ISRCTN54174557 https://doi.org/10.1186/ISRCTN54174557

Steroid Treatment Trial in JIA (STAR-JIA): A randomised trial to compare the effectiveness, safety and cost-effectiveness of intravenous versus oral corticosteroid induction regimens for children and young people with juvenile idiopathic arthritis

Submission date 15/07/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/09/2023	**Overall study status** Ongoing	
Last Edited 21/01/2025	**Condition category** Musculoskeletal Diseases	

Plain English summary of protocol

Background and study aims

The aim of this study is to compare two different steroid treatments in children and young people with new-onset polyarticular juvenile idiopathic arthritis (JIA) to find out which is best. Medications used in the long-term management of JIA take around 12 weeks to start working. Steroids act quickly, reducing inflammation whilst the other medications start to work but have many potential side effects. There is a lack of evidence to suggest whether intravenous steroids or oral steroids are more effective, safe, tolerable for patients and which have a greater impact on quality of life.

Who can participate?

Patients aged 1-18 years of age with at least five inflamed joints and newly diagnosed polyarticular JIA

What does the study involve?

They will be randomly allocated to either a 6-week course (reducing dose regimen) of prednisolone liquid or tablets, taken at home OR a 3-day course of intravenous methylprednisolone on a hospital day-case unit. Participants will be assessed before starting treatment (baseline) and four follow-up visits at 6, 12, 24 and 52 weeks, in line with standard care appointments. Study visits will include assessments in standard care however, additional study-specific assessments will include reporting of side effects, and steroid toxicity risk including extra blood tests, questionnaires relating to the impact of JIA and treatment on quality of life and cost. The study offers an option for participants to donate blood samples for storage in a biobank for future research. Samples will not be analysed as part of the study but adopted by Liverpool University Biobank.

What are the possible benefits and risks of participating?
The direct burden on participation will be minimal as all research visits have been scheduled at the same time as standard-of-care visits to minimise the burden to participants. Research blood samples are taken at the same time as standard-of-care bloods to reduce burden.
Participants will be asked to complete several questionnaires which will prolong their clinic appointments. Once complete the questionnaire will be handed to the research team.
Risks associated with being treated with steroids (the IMP and the comparator) via different routes for JIA with the IMP, These risks are stated in the trial information sheets and site teams are appropriately trained as both routes of administration are used as standard of care.
All of the above risks are minimized with appropriate training and following policies and procedures by hospital Trusts and as stated in the protocol. For participants receiving oral prednisolone from hospital pharmacies, the pharmacy will dispense the drug as prescribed with appropriate guidance for taking it. For participants receiving IV methylprednisolone over 3 days on a hospital day unit, nurses who normally work on the day unit and have been appropriately trained to give IV methylprednisolone will be responsible for administering the drug and monitoring participants. It will not be given by Research Nurses who may be less familiar with the administration of this drug and do not usually administer this drug. This will minimize the risk of drug preparation, administration and monitoring errors.

Where is the study run from?
Alder Hey Children's NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
July 2023 to December 2026

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
star-jia@liverpool.ac.uk

Study website
https://star-jia.org.uk/

Contact information

Type(s)
Scientific

Contact name
Dr Alison Hudak

Contact details
Liverpool Clinical Trials Centre
Block C
Waterhouse Building
Brownlow Street
Liverpool
United Kingdom

L69 3GL
+44 (0)151 7940619
star-jia@liverpool.ac.uk

Type(s)
Public

Contact name
Dr Alison Hudak

Contact details
Liverpool Clinical Trials Centre
Block C
Waterhouse Building
Brownlow Street
Liverpool
United Kingdom
L69 3GL
+44 (0)151 7940619
star-jia@liverpool.ac.uk

Type(s)
Principal Investigator

Contact name
Dr Clare Pain

Contact details
Eaton Road
Liverpool
United Kingdom
L12 2AP
+44 (0)151 2284811
Clare.Pain@alderhey.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1007610

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
AH23-05-006, IRAS 1007610, CPMS 58347

Study information

Scientific Title
Steroid Treatment Trial in JIA (STAR-JIA): A randomised trial to compare the effectiveness, safety and cost-effectiveness of intravenous versus oral corticosteroid induction regimens for children and young people with juvenile idiopathic arthritis

Acronym
STAR-JIA

Study objectives
Primary objectives:
To compare the clinical effectiveness of intravenous methylprednisolone versus oral prednisolone for controlling new-onset polyarticular juvenile idiopathic arthritis (JIA) in JIA Core Outcomes.

