Use of the NMF biomarker as predictive diagnostic for effective use of cyclosporine and dupilumab in the treatment of atopic dermatitis.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON54541

Source
ToetsingOnline

Brief title
NMF-CsA-dupi trial

Condition

- Epidermal and dermal conditions

Synonym
Atopic dermatitis, atopic eczema, eczema

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Atopic Dermatitis, Cyclosporine A (CsA), dupilumab, Filaggrin, Natural Moisturizing Factor (NMF)

Outcome measures

Primary outcome

- EASI (Eczema Area and Severity Index, EASI) at t = 1, 3 and 6 months

Secondary outcome

- Proportion of patients that achieved EASI75 (relative reduction of 75% from baseline EASI) without the use of rescue medication, at t = 1, 3 and 6 months - Proportion of patients that achieved IGA 0 or IGA 1 (Investigator*s Global Assessment) without the use of rescue medication at t = 1, 3 and 6 months - Proportion of patients that achieved a reduction >=4 points on the NRS-11 for itch intensity (Numeric Rating Scale) at t = 1, 3, and 6 months - POEM (Patient-Oriented Eczema Measure) at t = 1, 3, and 6 months - SCORAD (Scoring Atopic Dermatitis) at t = 1, 3 and 6 months - RECAP (Recap of Atopic Eczema) at t = 1, 3 and 6 months Cost-effectiveness Analysis: - EASI at t = 1, 3, 6 months - CDLQI (Children*s Dermatology Life Quality Index) >=4 years; IDQoL (Infants* Dermatitis Quality of Life Index) <4 years, at t = 0, 3 and 6 months - EQ-5D-Y at t = 0, 3 and 6 months - Emollients and steroid use in frequency and tubes used (per patient) over the course of 6 months - Healthcare costs related to the treatment of AD (medical specialist care, hospitalization, and costs directly associated with complications and recurrence) over the course of 6 months.

Study description

Background summary

If topical therapy fails, the next step for treatment of moderate-to-severe atopic dermatitis (AD) in children is systemic therapy (cyclosporine A (CsA) or dupilumab). Prognostic tools for effective use of CsA and dupilumab are currently lacking, resulting in over- and under treatment.

The strongest genetic risk factor for AD is a null mutation in the filaggrin gene (FLG). Stratification of patients based on the FLG null endotype could enable more targeted treatment. In current clinical practice FLG-null mutations are not determined for AD, since genotyping is costly, slow and requires a high level of expertise. The Natural Moisturizing Factor (NMF) biomarker, measured by Raman spectroscopy, is an accurate surrogate marker for the presence of FLG-null mutations.

Study objective

The current study has two main objectives:
- To investigate if the effectiveness of CsA differs for NMF low vs. NMF normal (corresponding with FLG mutation vs. FLG wild type) in children with moderate-to-severe AD.
- To investigate if the effectiveness of dupilumab differs for NMF low vs. NMF normal in children with moderate-to-severe AD.

Study design

This is a stratified biomarker study that investigates whether the NMF-biomarker status has an effect on the effectiveness of systemic treatment with respectively CsA or dupilumab in children with moderate-to-severe AD.

Intervention

After NMF measurement, patients are randomized to CsA treatment, to dupilumab treatment, or to no CsA and dupilumab treatment (control group). The duration of systemic treatment is 6 months. All groups will be treated with emollients and topical corticosteroids as topical therapy.

Study burden and risks

Risks: Patients may experience an exacerbation of their AD during the washout period, which may result in discomfort, necessitating escape medication. Patients may experience adverse effects from either CsA or dupilumab treatment, as can also occur during regular clinical care. Possible side-effects will be

closely monitored throughout the study.
A risk associated with this study is that some children who are treated gain no improvement of their AD. Step up therapy will be provided according to usual care.

Benefit: The majority of patients with CsA or dupilumab treatment will acquire improvement of clinical symptoms and achieve better disease control.

Burden: Patients may experience discomfort during additional study measurements such as drawing blood. Study visits and answering surveys will cost the patient and caretaker additional time.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015CN
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015CN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

children and adolescents, aged between 2 - 18 years, with moderate to severe atopic dermatitis
(AD diagnosed according to the UK working party criteria) - patient and parents/guardians able to
participate in the study and willing to give written informed consent - EASI (Eczema Area Severity
Index) >= 6 at screening and baseline (corresponding with moderate-to-severe disease) - IGA
(Investigators Global Assessment) >= 3 at screening and baseline (corresponding with moderate-to-severe
disease)

Exclusion criteria

children under the age of 2 years (due to the prescribe conditions of CsA) and patients older
than 18 years - contraindication for CsA - contraindication for dupilumab - patient (or one of the
parents/guardians) not willing to be randomized - children with a history of any known primary
immunodeficiency disorder - children with a history of cancer - EASI < 6 at screening or at baseline -
IGA - Pregnancy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-08-2021
Enrollment:	186
Type:	Actual

Ethics review

Approved WMO Date:	15-10-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-04-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	27-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-09-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-003247-30-NL
CCMO	NL71053.078.19