An exploratory trial to assess naturalistic safety and efficacy outcomes in patients trasitioned to ustekinumab from previous methotrexate therapy

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Primary Objective: The primary objective of this exploratory trial is to evaluate the comparative safety through Week 12 of two treatment transition strategies in patients with inadequate response to methotrexate: discontinuation of methotrexate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cornification and dystrophic skin disorders
Study type	Interventional

Summary

ID

NL-OMON33158

Source
ToetsingOnline

Brief title
An exploratory trial to assess naturalistic safety and efficacy outcomes

Condition

- Cornification and dystrophic skin disorders

Synonym
Psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: Janssen-Cilag medical Affairs EMEA

Intervention

Keyword: Methotrexate, Plaques Psoriasis, Safety, Ustekinumab

Outcome measures

Primary outcome

The primary objective of this exploratory trial is to evaluate the comparative safety through week 12 of two treatment transition strategies in patients with inadequate response to methotrexate: discontinuation of methotrexate with immediate initiation of ustekinumab versus initiation of ustekinumab with overlap and gradual dose reduction of methotrexate over 4 weeks.

Secondary outcome

Secondary Objectives of the study include evaluating the safety, efficacy, and quality of life through Week 52.

Study description

Background summary

Psoriasis is a chronic, immunologically-mediated inflammatory skin disease of unknown aetiology. The most common form is plaque psoriasis, characterised by symmetrically distributed, well-demarcated, scaly, erythematous plaques. Areas of the body that are frequently involved include the scalp, elbows, knees, and genitalia. Psoriatic lesions can cause pain, itching, and bleeding, and these physical discomforts combined with the potential psychological effects of the disease may interfere with everyday activities and negatively impact an individuals quality of life. Psoriasis has an impact similar to other major medical conditions on health-related quality of life (Rapp et al, 1999) and may be associated with a higher rate of depression (Gupta and Gupta, 1998). There is an unmet need for effective psoriasis therapies. Despite the large number of therapies available for the treatment of psoriasis, some agents are limited in efficacy, and many provide only temporary relief. Many patients require ultraviolet phototherapy or systemic therapies, which are often associated with

toxicities precluding long-term use. Currently, no treatments for psoriasis produce a curative response for the condition, including newer biological therapies. Thus, more effective and safer treatments that offer a longer duration of therapy are continually sought to fill this unmet therapeutic need.

Study objective

Primary Objective: The primary objective of this exploratory trial is to evaluate the comparative safety through Week 12 of two treatment transition strategies in patients with inadequate response to methotrexate: discontinuation of methotrexate with immediate initiation of ustekinumab versus initiation of ustekinumab with overlap and gradual dose reduction of methotrexate over 4 weeks.

Secondary Objectives: Secondary objectives of the study include evaluating the safety, efficacy, and quality of life outcomes through Week 52.

Study design

This is a phase IIIb/IV, multicentre, open label, two-arm, randomised study, lasting 56 weeks (including screening). The primary endpoint will be assessed after 12 weeks of treatment (Week 12). All treated patients will be followed for safety and efficacy through week 52. Patients will be stratified according to their body weight to ensure a similar distribution of patients >100 kg between the two treatment arms.

Intervention

In both treatment arms, patients weighing <=100 kg will receive ustekinumab 45 mg (0.5 ml) by subcutaneous injection at Weeks 0, 4 and every 12 weeks thereafter until Week 40. In both treatment arms, patients weighing >100 kg will receive ustekinumab 90 mg (1 ml) in two subcutaneous injections at Weeks 0, 4 and every 12 weeks thereafter until Week 40. The ustekinumab dose will be determined according to body weight recorded at randomisation and will remain the same for the duration of the trial. At Week 0, all eligible patients will be randomised to one of the following treatment regimens:

Arm 1: Immediate cessation of methotrexate therapy and administration of subcutaneous ustekinumab at Weeks 0, 4, and every 12 weeks thereafter until Week 40 (last dose of ustekinumab).

Arm 2: Gradual reduction of methotrexate therapy over a maximum of 4 weeks (see suggested *Gradual Reduction regimes in the table below) and administration of subcutaneous ustekinumab at Weeks 0, 4, and every 12 weeks thereafter until Week 40 (last dose of ustekinumab). Gradual Reduction of Methotrexate Dose in Arm 2 The methotrexate dose reduction regime will depend on the dose of

methotrexate at baseline.

All patients will stop methotrexate regardless of the final dose after 4 overlapping weeks (Weeks 0, 1, 2 and 3). The last dose of methotrexate will be given approximately 1 week before the second dose of ustekinumab. As methotrexate is taken once a week, patients in this group will preferably be given their second dose of ustekinumab on the same day of Week 4 that they normally take their methotrexate.

Study burden and risks

Follow up of patients will be 52 weeks at maximum during the trial. (exclusive of screenings period). After screening and randomisation patiënts will come every 2 weeks. After week 4 the next visit will take place and the next visit will be after 8 weeks; than another visit will be performed after 4 weeks and thereafter 1 visit every 3 months.
Patiënts receive subcutaneous injections, which will be administered by an expereinced trial nurse.

Risks: Methotrexate is a registered medication on the market with known side-effects. Ustekinumab is generally well tolerated by patients with psoriasis, but is a drug which influences the way the immune system of the body fights infections. In subjects who participated in earlier trials with Ustekinumab, infections of the upper respiratory tract were relatively often observed. Other infections which were observed were urinary tract infections or flue. Serious infections which led to hospital admission for medical observation and/or treatment were also observed in earlier trials with Ustekinumab. Allergic reactions might occur as well as reactions at the injection site.
The patient will have an extensive screening investigation, before randomization will take place. During the trial the patient will be followed-up intensively. Risks of blooddrawing are minimal.

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

Men and women, aged 18 years or older, with moderate to severe plaque psoriasis who have a Psoriasis Area and Severity Index (PASI) >=10 and who have failed or are intolerant to methotrexate therapy. Patient entering the study must be receiving a minimum dose of 10mg of methotrexate per week, and should have been receiving methotrexate for at least 8 weeks prior to screening.

Exclusion criteria

Currently receiving ciclosporin, fumarates, PUVA, etanercept, efalizumab, infliximab, adalimumab or alefacept.
Currently receiving any other systemic treatment (Except MTX) that may improve psoriasis.
Currently receiving biological therapy within the past 12 weeks or 5 half lives, whichever is greater.
Have received natalizumab, efalizumab or agents that deplete B or T cells within 12 months of screening, or, if later receiving these agents, evidence is available at screening of present depletion of the targeted lymphocyte population.
Have received, or are expected to receive a BCG vaccination within 12 months prior screening, during the stuy, or within 12 months after the last administration of study agent.
Have had or have serious infection, or have been hospitalized or received IV antibiotics for an infection during two months prior to screening.
Have evidence of current active infection, including TB or a nodule suspicious for lung malignancy on screening.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Stelara
Generic name:	Ustekinumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	06-07-2009

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-09-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-04-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-05-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-09-2010
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	EUCTR2008-008171-34-NL
CCMO	NL28173.091.09