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The treatment of severe atopic eczema trial (TREAT)

Submission date	Recruitment status	[X] Prospectively registered
09/03/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
09/03/2016	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
28/07/2025	Skin and Connective Tissue Diseases	

Plain English summary of protocol

Background and study aims
Eczema, also known as dermatitis, is a long-term medical condition which causes the skin to become dry, itchy and inflamed (swollen and red). Atopic eczema (AE) is the most common type of eczema, particularly in children. It can appear anywhere on the body, but it is usually found on the face, trunk (chest and back) and around the inside of the elbows or knees. This type of eczema is called “atopic” because sufferers are more sensitive to allergens (substances which can cause an allergic reaction). The exact cause of AE is not fully understood, but it is thought that their skin does not produce as many protective oils as it should do and so the skin loses water easily. This means that the protective barrier of the skin is not as good as it should be, and so it is more vulnerable to potential irritants. When the AE symptoms are particularly severe, it may be necessary to apply skin creams containing corticosteroids (powerful anti-inflammatory medicine). Although this type of treatment is generally effective, many children do not feel that it makes any difference to their condition. The aim of this study is to compare the short- and long-term effectiveness and safety of the immunosuppressive drugs methotrexate and ciclosporin for the treatment of severe atopic eczema in children.

Who can participate?
Children aged between 2 and 16 who have severe atopic eczema and have not responded well to previous corticosteroid skin cream treatments.

What does the study involve?
Participants are randomly allocated to one of two groups. Group 1 participants are treated with ciclosporin for 9 months. Group 2 participants are treated with methotrexate for 9 months. Participants in both groups are followed-up for another 6 months to assess the short- and long-term effectiveness and safety of the drugs.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Medicines for Children Clinical Trials Unit, University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
May 2016 to April 2019

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Miss Farhiya Ashoor

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2015-002013-29

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
20707

Study information

Scientific Title
A randomised controlled trial assessing the effectiveness, safety and cost-effectiveness of methotrexate versus ciclosporin in the treatment of severe atopic eczema in children: The TREatment of Severe Atopic Eczema Trial (TREAT)

Acronym
TREAT

Study objectives

The aim of this study is to compare the short- and long-term effectiveness and the safety profile of methotrexate vs ciclosporin in the treatment of severe atopic eczema in children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England: Cambridge central, 16/01/2016, ref: 15/EE/0328

Study design
Multi-centre randomised parallel trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Children, Dermatology; Subtopic: Children (all Diagnoses), Dermatology (Skin); Disease: All Diseases, Dermatology

Interventions
Participants are randomly allocated to one of two groups.
Group 1: Participants are treated with ciclosporin (Brand: Neoral) for 9 months.
Group 2: Participants are treated with methotrexate (any brand with marketing authorisation within EEA) for 9 months.

Participants in both groups are followed-up for another 6 months to assess short- and long-term effectiveness and the safety profile of both drugs.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure

1. Atopic eczema severity is measured using the o-SCORAD index at baseline and 12 weeks
2. Disease remission (time to first significant flare) is measured using the o-SCORAD index during the 24 weeks after treatment cessation

Secondary outcome measures
1. Atopic eczema severity is measured using the Eczema Area & Severity Index (EASI), Investigator Global Assessment (IGA), and Patient orientated Eczema Measure (POEM) scores at baseline, 12, 36, 48, and 60 weeks and using the o-SCORAD at 36, 48 and 60 weeks
2. Number of flares in each study arm as well as the proportion of children who re-flared during the 24 weeks after treatment cessation
3. Quality of life is measured using the Children's Dermatology Life Quality Index (CDLQI)/Infant's Dermatitis Quality of Life index (IDQOL) & Dermatitis Family Impact questionnaire (DFI) scores at baseline, 12, 36, 48, and 60 weeks
4. Proportion of participants achieving 50% improvement in the o-SCORAD and EASI index is assessed at 12, 36, 48, and 60 weeks
5. Proportion of participants who withdraw from treatment because of adverse events
6. Cost-effectiveness of treatment based on utility is measured using the CHU-9D
7. Immuno-metabolic effects of MTX and CyA, especially in relation to markers of glycolytic activation and T cell cytokine signature, is measured at baseline, during treatment and up to 24 weeks after completion of treatment
8. Drug side effects/toxicity profiles
9. Association between MTX polyglutamate and CyA trough levels and reduction in atopic eczema severity as well as drug-related side effects
10. Impact of FLG genotype (yes/no) on reduction in atopic eczema severity

