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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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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23450

Bron
NTR

Verkorte titel
NMF-CsA-Dupi Trial

Aandoening

Atopic dermatitis

Ondersteuning

Primaire sponsor: Erasmus MC
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- 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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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).

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

Systemic cyclosporine A or dupilumab for 6 months

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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)

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	06-10-2019
Aantal proefpersonen:	318
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	16-08-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7967
Ander register	METC Erasmus MC Rotterdam : MEC-2019-0568

Resultaten