Reduction of adverse effects by systemic antihistamines in drug therapy with fumarates in severe chronic plaque psoriasis: a doubleblind, randomized, placebo controlled clinical trial

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

Summary

ID

NL-OMON37148

Source
ToetsingOnline

Brief title
Reduction of adverse effects of fumarates with antihistamines.

Condition

- Epidermal and dermal conditions

Synonym
fumarates, side-effects

Research involving
Human

Sponsors and support

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

Intervention

Keyword: antihistamines, fumarates, side-effects, therapy

Outcome measures

Primary outcome

To attempt to decrease the side effects in patients by using fumarates in

combination with antihistamines (Cetirizine).

Secondary outcome

We will attempt to show that antihistamines can also support fumarate therapy

with an antipsoriatic effect through immunomodulation.

Study description

Background summary

Psoriasis is a T-cell mediated skin disease affecting 2-3 % of the world*s population.
The anti-psoriatic drug, Fumaderm® or Fumarate '120', further referred to as *fumarate therapy* or *fumarates* has proven to be effective in psoriasis vulgaris. Systemic therapy with fumarates may be given to patients for prolonged periods because of its lack of serious side effects. Commonly reported side-effects of fumarates are flushing, gastrointestinal complaints, nausea, and tiredness. These side effects usually occur during the induction of fumarate therapy. H1- histamine receptors are thought to be responsible for these side- effects.Anti-histamines, more precisely H1-receptor blockers may be of clinical value in overcoming the common side effects of fumarate therapy. H1-receptor blockers may also have anti-psoriatic effects, supporting those of fumarates, by shifting the balance of proinflammatory cytokines produced by Th-1 T cells (IFN-γ,TNF-α, IL-12) to Th2-type cytokines, including IL-4,IL-5,IL-10 and IL-13. H1-receptor blockers would then be as effective as fumarates, which also shift the balance from type-1 to type-2 cytokine

production.

Study objective

The aim of this study is to determine the effects of fumarate therapy in combination with the H1-receptor blocker Cetirizine in psoriasis patients. Further to evaluate whether there is a decrease in the side effects of fumarate therapy during the first three months. This study is also to investigate the possible synergestic/additional anti-psoriatic effects of H1-receptor blocker Cetirizine during fumarate therapy and to study the immunological effects of this combination therapy.

Study design

Patients will be randomized into 2 groups consisting of 25 patients each. One group (25 patients) will receive fumarate therapy combined with Levocetirizine. The other group (25 Patients) will receive fumarate therapy* combined with a placebo instead of Levocetirizine. All patients will be treated for 12 weeks with a follow-up period of 8 weeks. Laboratory tests and skin biopsies will be taken at weeks 0, 4, 8, 12 and 20.
*Treatment scheme:

Week 1 1 dd 1 Fumaderm initial® + 1 dd 1 Xyzal®
Week 2 2 dd 1 Fumaderm initial® + 1 dd 1 Xyzal®
Week 3 3 dd 1 Fumaderm initial® + 1 dd 1
Xyzal®
Week 4 1 dd 1 Fumaderm® + 1 dd 1 Xyzal®
Week 5 2 dd 1 Fumaderm® + 1 dd 1
Xyzal®
Week 6 3 dd 1 Fumaderm® + 1 dd 1
Xyzal®
Week 7 2 dd 2 Fumaderm® + 1 dd 1
Xyzal®
Week 8 2 dd 2 Fumaderm® + 1 dd 1
Fumaderm® + 1 dd 1
Xyzal®
Week 9 - Week 12 3 dd 2 Fumaderm® + 1 dd 1 Xyzal®

Intervention

psoriasis vulgaris

Study burden and risks

There will be a significant chance for the patient of a secondary woundinfection of the injection- and biopsie place and collaps during taking

the bloodsamples. Furthermore patients might experience the side-effects of the fumaratetherapy.

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)Patients with known severe psoriasis of the chronic plaque type
2)PASI >= 10
3)Age >= 18 years
4)Signed informed consent

Exclusion criteria

1)Pregnancy and breast feeding
2)Patients with Prostate hyperplasia, Glaucoma, Stomach ulcer
3)Patients with liver diseases
4)Patients with kidney diseases
5)Patients with blood test deviations
6)Patients with gastro-intestinal diseases
7)Patients with a history of malignancies

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-11-2009
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Levoceterizine
Generic name:	Xyzal
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-08-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-10-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-05-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
Other	ISRCTN12758639
EudraCT	EUCTR2009-010137-41-NL
CCMO	NL26484.078.09