Dupilumab in adults with severe chronic hand eczema with an inadequate response or intolerance to alitretinoin: a randomized, double-blind, placebo-controlled proof of concept efficacy study

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Main study:To evaluate the efficacy of dupilumab in patients with inflammatory subtypes of severe chronic hand eczema with an inadequate response or intolerance to alitretinoin and in patients with concomitant positive patch test results.Substudy:...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON48247

Source
ToetsingOnline

Brief title
Dupilumab in severe chronic hand eczema

Condition

- Epidermal and dermal conditions

Synonym
hand dermatitis, Hand eczema

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Farmaceutische industrie,Sanofi-aventis

Intervention

Keyword: Biologics, Dupilumab, Efficacy, Hand eczema

Outcome measures

Primary outcome

Main study:

Severity of hand eczema, measured with the proportion of patients reaching 75% improvement on the Hand Eczema Severity Index (HECSI-75).This instrument is being used in the standard care of patients with hand eczema.

The amount of positive patch test results compaired to baseline.

Substudy:

Difference in gene expression profile before and after treatment.

Secondary outcome

• health related quality of life.

• improvement in severity of hand eczema, assessed by the patient.

• improvement in severity of hand eczema, assessed by the photographic guide for hand eczema.

• improvement in severity of hand eczema, assessed by the hand eczema severity index (mean percentage change, HECSI-50, HECSI-90).

• work productivity and impairment.

• the safety and tolerability of treatment.

• treatment-related changes in the serum biomarkers.

• the effects of dupilumab treatment on histologic morphology.

• the effects of dupilumab treatment on the microbiome colonization profiles.

Study description

Background summary

Hand eczema is a common condition with a 1-year prevalence up to 10%. Alitretinoin is the only approved systemic treatment for all clinical types of hand eczema. However, it is less effective in non-hyperkeratotic forms, such as the inflammatory subtypes of hand eczema. In our current clinical experience with dupilumab, patients with atopic dermatitis and concomitant hand eczema also have beneficial effects on hand eczema. Among these patients were also patients who were refractory to alitretinoin and other off-label immunosuppressive drugs.

Study objective

Main study:
To evaluate the efficacy of dupilumab in patients with inflammatory subtypes of severe chronic hand eczema with an inadequate response or intolerance to alitretinoin and in patients with concomitant positive patch test results.

Substudy:
To compare genomic changes due to dupilumab in active HE lesions and changes in the HE transcriptome defined by gene expression differences between lesional and non-lesional skin.

Study design

A randomized, double-blind, placebo-controlled proof of concept efficacy study, set in a university dermatology clinic, tertiary referral center.

Intervention

Group I: dupilumab in starting dose of 600mg s.c. and subsequently 300mg s.c. every two weeks.
Group II: placebo in starting dose of 600mg s.c. and subsequently 300mg s.c. every two weeks.
The treatment period is 16 weeks.

Study burden and risks

Eligible patients will be recruited during routine clinical consultations in the department of Dermatology of the UMCG. There is a total of 6 visits. The screening comprises a short medical exam, disease severity assessment, epicutaneous allergy test, serum test and for women also a pregnancy test. Participants will be asked to fill out the questionnaires five times. Clinical photographs will be taken at defined intervals. At every visit a short medical exam will be performed and patients will be asked about possible side effects. Extra biomarker laboratory measurements will be carried out, but these will be carried out during the laboratory measurements that are routinely assessed in treatment with dupilumab in AD patients. If patients participate in the substudy, skin biopsies will be performed. This is a standard dermatological procedure, performed on a daily base. It is a generally safe procedure with minimal burden to the patient. Biopsies can be mainly associated with a small risk of scarring, prolonged bleeding and/or infection. One extra visit is needed to give patients consideration time before participation in the study. Results of the trial can be related to the population of patients with severe hand eczema.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age >= 18 years and <= 75 years.
• Severe or very severe chronic hand eczema as defined by a Physician Global Assessment (PGA) using a validated Photoguide.
• Inflammatory subtypes of hand eczema: recurrent vesicular hand eczema or chronic fissured hand eczema.
• An inadequate response to topical corticosteroids within 6 months before screening.
• A history of prior alitretinoin exposure and inadequate response or intolerance to alitretinoin.
• Patients has also received standard skin care, including emollients and barrier protection as appropriate, without significant improvement.
• Patients has avoided irritants and contact allergens, if identified, without significant improvement.
• Women of childbearing potential are required to use a highly effective method of birth control, prior to receiving study intervention, during the study and for at least 10 weeks after receiving the last administration of study intervention.
• A woman of childbearing potential must have a negative serum or urine pregnancy test (β-human chorionic gonadotropin [β-hCG]) at screening and at Week 0 prior to administration of study intervention;
• Agree not to receive a live virus or live bacterial vaccination during the study, or within 12 weeks after the last administration of study intervention.
• Agree not to receive a BCG vaccination during the study, or within 12 months after the last administration of study intervention.
• Be willing and able to adhere to the prohibitions and restrictions specified in this protocol.
• Must sign an informed consent form (ICF) indicating that he or she understands the purpose of and procedures required for the study, and is willing to participate in the study.

Exclusion criteria

• Other clinical subtypes of hand eczema, e.g. hyperkeratotic hand eczema, as defined by the Danish Contact Dermatitis Group.
• Treatment with alitretinoin, systemic immunosuppressive medication or UV

radiation within the previous 4 weeks.
• Patients with predominantly atopic dermatitis, in whom the hands are also involved, but no main concern. Patients with controlled atopic dermatitis, in which the hands are mainly affected, are eligible for inclusion.
• Psoriasis of the hands.
• Active bacterial, fungal, or viral infection of the hands.
• Pregnant/lactating or planning to become pregnant during the study period.
• Current malignancy (other than successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma and*or localized carcinoma in situ of the cervix).
• Participant has known allergies, hypersensitivity, or intolerance to dupilumab or its excipients: L-arginine hydrochloride, L-histidine, polysorbate 80, sodium acetate, acetic acid, sucrose, water for injections.
• Participants with active helminth and other parasitic infections.
• Patients infected with human immunodeficiency virus (HIV) (positive serology for HIV antibody).
• Patients testing positive for hepatitis B virus (HBV) or hepatitis C (HCV) infection.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-08-2020
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dupixent
Generic name:	Dupilumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-01-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-04-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2019-001561-32-NL
CCMO	NL71585.042.19