Secondary objectives:
1. To compare the differences in JIA Core Outcomes for intravenous methylprednisolone versus oral prednisolone for the following domains:
1.1. Pain
1.2. Function
1.3. Health-related Quality of Life (HRQOL)
2. To assess the effectiveness of intravenous versus oral corticosteroids in minimising the need for additional treatments including all corticosteroid routes and additional disease-modifying anti-rheumatic drugs (DMARDs)/biologics.
3. To evaluate short/medium-term safety and tolerability of IV versus oral corticosteroids, with regards to adverse reactions, serious adverse events, laboratory assessments and paediatric glucocorticoid toxicity index (pGTI).
4. To determine if a dose-response relationship can be identified in the efficacy/adverse responses to corticosteroids across all participants by secondary analysis, normalising corticosteroids received for dose, bioavailability and potency using previously published data.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 08/09/2023, Yorkshire and the Humber - Leeds East (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle-upon-Tyne, NE2 4NQ, United Kingdom; +44 (0)207 1048171, (0) 207 104 8141; leedseast.rec@hra.nhs.uk), ref: 23/YH/0173

Study design
Open randomized controlled parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment, Safety, Efficacy

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

Health condition(s) or problem(s) studied
Juvenile idiopathic arthritis (polyarticular)

Interventions
IMP: Intravenous methylprednisolone administered over 3 days on a hospital day unit
Comparator: Oral prednisolone taken/administered over 6 weeks at home

The doses, frequency and method of administration of the IMP and comparator drug are provided below.

IMP: Methylprednisolone
Route: Intravenous administration
Form: Powder for injection to be prepared for intravenous administration
30 mg/kg per day for 3 consecutive days (Maximum dose: 1g per day)

Comparator: Prednisolone
Route: Oral administration
Form: Tablet or solution
The initial dose of prednisolone will be 1 mg/kg per day with a maximum dose of 40 mg. For participants weighing ≥40 kg, the weaning will be a reduction in line with the percentage decrease used for lighter patients.

Week of oral prednisolone 1: Dose (patient <40 kg): 1 mg/kg per day; Dose (patient ≥40 kg): 40 mg
Week of oral prednisolone 2: Dose (patient <40 kg): 0.75 mg/kg per day; Dose (patient ≥40 kg): 30 mg
Week of oral prednisolone 3: Dose (patient <40 kg): 0.5 mg/kg per day; Dose (patient ≥40 kg): 20 mg
Week of oral prednisolone 4: Dose (patient <40 kg): 0.375 mg/kg per day; Dose (patient ≥40 kg): 15 mg
Week of oral prednisolone 5: Dose (patient <40 kg): 0.25 mg/kg per day; Dose (patient ≥40 kg): 10 mg
Week of oral prednisolone 6: Dose (patient <40 kg): 0.125 mg/kg per day; Dose (patient ≥40 kg): 5 mg

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Bioequivalence, Pharmacoeconomic

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Methylprednisolone, prednisolone

Primary outcome measure
Primary clinical outcome:
Disease activity measured using the JADAS10 score at 0 weeks (Baseline) and 6 weeks

Primary economic outcomes:
1. Incremental cost per quality-adjusted life year (QALY) gained measured using Resource Use Questionnaires and Patient Level Information and Costing System (PLICS) data at 0 weeks (Baseline), 6 weeks, 12 weeks, 24 weeks and 52 weeks.
2. Resource use, costs and health utilities associated with IV and oral corticosteroids measured using Resource Use Questionnaires and Patient Level Information and Costing System (PLICS) data at 0 weeks (Baseline), 6 weeks, 12 weeks, 24 weeks and 52 weeks.

