Efficacy of oral alitretinoin treatment in patients with palmo-plantar pustulosis (PPP) inadequately responding to standard topical treatment

Published: 03-12-2010
Last updated: 04-05-2024

- To determine the response based on Palmo-plantar Pustulosis Psoriasis Area and Severity Index (PPPASI) at the end of treatment (week 24), or at the latest assessment for patients who withdraw prematurely

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

Summary

ID

NL-OMON36734

Source
ToetsingOnline

Brief title
Oral alitretinoin in PPP

Condition

- Epidermal and dermal conditions

Synonym
hand and foot pustulosis; Palmo-plantar pustulosis

Research involving
Human

Sponsors and support

Primary sponsor: Basilea Pharmaceutica

Source(s) of monetary or material Support: Basilea Pharmaceutica Ltd

Intervention

Keyword: alitretinoin, Efficacy, palmo-plantar pustulosis

Outcome measures

Primary outcome

- Percentage change in PPPASI

Secondary outcome

Efficacy

- PPPASI 50 response and PPPASI 75 response defined as a 50% and 75% decrease

in PPPASI from baseline, respectively.

- Value and change in pustule count on palms and soles to assess the response

with regard to pustular lesions

- Value and percentage change in mPASI, mPASI 50 response, and mPASI 75 response

- Value and change in NAPSI

Safety

- Overall incidence and severity of AEs

- Laboratory test results (fasted lipid tests) and incidence of abnormal

laboratory values

- Value and change in CES D

Study description

Background summary

Alitetinoin has shown efficiency in severe chronic hand eczema and is licensed for this indication. Case reports of Alitetinoin treatment in PPP warrant further study as PPP is difficult to treat with limited options available.

Study objective

- To determine the response based on Palmo-plantar Pustulosis Psoriasis Area and Severity Index (PPPASI) at the end of treatment (week 24), or at the latest assessment for patients who withdraw prematurely

Study design

Randomized, double-blind, placebo-controlled, parallel-group, multicenter

Intervention

oral treatment: 30 mg/day Alitritoin or placebo for 24 weeks.

Study burden and risks

Alitretinoin is a known teratogen. Alitretinoin is licenced for treating severe chronic hand eczema, a skin condition with a similar disease burden and therapy challenge to PPP. The dose chosen is the licenced dose in other indications.

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

1. Male patients, or female patients if post-menopausal as defined in protocol section 7.4.1., or hysterectomized, or bilaterally ovarectomized, or if pre-menopausal and willing to use at least 1 but preferably 2 methods of contraception under supervision of the investigator or a gynecologist
2. Aged 18 to 75 years
3. Patients with PPP for at least 6 months, with or without psoriasis lesions on other areas of the skin
4. A PPPASI score of at least 8 with involvement of at least 10% of the palms and/or the soles
5. Refractory to standard topical therapy
6. Written informed consent provided

Exclusion criteria

1. Patients unable to comply with the requirements of the study
2. Female patients who are pregnant or who plan to become pregnant or who are breast feeding
3. Female patients of childbearing potential who cannot use or will not commit to using at least one but preferably two effective forms of contraception simultaneously under supervision of the investigator or a gynecologist
4. Patients whose disease is adequately controlled by standard non-medicated therapy (skin moisturizing and protection) and standard topical corticosteroid therapy, but whose disease has relapsed following discontinuation of these treatments
5. Patients with known hypersensitivity to other retinoids or vitamin A derivatives, or to any study medication component, especially soybean oil and partly hydrogenated soybean oil
6. Patients treated with any of the following treatments 4 weeks before the start of study treatment:
a. systemic drugs: corticosteroids, immunosuppressants, methotrexate
b. phototherapy: ultraviolet B light therapy [UVB], Psoralen with ultraviolet A combination therapy [PUVA], Grenz rays, X-rays
7. Patients treated with biologic treatments within 12 weeks prior to start of study treatment.
8. Patients treated with any systemic or topical retinoids within 1 year or 1 month,

respectively, before start of study treatment, and patients who received systemic retinoids for treatment for PPP at any time
9. Patients with severe generalized pustular psoriasis
10. Patient has a skin condition of palms and/or soles which is assessed as unrelated to PPP by the investigator
11. Patients with any serious medical condition which, in the opinion of the investigator, may interfere with the safety of the patient
12. Patients with hepatic insufficiency, severe renal failure, uncontrolled hypercholesterinemia, uncontrolled as characterized by:
a. AST/ ALT > 2,5 x ULN
b. Creatinine clearance <60ml/min (calculated, Cockcroft-Gault)
c. Fasting triglyceridemia > 1.5 x ULN
d. Fasting cholesterol > 1.5 x ULN
e. Fasting LDL cholesterol > 1.5x ULN
13. Patients with hypothyroidism as indicated by TSH/T4 test <0.9 x LLN or hypervitaminosis A
14. Patients with cardiovascular risk factors that would exclude a starting dose of 30 mg of alitretinoin
15. Patients receiving drugs with a potential for drug-drug interaction, such as systemic tetracyclines, ketoconazole, or St. John*s Wort within 1 week, or receiving systemic itraconazole within 2 weeks, before start of study treatment
16. Patients included in the study of an investigational drug within 2 months before start of study treatment (3 months for biologics)
17. Patients with a score of 20 or more on CES-D, or with active major psychiatric disorder (e.g. Major Depressive Disorder, Generalized Anxiety Disorder, Bipolar Disorder (I or II), or schizophrenia)

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):	05-09-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Toctino
Generic name:	Alitretinoin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	03-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-05-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2010-022843-39-NL
ClinicalTrials.gov	NCT01245140
CCMO	NL34464.091.10