A phase 3b, Multicenter, Randomized, Placebo-Controlled, Double-Blind, Double-Dummy, Study of the Efficacy and Safety of Apremilast (CC-10004), Etanercept, and Placebo, In Subjects with Moderate to Severe Plaque Psoriasis

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Primary Objective- To evaluate the clinical efficacy and safety of oral apremilast (APR) 30 mg twice a day (BID) compared with placebo, in subjects with moderate to severe plaque psoriasis at Week 16.Secondary Objectives- To evaluate the clinical...

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

Summary

ID

NL-OMON44059

Source
ToetsingOnline

Brief title
A study to evaluate the efficacy and safety of Apremilast

Condition

- Autoimmune disorders

Synonym
chronic plaque psoriasis; skin disorder

Research involving

Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Apremilast, CC-10004, Etanercept, Plaque Psoriasis

Outcome measures

Primary outcome

Proportion of subjects with either apremilast 30 mg BID or placebo who achieve

at least a 75% reduction in PASI (PASI-75) at Week 16 from baseline.

Secondary outcome

- Proportion of subjects with an sPGA score of clear (0) or almost clear (1)

with at least 2 points reduction at Week 16

- Percent change from baseline in the affected body surface area (BSA %) at

Week 16

- Proportion of subjects who achieve PASI-50 at Week 16

- Change from baseline in DLQI total score at Week 16

- Change from baseline in Mental Component Summary (MCS) score of SF-36 at Week

16

- Proportion of subjects with an LS-PGA score of clear (0) or almost clear (1)

at Week 16

Study description

Background summary

Psoriasis is a chronic disease that requires long-term treatment, ideally with effective agents that offer convenient dosing and a low incidence of adverse events. Currently available systemic therapies are limited by risks of hepatic, renal and neurological toxicities, teratogenicity, as well
as an increased risk of infections and malignancies. Etanercept is the most widely used biologic for psoriasis (Decision Resources- Psoriasis, 2011). Like other biologics, etanercept is administered parenterally. Given the limitations of current systemic psoriasis treatments, there is an unmet medical need for an effective oral agent that is well tolerated and less immunosuppressive than the current oral agents and parenteral biologics.

Apremilast (CC-10004) is a specific phosphodiesterase type 4 (PDE4) inhibitor under development for use in the treatment of inflammatory conditions. PDE4 is one of the major phosphodiesterases expressed in leukocytes. Inhibitors of PDE4 cause accumulation of
intracellular cyclic adenosine monophosphate (cAMP), resulting in inhibition of proinflammatory cytokine transcription and other cellular responses, such as neutrophil degranulation and chemotaxis.

In completed Phase 2 studies in subjects with psoriasis and psoriatic arthritis, apremilast has demonstrated broad anti-inflammatory and immunomodulatory activity, as well as efficacy in psoriasis and psoriatic arthritis. Based on preclinical and clinical data to date, apremilast is expected to have a more favorable safety profile than the currently available systemic psoriasis treatments, while delivering efficacy with convenient oral dosing.

Study objective

Primary Objective
- To evaluate the clinical efficacy and safety of oral apremilast (APR) 30 mg twice a day (BID) compared with placebo, in subjects with moderate to severe plaque psoriasis at Week 16.

Secondary Objectives
- To evaluate the clinical efficacy and safety of etanercept 50 mg subcutaneous (SC) once weekly (QW) compared with placebo, in subjects with moderate to severe plaque psoriasis at Week 16.
- To evaluate the relative safety of a crossover from etanercept 50 mg subcutaneous (SC) once weekly to apremilast 30 mg BID, as compared with apremilast dosed since Week 0 in subjects with moderate to severe plaque psoriasis after Week 16.
- Explore relative safety/tolerability of subjects starting apremilast therapy without the 7 day dose titration.