Overall study start date
01/03/2016

Completion date
31/07/2020

Eligibility

Key inclusion criteria
1. Written informed consent for study participation obtained from the patient or parents/legal guardian, with assent as appropriate by the patient, depending on the level of understanding
2. Aged 2-16 years at the time of the screening and randomisation visit
3. Diagnosis of severe recalcitrant atopic ezcema
4. History of inadequate clinical response (in the opinion of the treating clinician) to mild to potent topical corticosteroids
5. An objective (o)-SCORAD severity score of at least 30
6. Participants must live within travelling distance of the recruiting centre
7. Females of childbearing potential, who are sexually active, must commit to consistent and correct use of an acceptable method of contraception for the duration of the trial and for 3 months after the last dose of study drug
8. Willingness to comply with study requirements
9. Ability to swallow tablets/capsules
10. Baseline visit within 2 weeks of the screening visit

Participant type(s)
Patient

Age group
Child

Lower age limit
2 Years

Upper age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 98; UK Sample Size 98

Total final enrolment
103

Key exclusion criteria
1. Serious underlying medical condition which in the opinion of the Investigator would compromise the safety of the patient
2. Pregnant or nursing (lactating) females, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
3. Any active and/or chronic infection at screening or baseline (randomisation) visit that, based on the investigator's clinical assessment, makes the subject an unsuitable candidate for the study
4. Presence of moderate to severe impaired renal function as indicated by clinically significantly abnormal creatinine (≥ 1.5 x upper normal limit (ULN) for age and sex) or eGFR <60ml/min/1. 73m2 at screening visit*
5. Clinical evidence of liver disease or liver injury at screening visit as indicated by abnormal liver function tests such as AST, ALT, GGT, alkaline phosphatase, or serum bilirubin (must not exceed 1.5 x the upper limit value of the normal range for age and sex)
6. Total WBC count <3x109/L, or platelets <150x109/L or neutrophils <1.5x109/L or haemoglobin <8.5 g/dL at screening visit
7. Blood pressure values > 95th percentile for age and sex at screening and baseline visit
8. Received systemic cortico-steroids within 14 days prior to screening visit and 28 days of baseline visit
9. Received phototherapy within 4 weeks prior to screening visit and 6 weeks of the baseline visit
10. Previous exposure to any biologic agents or systemic immuno-suppressive therapy, except for oral corticosteroids (CS) for acute flare management
11. Concomitant use of disease-modifying and/or immunosuppressive drugs
12. Received live vaccines within 4 weeks prior to baseline visit
13. Currently participating in a conflicting study or participation in a clinical study involving a medicinal product in the last 28 days or less than 5 half-lives of the medicinal product prior to the screening visit
14. Known hypersensitivity to methotrexate or ciclosporin products
15. Insufficient understanding of the trial

*Formula for measuring eGFR = height (cm) x 40 / Plasma creatinine (micromol/l)

Date of first enrolment
11/05/2016

Date of final enrolment
31/01/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Liverpool
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Clinical Trials Research Centre
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Sponsor information

Organisation
King's College London (UK)

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Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/12/2020

Individual participant data (IPD) sharing plan

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	protocol	01/12/2018	11/07/2019	Yes	No
HRA research summary			28/06/2023	No	No
Results article		16/11/2023	20/11/2023	Yes	No
Results article	secondary analysis	24/07/2025	28/07/2025	Yes	No