Efficacy of oral alitretinoin versus oral azathioprine in patients with severe chronic non-hyperkeratotic hand eczema. A randomized prospective open-label trial with blinded outcome assessment.

Published: 12-06-2015
Last updated: 13-04-2024

To compare the efficacy of alitretinoin and azathioprine in the treatment of severe chronic non-hyperkeratotic hand eczema.

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

Summary

ID

NL-OMON41737

Source
ToetsingOnline

Brief title
ALIAZ-trial

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, Azathioprine, Clinical trial, Hand eczema

Outcome measures

Primary outcome

The primary endpoint for efficacy is response to treatment, defined as an improvement of * 2 steps on the Physician Global Assessment (PGA), developed by Ruzicka et al, after 24 weeks of treatment.

Secondary outcome

Secondary endpoints are improvement in: mean PGA after 12 and 24 weeks, the Hand Eczema Severity Index (HECSI) score, the Health related QoL questionnaire for hand eczema (QOLHEQ), and a Patient Global Assessement (PaGA) of improvement. 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 1-year period prevalence up to 10%. Systemic treatment with alitretinoin is registered for all clinical types of hand eczema. However, it is especially effective in the hyperkeratotic subtype, and less effective in non-hyperkeratotic forms. Azathioprine is often prescribed 'off-label' for hand eczema in daily practice, and has a beneficial

effect in non-hyperkeratotic subtypes. A few small studies support this observation. The efficacy of azathioprine in non-hyperkeratotic hand eczema could prove superior to that of alitretinoin.

Study objective

To compare the efficacy of alitretinoin and azathioprine in the treatment of severe chronic non-hyperkeratotic hand eczema.

Study design

Randomized prospective open-label trial with blinded outcome assessment, set in a university dermatology clinic, tertiary referral center. Assessment of severity and laboratory measurements in this study will be conducted corresponding to daily practice in our department.

Intervention

Group I: alitretinoin 30mg once daily. Group II: azathioprine 1.5 or 2.5mg/kg/day in 2 doses. The treatment period 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. No additional laboratory measurements will be carried out next to measurements that are routinely assessed in treatment with one of both study drugs. 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 chronic non-hyperkeratotic hand eczema.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:;- Age * 18 years and * 75 years;- Severe chronic non-hyperkeratotic hand eczema for a minimum duration of 3 months as defined by a Physician Global Assessment (PGA) using a validated Photoguide;- Refractory to standard therapy, defined as:
-> 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
-> Patients had also received standard skin care, including emollients and barrier protection as appropriate, without significant improvement
-> Patients had avoided irritants and 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

A potential subject who meets any of the following criteria will be excluded from participation in this study:;General criteria prior to randomization
- Hyperkeratotic palmar eczema as defined by the Danish Contact Dermatitis Group
- Patients with predominantly atopic dermatitis, in which the hands are also involved. Patients with mild atopic dermatitis, in which the hands are mainly affected are eligible for inclusion.
- Psoriasis
- 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
- Mentally incompetent
- Immunocompromised status
- 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
- 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
- Evidence of alcohol abuse or drug addiction
- 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);Azathioprine specific
- Patients with low or absent thiopurine methyltransferase (TPMT) activity (defined in our center as <52 nmol/gHb/hour, combined with genotyping showing homozygous of compound heterozygous mutations) and a subsequent risk for life-threatening myelotoxicity

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:	Recruitment stopped
Start date (anticipated):	09-05-2016
Enrollment:	116
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Imuran, Azasan
Generic name:	Azathioprine
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:	12-06-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-06-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-09-2015
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
EudraCT	EUCTR2015-001447-37-NL
CCMO	NL52232.042.15