A phase IV open label study in moderate to severe chronic plaque psoriasis subjects transitioning from previous systemic antipsoriasis therapies (methotrexate, cyclosporine, retinoids or PUVA, NBUVB) to Raptiva 1 mg/kg/ week therapy.

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Objectives:To assess the safety of transitioning subjects to Raptiva therapy from standard oral systemic or phototherapy by overlapping with Raptiva whilst tapering the initial systemic therapy or phototherapy dose. The secondary objective is to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON31969

Source
ToetsingOnline

Brief title
Open label trial investigating transition from systemic agents to Raptiva.

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym

not found

Research involving
Human

Sponsors and support

Primary sponsor: Merck
Source(s) of monetary or material Support: Merck Serono International SA - Genève

Intervention

Keyword: Phase IV, Psoriasis, Raptiva, transition

Outcome measures

Primary outcome

The primary endpoint is safety, and will include all AEs, SAEs, and laboratory data (haematology and biochemistry) and urinalysis at all time points, divided by tapering and previous treatment.

Secondary outcome

The secondary endpoint will be the efficacy of Raptiva after 12 weeks therapy, measured as the proportion of subjects who achieve an sPGA assessment of minimal or clear at Week 12 (Day 85).

Tertiary endpoints will be the proportion of subjects with >=50% improvement of PASI score and the proportion of subjects with >=75% improvement of PASI score at Week 12 (Day 85) relative to Baseline and the median improvement of DLQI scores at Week 12 (Day 85) relative to Baseline.

Study description

Background summary

Psoriasis is an inflammatory skin disorder that affects between 1 and 2% of the

general population. It is characterised by an increased proliferation of the epidermis, and presents as well-defined thickened erythematous patches typically covered with a silver scale. Current therapies for psoriasis are unsatisfactory as none are curative, and in addition the most effective agents are associated with potentially serious side effects. In all cases, psoriasis is a chronic condition requiring long-term medication.
Although the aetiologies and pathologies of psoriasis are not well understood, the discovery that T-cells are centrally involved in the development of psoriasis, and the continued elucidation of the inflammatory pathways in psoriasis, are leading to the development of new biological therapeutic agents to treat these conditions.
Physicians anticipate using cell-adhesion molecule (CAM) antagonists, which affect T-cell function in the treatment of psoriasis and using tumour necrosis factor (TNF) inhibitors, which affect TNF in the inflammatory cascade, in the treatment of psoriasis.
For further information, please refer to the current Raptiva Investigator Brochure (11).

Study objective

Objectives:
To assess the safety of transitioning subjects to Raptiva therapy from standard oral systemic or phototherapy by overlapping with Raptiva whilst tapering the initial systemic therapy or phototherapy dose.
The secondary objective is to evaluate the efficacy of Raptiva in subjects with moderate to severe chronic plaque psoriasis over a 12-week period
The study aims to provide management guidance to physicians who are transitioning subjects with moderate to severe chronic plaque psoriasis from phototherapy or systemic anti-psoriatic medication to Raptiva.

Study design

Trial Design:
The trial is an open-label, non-comparative, non-randomised study in subjects with moderate to severe chronic plaque psoriasis who have failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies, including methotrexate, cyclosporine and PUVA, and are transitioned to Raptiva.
Subjects meeting these criteria but currently on systemic treatments not listed above, as e.g. retinoids or phototherapies e.g. NBUVB can also be included in the trial.
The multi-centre trial will be conducted at approximately (but not limited to) 20 sites in Canada and EU countries.
Subjects will start Raptiva on Day 1 with a first dose 0.7mg/kg/SC, followed by 1 mg/kg/wk SC for the following 11 weeks, while gradually tapering off their current systemic therapy over 6 weeks.

The tapering of systemic treatment will be as follows:
• Wk 0-1 (Day 1-14) at pre-trial dose systemic or UV;
• Wk 2-3 (Day 15-28) at approximately half dose systemic (or approximately half of the cumulative dose of UV sessions);
• Wk 4-5 (Day 29-42) at approximately one quarter of the pre-trial dose of systemic or approximately one quarter of the cumulative dose of UV;
• No systemic or UV from Wk 6-12 (Day 43-85)
The study will be of 12 weeks duration with a 14 day screening period. A 30-day safety follow-up visit will be conducted for all subjects following study completion or withdrawal.

Study burden and risks

Psoriasis is a life-long systemic disease that starts early in life and affects the quality of life significantly. Current therapies are limited due to cumulative toxicities that leave unmet medical needs. The main oral drugs used to control psoriasis have known serious systemic side effects e.g. cyclosporine may cause nephrotoxicity and arterial hypertension, while methotrexate is an immunosuppressive agent with known hepatotoxicity especially if alcohol is taken with the drug.

Raptiva has not been studied extensively in combination with systemic antipsoriasis drugs such as cyclosporine, and their concomitant use may increase the risk of malignancies and lymphoproliferative disorders.
The Investigator Brochure details the safety profile of Raptiva. Estimated total exposure from clinical trials and post-marketing treatment is about 30,000 subject-years.
Very common adverse drug reactions (ADRs) seen during treatment with Raptiva in large placebo-controlled clinical trials were mild to moderate dose-related flu-like symptoms including headache, fever, chills, nausea or myalgia, as well as reversible lymphocytosis and leucocytosis up to 3.5 times the upper limit of normality (ULN).
Common ADRs include back pain, asthenia, human anti-human antibody (HAHA) (HAHA to Raptiva was detected in 6% of subjects, with no differences in pharmacokinetics, clinically noteworthy adverse events or clinical efficacy between subjects with or without HAHA response), reversible alkaline phosphatase increase (less than 3 times ULN), asymptomatic and transient ALT increase (less than 2.5 times ULN), arthralgia and erythrodermic and pustular forms of psoriasis.
Uncommon ADRs include injection site reactions, thrombocytopenia and psoriasis arthritis as well as uticaria, rash and allergic reactions.
Additional ADRs have been identified during post-marketing surveillance, but an exact quantification of frequency has not been established. These reactions include aseptic meningitis, severe infections, inflammatory polyradiculoneuropathy, and facial palsy.
The combination of safety, efficacy, and quality of life endpoints provides a comprehensive benefit: risk assessment of psoriasis therapies.

Using this combination, a favourable absolute benefit: risk has been established during development of Raptiva marked by improvement of skin and health status with a favourable safety profile. Previous Raptiva studies have shown that about 40% of the subjects achieved favourable benefit -risk control of their disease.

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

Mature subjects with moderate to severe chronic plaque-type psoriasis who have failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including cyclosporine, methotrexate and PUVA and meet all eligibility criteria will be eligible for the study.
Subjects must be willing and able to comply with the study requirements and give their

written, informed consent.

Exclusion criteria

Subjects who have a contraindication to Raptiva, are participating in another clinical trial (except non-interventional studies, e.g. registries) or are experiencing an acute exacerbation of psoriasis at the time of screening will be excluded.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-09-2008
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ledertrexate
Generic name:	methotrexate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Neoral
Generic name:	cyclosporine
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Neotigason
Generic name:	acitretine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	PUVA
Generic name:	Psoraleen (+ ultraviolet A light (PUVA), see C16k.)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Raptiva
Generic name:	efalizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-04-2008
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	23-05-2008
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	19-08-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	08-12-2008
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO	

Date:	02-02-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	25-02-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

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	EUCTR2007-004243-29-NL
CCMO	NL21429.003.08