Secondary outcome measures
1. Disease activity in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured using the American College of Rheumatology (ACR) Pediatric Response Criteria (30, 50, 70, 90, 100) at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
2. Disease activity in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA), randomised to IV methylprednisolone or oral prednisolone measured using the JADAS (10,27,71) at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
3. Disease activity in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured by JADAS10 cut-off scores at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
4. Pain in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured using the Pain Visual Analogue Scale (Pain VAS) at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
5. Function in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured using the Childhood Health Assessment Questionnaire (CHAQ) at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
6. Health-related Quality of Life (HRQoL) in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured using Child Health Utility 9D Questionnaire (CHU-9D) and CAPTURE-JIA PROM at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks.
7. Requirement for additional treatment for subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) due to failure to respond to IV methylprednisolone or oral prednisolone measured using concomitant medications recorded at 6 weeks, 12 weeks, 24 weeks, 52 weeks.
8. Glucocorticoid toxicity in subjects with polyarticular Juvenile Idiopathic Arthritis (JIA) randomised to IV methylprednisolone or oral prednisolone measured using Paediatric Glucocorticoid Toxicity Index (pGTI) scores at 0 weeks (baseline), 6 weeks, 12 weeks, 24 weeks, 52 weeks

Overall study start date
13/07/2023

Completion date
06/02/2027

Eligibility

Key inclusion criteria
1. Participants must be between 1-18 years of age inclusive
2. New onset pcJIA diagnosed by a paediatric rheumatologist (to include polyarticular rheumatoid factor (RF+) positive, polyarticular RF negative, enthesitis-related arthritis, psoriatic arthritis and extended oligo-articular). This includes new diagnosis of JIA with at least 5 joints affected and patients previously categorised as oligoarticular JIA (with 4 joints or less) who have extended to at least 5 joints.
3. Participants are expected to be able to commence allocated treatment within 1 week of randomisation
4. Written, informed consent and where appropriate, assent obtained from participant or their legal representative
5. Participants of child-bearing potential must be willing to abstain from sexual intercourse from consent to their final visit and/or use another acceptable contraception method as described in section 9.10.5 of this protocol

Participant type(s)
Patient

Age group
Child

Lower age limit
1 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
130

Key exclusion criteria
1. Any contraindication to starting corticosteroids
2. Any contraindication to starting methotrexate
3. Pregnancy
4. Treatment with systemic corticosteroids within 4 weeks preceding screening (includes IV, IA, IM and oral)
5. Treatment with methotrexate within 12 weeks preceding screening
6. Any co-morbidity which in view of the treating clinician makes participation inappropriate

Date of first enrolment
05/03/2024

Date of final enrolment
05/02/2026

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Wales

Study participating centre
Alder Hey Hospital
Eaton Road
West Derby
Liverpool
United Kingdom
L12 2AP

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
University Hospitals Sussex NHS Foundation Trust
Worthing Hospital
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Study participating centre

The Royal Belfast Hospital for Sick Children
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Noahs Ark Childrens Hospital for Wales
Cardiff & Vale University Health Bd
Heath Park
Cardiff
United Kingdom
CF14 4XW

Sponsor information

Organisation
Alder Hey Children's NHS Foundation Trust

Sponsor details
Eaton Road
Liverpool
England
United Kingdom
L12 2AP
+44 (0)151 2824521
Kelly.Davies@alderhey.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.alderhey.nhs.uk/

ROR
https://ror.org/00p18zw56

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

The results of STAR-JIA will be published regardless of the magnitude or direction of effect. After the primary results have been published, the anonymised individual participant data and associated documentation (protocol, statistical analysis plan, annotated blank CRF will be prepared in order to be shared with external researchers.

Dissemination animations will be created with input from PPIE group for both participants, families and the public as well as healthcare professionals to increase impact of the findings,

There is a JIA patient and public involvement focus group that contribute to development of study information sheets and animation videos for participants and parents/guardians, protocol and dissemination of results. Results of this research study will be shared with healthcare professionals, participants/care-givers and the public including medical conferences and online journals.

Intention to publish date
30/12/2027

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