Study design

This is a phase 3b, multicenter, randomized, placebo-controlled, double-blind, double-dummy study of the efficacy and safety of apremilast (CC-10004), etanercept, and placebo in subjects with moderate to severe plaque psoriasis. Approximately 240 subjects will be randomized 1:1:1 to the three treatment groups. Subject randomization for treatment assignments will be stratified according to their calculated body mass index (BMI) categories at Screening (BMI < 30 or BMI * 30). All subjects will receive both tablets and injections through Week 16:
- Subjects randomized to the apremilast treatment group will receive apremilast 30 mg tablets orally twice daily and evaluator/subject-blinded SC saline (placebo) injections once weekly for 16 weeks
- Subjects randomized to the etanercept treatment group will receive placebo tablets (identical in appearance to apremilast 30 mg tablets) orally twice daily and etanercept as two SC 25 mg injections (50 mg total dose) once weekly for 16 weeks
- Subjects randomized to the placebo treatment group will receive placebo tablets (identical in appearance to apremilast 30 mg tablets) orally twice daily and evaluator/subject-blinded SC saline (placebo) injections once weekly for 16 weeks

The study will consist of four phases:
*Screening Phase * up to 35 days
* Double-blind Placebo-controlled Phase * Weeks 0-16
Subjects will receive treatment with one of the following:
- apremilast 30 mg tablets orally BID plus once weekly saline (placebo) injections (1 mL x 2 injections SC), or
- etanercept 50 mg SC QW plus placebo tablets orally BID, or
- placebo tablets and evaluator/subject-blinded SC saline (placebo) injections.

Subjects will take oral tablets (either 30 mg APR or placebo) BID and receive two SC injections (either etanercept 25 mg each dose or saline placebo) QW.

* Apremilast Extension Phase * Weeks 16-104
- All subjects will be switched to (or continue with) 30 mg BID apremilast at Week 16. All subjects will maintain this dosing through Week 104.
- Starting at Week 32, all non-responders (< PASI-50) will have the option of adding topical therapies (including, but not limited to, topical corticosteroids, retinoids or vitamin D analog preparations) and/or phototherapy (excluding oral PUVA) to their treatment regimen.
* Post-treatment Observational Follow-up Phase
- Four-week Post-treatment Observational Follow-up Phase for all subjects who complete the study or discontinue from the study early.

Study burden and risks

In completed Phase 2 studies in subjects with psoriasis and psoriatic arthritis, apremilast has demonstrated broad anti-inflammatory and

immunomodulatory activity, as well as efficacy in psoriasis and psoriatic arthritis. Based on preclinical and clinical data to date, apremilast is expected to have a more favorable safety profile than the currently available systemic psoriasis treatments, while delivering efficacy with convenient oral dosing.

Contacts

Public
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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. Males or females, * 18 years of age at the time of signing the informed consent document.
2. Understand and voluntarily sign an informed consent document prior to any study related assessments/procedures being conducted.
3. Able to adhere to the study visit schedule and other protocol requirements.
4. Diagnosis of chronic plaque psoriasis for at least 12 months prior to Screening.

5. Have moderate to severe plaque psoriasis at Screening and Baseline as defined by
a. PASI score * 12 and
b. BSA * 10%, and
c. sPGA * 3 (moderate)

Exclusion criteria

1.Other than psoriasis, history of any clinically significant cardiac, endocrinologic, pulmonary, neurologic, psychiatric, hepatic, renal, hematologic, immunologic disease, or other major uncontrolled disease.
2.Any condition, including the presence of laboratory abnormalities, which would place the subject at unacceptable risk if he/she were to participate in the study.
3.Any condition, including other inflammatory diseases or dermatologic conditions, that confound the ability to interpret data from the study.

Study design

Design

Study phase:	3
Study type:	Observational invasive
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):	01-10-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Apremilast
Generic name:	Apremilast
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-11-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-06-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-09-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-11-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-07-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-05-2016

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	EUCTR2012-000859-14-NL
ClinicalTrials.gov	NCT01690299
CCMO	NL42206.091.12