Efficacy of oral alitretinoin versus oral cyclosporine in patients with moderate to very severe hand eczema. A randomized prospective open-label trial with blinded outcome assessment.

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This study has been transitioned to CTIS with ID 2024-515140-23-00 check the CTIS register for the current data. To compare the efficacy of alitretinoin and cyclosporine in the treatment of hand eczema.

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

Summary

ID

NL-OMON55401

Source
ToetsingOnline

Brief title
Alitretinoin vs cyclosporine in hand eczema

Condition

- Epidermal and dermal conditions

Synonym
hand eczema

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Alitretinoin, clinical trial, cyclosporine, hand eczema

Outcome measures

Primary outcome

The primary endpoint for efficacy is response to treatment, defined as achieving *clear*/*almost clear* in the PGA (Physician Global Assessment) score, based on a validated Photographic Guide developed by Coenraads et al (16) at 24 weeks of treatment

Secondary outcome

Secondary endpoints are: improvement of >=2 steps on the PGA score, based on a validated Photographic Guide developed by Coenraads et al at 24 weeks of treatment; improvement in the Hand Eczema Severity Index (HECSI) score; improvement in the Health related Quality of Life questionnaire for hand eczema (QOLHEQ); and a Patient Global Assessement (PaGA) of improvement after 12 en 24 weeks. Adverse events will be registered, as well as time to response. Furthermore, cost-utility, quality adjusted life years (QALYs) and cost-effectiveness will be assessed with the EQ-5D-5L questionnaire while monitoring treatment related costs.

Study description

Background summary

Hand eczema is a common condition, with a point prevalence of 4% and a 1-year-period prevalence up to 10% in the general population.
Systemic treatment with alitretinoin is registered for all clinical types of hand eczema. However, it is especially effective in hyperkeratotic subtype, and less effective in non-hyperkeratotic forms. Cyclosporine is often prescribed 'off-label' for hand eczema in daily practice and has a benefical effect in recurrent vesicular hand eczema. However, there is no international consensus on the classification of clinical types of hand eczema. The efficacy of cyclosporine in hand eczema could prove superior to that of alitretinoin.

Study objective

This study has been transitioned to CTIS with ID 2024-515140-23-00 check the CTIS register for the current data.

To compare the efficacy of alitretinoin and cyclosporine in the treatment of hand eczema.

Study design

Randomized prospective open-label trial with blinded outcome assessment, set in a university dermatology clinic and at dermatology departments of other hospitals in the Netherlands. The researchers of the dermatology department from UMCG will include patients in UMCG or at dermatology departments of other hospitals in the Netherlands. The other hospitals only have a facilitating role. In this way, patients can be treated and included in the study at their own hospital. Assessment of severity and laboratory measurements in this study will be conducted correspondending to daily practice in our department.

Intervention

Group I: alitretinoin 30mg/day
Group II: cyclosporine 5mg/kg/day (startdose). After 8 weeks decreased to 3-3.5 mg/kg/day.
Treatment duration is 24 weeks.

Study burden and risks

This trial is designed in a way that minimizes the burden and risks for the patient, because it will be carried out according to daily practice at our department. Moreover, patients can be treated and included in the study at their own hospital by the researchers of the dermatology department from UMCG and therefore travel as little as possible. No additional laboratory measurements will be carried out next to measurements that are routinely assessed in treatment with one of both study drugs. Evaluation of cost-utility and cost-effectiveness of both treatments is additional compared to daily

practice. A maximum of 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 moderate to very severe hand eczema.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age >= 18 years and <= 75 years
- Moderate, severe or very severe hand eczema for a minimum duration of 3 months as defined by a validated Photoguide
- Refractory to standard therapy, defined as:
o Patients received treatment with topical corticosteroids of class II or higher for at least 8 weeks within 3 months before enrolment, with either no response or a transient response
o Patients had also received standard skin care, including emollients and

barrier protection as appropriate, without significant improvement
o Patients had avoided irritants and contact allergens, if identified, without significant improvement
- Women of childbearing potential are required to use at least two forms of contraception for at least 1 month before starting treatment, during treatment, and for at least 1 month after finishing treatment; these women are required to take monthly pregnancy tests
- Able to provide written Informed Consent
- Able to speak and read the Dutch language

Exclusion criteria

- Treated with alitretinoin or cyclosporine in the previous 3 months
- Patients with predominantly atopic dermatitis, in which the hands are also involved. 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
- Treatment with systemic medication or UV radiation within the previous 4 weeks. For systemic prednisolone; patients with treatment within the previous 2 weeks will be excluded
- Mentally incompetent
- Immunocompromised status
- Uncontrolled arterial hypertension (minimally 3 measurements). Systolic pressure > 160 mmHg or diastolic pressure > 95 mmHg, despite starting anti-hypertensive medication (first choice amlodipine 5 mg/day)
- Known or suspected allergy to ingredients in the study medications
- Inclusion in a study of an investigational drug within 60 days prior to start of treatment
- Current malignancy (other than successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma and*or localized carcinoma in situ of the cervix)
- Current active pancreatitis
- Evidence of alcohol abuse or drug addiction
- Malabsorption
- Currently active gout
- Recurring convulsions/epilepsy
- Living vaccine (including bacillus Calmette-Guérin (BCG), varicella, measles, mumps, rubella, yellow fever, oral polio and oral typhoid) in the last 2 weeks or the planned application of such a vaccine during the study period
- Chronic or recurrent infectious diseases
- Contact sensitizations with clinical relevance to the hands, in which exposure to allergens is not avoided.
- Hypervitaminosis A due to the use of vitamin A supplements containing >2000 IU

- Use of drugs with potential to change the effective dosis of study drugs within the previous 2 weeks, Laboratory exclusion criteria post randomization:
- Alanine aminotransferase (ALAT) and *or aspartate aminotransferase (ASAT) values > 200% of the upper limit of normal
- Impaired renal function as indicated by a clinically relevant abnormal creatinine value (to be determined by investigator or treating physician)
- Anemia as indicated by a clinically relevant lowered hemoglobin value (to be determined by investigator or treating physician), Alitretinoin specific:
- Triglycerides > 200% of the upper limit of normal,
- Cholesterol or low density lipoprotein (LDL) cholesterol values > 200% of the upper limit of normal
- Uncontrolled hypothyroidism (to be determined by investigator or treating physician), Cyclosporine specific:
- Impaired renal function as indicated by a clinically relevant abnormal creatinine value (to be determined by investigator or treating physician)
- Uremia
- Hyperkalemia
- Hyperuricemia in patients with a medical history of gout

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-05-2017
Enrollment:	78
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	neoral
Generic name:	cyclosporine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Toctino
Generic name:	alitretinoin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-05-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-08-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-08-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-01-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-08-2024
Application type:	Amendment
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
EU-CTR	CTIS2024-515140-23-00
EudraCT	EUCTR2015-003488-12-NL
ClinicalTrials.gov	NCT03026946
CCMO	NL54659.042.15