on the baricitinib arm will start on a “lower” dose (2mg or 4mg) which is dependent upon their weight at the Baseline and Randomisation visit. At Week 12 and Week 24, if participants are clinically worsening or showing inadequate improvement, the baricitinib dose will be increased to a “higher” dose (6mg, 8mg, or

10 mg), dependent upon their estimated glomerular filtration rate and weight at that visit.
ii. Dose frequency: Tablets to be taken once a day for first 12 weeks, then either twice a day or four times a day dependent upon dose for remainder of duration of treatment.
iii. Route of administration: Oral (if children cannot swallow whole tablets, soluble form in water is acceptable).
iv. Duration of treatment: 52 weeks (+/- 2 week protocol window).

c. Methotrexate:
i. Dose range: 15 mg/m2. Body weight, height, and body surface area will be assessed at every visit and used to determine methotrexate dosing and dispensing.
ii. Dose frequency: Injection to be taken once weekly for duration of treatment.
iii. Route of administration: Subcutaneous injection.
iv. Duration of treatment: 52 weeks (+/- 2 week protocol window).

d. Glucocorticoids (prednisolone):
i. Dose range: All participants will receive the same protocolised oral prednisolone dosing regimen (and recommended non-mandatory supportive measures) starting from 2 mg/kg/day at the Baseline and Randomisation visit reducing to 0 mg/kg/day from Week 25. The Baseline and Randomisation body weight will be used to determine the glucocorticoid doses (prednisolone and methylprednisolone) for the duration of the trial. Maximum daily dose of oral prednisolone is 60 mg.
ii. Dose frequency: Tablets to be taken once a day.
iii. Route of administration: Oral (if children cannot swallow whole tablets, soluble form in water is acceptable). Intravenous methylprednisolone may be substituted for oral prednisolone at an equivalent (0.8 x prednisolone) dose at the discretion of the local investigator, if required for clinical or practical reasons.
iv. Duration of treatment: First 24 weeks of treatment.

e. Follow-up activity for all trial arms:
After attending a Screening visit, participants eligibility will be confirmed at a Baseline and Randomisation visit. Progress will be checked at participants local research hospital at Week 12, 24, 39, and 52, where questionnaires, assessments, and blood/urine tests are completed. There is an end of trial visit which may be a call or clinic visit.

f. Randomisation process: Participants will be randomised (2:1, baricitinib: methotrexate) using Sealed Envelope randomisation software customised for the trial by the UCL CCTU.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Baricitinib, methotrexate

Primary outcome(s)
The primary endpoint is the proportion of participants achieving clinically inactive disease, as per modified PRINTO criteria, at Week 52 AND off glucocorticoids from Week 40.

Clinically inactive disease as per modified PRINTO criteria is achieved if a participant fulfils the following criteria:
a. No active skin disease, and
b. Physician global assessment (PhyGLOVAS) ≤0.2/10 on a visual analogue scale, and
c. Two of the following three criteria:
i. Creatine kinase (CK) ≤150 U/L.
ii. Childhood Myositis Assessment Scale (CMAS) ≥48/52.
iii. Manual Muscle Testing 8 (MMT8) ≥78/80.

Key secondary outcome(s)

1. Proportion of participants requiring protocoled baricitinib dose escalation at Week 12 or Week 24.
2. Proportion of participants achieving clinically inactive disease and off glucocorticoids from Week 25.
3. Proportion of participants achieving clinically inactive disease at Week 52 but received prednisolone beyond Week 25.
4. Proportion of participants requiring rescue treatment.
5. Cumulative dose of prednisolone (mg/kg) at trial end.
6. Cumulative dose of methylprednisolone (mg/kg) at trial end.
7. Time to clinically inactive disease (see Appendix 1 of protocol for definition) following the protocoled glucocorticoid tapering schedule.
8. Number of grade 3 to 5 adverse events (AEs), including deaths, and serious adverse events (SAEs) reported.
9. Toxicity of glucocorticoids as assessed by the paediatric glucocorticoid toxicity index.
10. Proportion of patients with disease flares defined as worsening disease after clinically inactive disease as assessed at the time of trial visits within 52 weeks.
11. Cumulative weight adjusted dose of prednisolone or methylprednisolone received.
12. Duration of glucocorticoid treatment from the Baseline and Randomisation visit.
13. JDM Paediatric Rheumatology International Trials Organisation (PRINTO) 20, 50, 70, and 90 levels of improvement (20%, 50%, 70%, and 90% improvement from the Baseline and Randomisation visit in three of six core set variables at a given visit with one or no variable worsening by more than 30% (muscle strength excluded)) at Weeks 12, 24, 39 and 52, with adherence to glucocorticoid schedule.
14. Minimal clinical response according to the International Myositis Assessment and Clinical Studies (IMACS) Group criteria at Weeks 12, 24, 39 and 52, with adherence to glucocorticoid schedule (Web calculator for 2016 ACR/EULAR Criteria for Minimal, Moderate, and Major Clinical Response in Juvenile Dermatomyositis (nih.gov)).
15. Total improvement score at Week 12, 24, 39 and 52, with adherence to glucocorticoid schedule (Web calculator for 2016 EULAR/ACR Criteria for Minimal, Moderate, and Major Clinical Response in Juvenile Dermatomyositis (nih.gov)).
16. Health-related quality of life (Physical Summary Score of the Child Health Questionnaire - Parent Form 50 (CHQ-PF50) and Paediatric Quality of Life Inventory (PedsQL)), functional ability (Childhood Health Assessment Questionnaire (CHAQ)) and disease activity (patient/parent global activity Visual Analogue Score (VAS)) evaluation at the Baseline and Randomisation visit, Week 12, 24, 39 and Week 52 visit.
17. Healthcare resource use and health-related quality of life (Child Health Utility 9D (CHU-9D)) for use in health economics analysis at the Baseline and Randomisation visit, Week 24 and Week 52 visit.

