Use of the NMF Biomarker as Predictive Diagnostic for Effective Use of Cyclosporine and Dupilumab in the Treatment of Atopic Dermatitis

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23450

Source
NTR

Brief title
NMF-CsA-Dupi Trial

Health condition

Atopic dermatitis

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: ZonMW

Intervention

Outcome measures

Primary outcome

- Relative reduction in EASI (Eczema Area and Severity Index, EASI) at t = 6 months

- Proportion of patients that achieved EASI75 (relative reduction of 75% from baseline EASI) without the use of rescue medication, at t = 6 months

Secondary outcome

- Relative and absolute reduction in EASI from baseline at t = 1, 2, 3 and 6 months
- Relative and absolute reduction in SCORAD (Scoring Atopic Dermatitis) from baseline at t = 1, 2, 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, 2, 3 and 6 months
- Absolute reduction and proportion of patients that achieved a reduction ≥4 points on the NRS-11 for itch intensity (Numeric Rating Scale) at t = 1, 2, 3 and 6 months
- Relative and absolute reduction in POEM (Patient-Oriented Eczema Measure) from baseline at t = 1, 2, 3 and 6 months
- Emollients and steroid use in frequency and tubes used (per patient) over the course of 6 months
- Quality of life by patients (aged 16-18 years DLQI (Dermatolgy Life Quality Index); 4-15 years CDLQI (Children's Dermatology Life Quality Index); <4 years IDQoL (Infants' Dermatitis Quality of Life Index)) and by parents (EQ-5D-Y (Parents' Dermatitis Family Impact Questionnaire)) at t = 0, 6 and 12 months
- Healthcare costs related to the treatment of AD (medical specialist care, hospitalization, and costs directly associated with complications and recurrence).

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. Systemic cyclosporine A (CsA), is the first choice according to the national guidelines. Unfortunately, about 22.5-36% patients are refractory to CsA. In addition, treatment of AD in children with systemic CsA is expensive (€7.000/year). Prognostic tools for effective use of CsA are lacking, resulting in over- and under treatment. AD is a heterogeneous disease with various biological origins and clinical appearances. Dupilumab (Dupixent) is a newly registered biological for the treatment of pediatric atopic dermatitis with promising results, but also lacking in prognostic tools. It is likely that different therapies or treatment intensities are not equally effective for all AD endotypes. 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. The goal of this study is to investigate whether stratification of children with atopic dermatitis on the NMF biomarkers results in an improvement of effectiveness and efficiency in the use of systemic treatment (ciclosporin and dupilumab) in moderate-to-

severe atopic dermatitis.

Study objective

The effectiveness and cost-effectiveness of treatment with systemic cyclosporine or dupilumab in children with moderate-to-severe atopic dermatitis is different for patients with low NMF (corresponding with filaggrine-gene mutation) versus children with normal NMF (corresponding with filaggrine wildtype).

Study design

t = 0, 1, 2, 3 and 6 months

Intervention

Systemic cyclosporine A or dupilumab for 6 months

Contacts

Public
ErasmusMC
Suzanne Pasmans

0031653524299
Scientific
ErasmusMC
Suzanne Pasmans

0031653524299

Eligibility criteria

Inclusion criteria

- Children and adolescents, aged between 2 and 18, with moderate to severe atopic dermatitis (diagnosed according to the UK working party criteria)
- Patients 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 or dupilumab
- use of topical corticosteroids (TCS) or topical calcineurine inhibitors (TCI) 2 weeks before randomization (during the washout period)
- use of systemic anti-inflammatory medication 4 weeks before randomization
- 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 <3 at screening or at baseline

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	06-10-2019
Enrollment:	318
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	16-08-2019
Application type:	First submission

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
NTR-new	NL7967
Other	METC Erasmus MC Rotterdam : MEC-2019-0568

Study results