Completion date

02/06/2029

Eligibility

Key inclusion criteria
1. Patients with newly diagnosed (treatment naïve) juvenile dermatomyositis (JDM) who meet European League Against Rheumatism (EULAR)/ American College of Rheumatology (ACR) classification criteria for possible, probable or definite JDM; or modified (i.e. incorporating MRI muscle findings in place of EMG) Peter and Bohan criteria for possible, probable or definite JDM.
2. Active disease for JDM using the following pre-specified definition:
a. Active inflammatory disease based on persisting or worsening muscle weakness (for example, Manual Muscle Testing 8 (MMT8) <78/80 or CMAS <49/52), and
b. At least one other sign of active disease:
i. Elevated serum levels of at least one muscle enzyme (creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT)) above upper limit of normal and being explained by muscle involvement and no other cause such as liver disease, or
ii. Inflammation in recent (<12 weeks) muscle biopsy or MRI scan, or
iii. Active extra muscular disease: dermatomyositis-specific skin rash, arthritis, or interstitial lung disease (ILD) as suggested by chest x-ray or high-resolution computerised tomography (HRCT) or pulmonary function test.
3. Participants aged ≥2 years to <17 years at the Baseline and Randomisation visit.
4. Written informed consent from:
a. Participants who have reached the age of consent (16 years), or
b. Parent/legal representative of participants who have not reached the age of consent (16 years); and assent, where possible, from the participant.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 Years

Upper age limit
17 Years

Sex
All

Total final enrolment
0

Key exclusion criteria

1. Participants with other types of inflammatory myopathies.
2. Participants where the use of baricitinib, methotrexate or glucocorticoids would be contraindicated, including known hypersensitivity or history of severe allergic reaction to any of the study medications or their excipients.
3. Participants who are pregnant or breastfeeding at the screening visit.
4. Participants of childbearing potential that are unwilling to have pregnancy testing done according to the protocol schedule for the duration on the trial.
5. Participants of childbearing potential or fertile men that are either considering becoming pregnant/having children or are unable/unwilling to use an acceptable method of contraception to avoid pregnancy for the duration on the trial and for 6 months after the last dose of trial medication.
6. Participants who have an active varicella zoster infection (chickenpox) or have had exposure to a case of varicella (chickenpox or shingles) within 21 days of the screening visit.
7. Participants who have active herpes zoster that resolved within 8 weeks of the screening visit.
8. Participants who have a serious systemic or local infection or who have had a serious systemic or local infection within 12 weeks of the screening visit.
9. Participants who have received live/attenuated vaccines in the 4 weeks prior to screening or who plan to receive live/attenuated vaccines for the duration on the trial.
10. Participants with a history of active hepatitis B, hepatitis C or human immunodeficiency virus.
11. Participants with evidence of active or latent tuberculosis.
12. Participants with any of the following laboratory values at screening:
a. Haemoglobin (Hb) <80 g/L (alternative units <8 g/dL), or
b. Absolute lymphocyte count (ALC) <0.5x109/L (alternative units <500 cells/mm^3), or
c. Absolute neutrophil count (ANC) <1x109/L (alternative units 1000 cells/mm^3), or
d. Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73m^2.
13. Any other clinical feature or laboratory test result that, in the opinion of the investigator, might place the subject at unacceptable risk for participation in this trial.
14. Current participation in another clinical trial of a device, interventional medicinal product, advanced therapy, or surgical procedure; or previous participation within 12 weeks of the screening visit.
15. Participants who have received > 3 g of intravenous methylprednisolone within 4 weeks prior to randomisation.
16. Participants who have received oral prednisolone/prednisone at a dose ≥2 mg/kg once daily for more than 4 weeks and completing the course in the 4 weeks prior to randomisation.

Date of first enrolment
01/07/2025

Date of final enrolment
31/03/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
England
WC1N 3JH

Study participating centre
Royal Hospital for Sick Children (Glasgow)
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Alder Hey Children's Hospital
E Prescot Rd
Liverpool
England
L14 5AB

Study participating centre
Evelina London Children's Hospital
Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
Manchester Royal Infirmary
Cobbett House
Manchester Royal Infirmary
Oxford Road
Manchester
England
M13 9WL

Study participating centre
Southampton Children's Hospital
Tremona Road

Southampton
England
SO16 6YD

Study participating centre
Cambridge University Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Leeds Children's Hospital
Clarendon Wing
Leeds
England
LS1 3EX

Study participating centre
Great North Children's Hospital Newcastle
Victoria Wing
Royal Victoria Infirmary
Newcastle upon Tyne
England
NE1 4LP

Study participating centre
Nottingham Children's Hospital
Derby Road
Lenton
Nottingham
England
NG7 2UH

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
England
B4 6NW

Study participating centre
Bristol Royal Hospital for Children
Paul O'Gorman Building
Upper Maudlin Street
St Michael's Hill
Bristol
England
BS2 8BJ

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Versus Arthritis

Alternative Name(s)
Arthritis UK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Applications for access to the trial dataset, at the end of the trial, can be submitted formally in writing to UCL CCTU and will be considered and approved in writing after formal consideration by the trial oversight committees and the Chief Investigator.

Data, including sample data, collected may be shared with regulators and other researchers either at academic sites, nationally or internationally, or academic, commercial or charitable organisations approved by the Sponsor, in other future ethically approved research or regulatory approval process.

Participants provide consent to their data being shared by signing the informed consent form. All relevant data sharing agreements will be in place.

IPD sharing plan summary

Available on request