A Phase 3, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo- And Active-Controlled Study Followed By A Placebo-Controlled Maintenance Period And Open-Label Follow-Up To Evaluate The Efficacy And Safety Of Certolizumab Pegol In Subjects With Moderate To Severe Chronic Plaque Psoriasis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON47061

Source
ToetsingOnline

Brief title
CIMPACT

Condition

- Immune disorders NEC
- Epidermal and dermal conditions

Synonym
Chronic Plaque Psoriasis, Psoriasis

Research involving
Human

Sponsors and support

Primary sponsor: UCB Biopharma, SPRL
Source(s) of monetary or material Support: Dermira,UCB Biopharma SPRL

Intervention

Keyword: Chronic plaque psoriasis, Cimzia, Enbrel, Psoriasis

Outcome measures

Primary outcome

(Protocol v1.0 25Jul2014 p.18)

The primary outcome measure will be the proportion of subjects achieving a

PASI75 response at Week 12.

Secondary outcome

(Protocol v1.0 25Jul2014 p.19-20)

The secondary efficacy variables are:

- PGA Clear or Almost Clear (with at least 2 category improvement) at Week 12

- PASI75 at Week 16

- PGA Clear or Almost Clear (with at least 2 category improvement) at Week 16

- PASI75 at Week 48 for those achieving PASI75 at Week 16

The other efficacy variables are (at all visits [as applicable], except those

specified as primary or

secondary variables):

- PASI50, PASI75, PASI90, and PASI100

- PGA Clear or Almost Clear (with at least 2 category improvement)

- Time to onset of action, defined as the time to PASI50

- Time to onset of action, defined as the time to PASI75

- Time to relapse (not achieving PASI50 response) for those achieving PASI75 at Week 16

- Time to loss of PASI75 response for those achieving PASI75 at Week 16

- Absolute PASI score

- Absolute and percent change from Baseline in PASI score

- PGA score distribution

- Absolute body surface area (BSA) affected by PSO and absolute and percent change from Baseline in the BSA affected by PSO

- Change from Baseline in mNAPSI

- Change from Baseline in DLQI mean scores, percent of subjects achieving MCID, and percent achieving DLQI Remission

- Change from Baseline in WPAI-SHP v2.0 adapted to PSO scores

- Health status assessed by EQ-5D 3L

- Change from Baseline in fatigue (FASca)

- Direct medical resource use: all medical procedures, hospital stays, health care consultations not foreseen by protocol: Number of concomitant medical procedures, Number of health care provider consultations, Number of hospitalizations, Number of emergency room (ER) visits, Length of hospital stay

The pharmacokinetic variable is the CZP concentration prior to and following

study treatment.

The Immunological variable is the CZP antibody concentrations prior to and

following study treatment

The Safety variables to be assessed are:

- AEs

- Blood pressure

- Physical examination

- Clinical laboratory values (hematology, biochemistry, and urinalysis)

- IGRA test for tuberculosis

- Subject Questionnaire for tuberculosis

Study description

Background summary

(Protocol v1.0 25Jul2014 p.13-14)
Psoriasis (PSO) is a common, chronic inflammatory disease characterized by a series of linked cellular changes in the skin: hyperplasia of epidermal keratinocytes, vascular hyperplasia and ectasia, and infiltration of T lymphocytes, neutrophils, and other types of leucocytes in affected skin.
Though the pathophysiology of PSO is not fully understood, the importance of T-cells and inflammatory cytokines has been demonstrated by the clinical benefit provided by therapies directed at these targets.
Psoriasis affects approximately 3% of the adult US population and its onset can begin at any age. Although its onset can occur at any age and has been reported even at, or near, birth, it is unusual before late adolescence and most patients develop the disease in the third decade of life.
The prevalence of PSO varies widely and ranges from about 1% in South America to up to about 2.5% in parts of Europe. It is rare in West African blacks and displays low incidence in Japanese and Eskimo populations.
Various forms of PSO exist including plaque, guttate, inverse, pustular, and

erythrodermic. Plaque PSO is the most common, comprising approximately 80% to 90% of all cases. Approximately 17% of those with PSO have moderate to severe disease.
Increased severity of the disease tends to be correlated with a strong family history, earlier onset of the disease (eg, in the late teens) and is often manifested by more extensive involvement of the skin (ie, greater body surface area). In addition to the impact on skin, PSO has a multitude of psychosocial and emotional effects on patients, including increased selfconsciousness, frustration, fatigue, depression, and suicidal ideation.
As a result, patients frequently report sleeping problems, difficulties at work, problems interacting with family
members, disrupted leisure activities, and sexual difficulties. [...]

Therapy for patients with PSO varies according to the severity of disease. Limited or mild disease is often treated with topical therapies, such as corticosteroids and vitamin D analogs, and phototherapy. Patients with more severe disease are often treated with photochemotherapy, cyclosporine, methotrexate (MTX), or biologic agents, such as TNF inhibitors and IL12/23 inhibitors. The effectiveness of TNF inhibitors in the treatment of PSO has been demonstrated in many Phase 3 clinical trials and has led to FDA approval of multiple TNF inhibitors for use in patients with moderate to severe chronic plaque PSO.
The efficacy of TNFα inhibitors in treating PSO has been attributed to their inhibition of Th17 T cells. Different from the traditional systemic drugs that impact the entire immune system, biologics target specific parts of the immune system. The efficacy and safety of these molecules is now well established and accepted in the management of the disease, yet a recent study has shown that patients who switched to a different TNFα inhibitor as a result of secondary loss of efficacy, adverse events (AEs), or intolerance were more likely to reach a PASI75 response than those who switched as a result of primary inefficacy. Data consistently demonstrate that >50% of severely affected patients are dissatisfied with current treatments and up to 30% of severe patients are not receiving treatment in accordance with accepted therapy guidelines.

Study objective

(Protocol v1.0 25Jul2014 p.18)
The primary objective of the study is to compare the efficacy of certolizumab pegol (CZP) administered subcutaneously at the doses of CZP 400mg every two weeks and CZP 200mg every two weeks after a loading dose of CZP 400mg every two weeks at Weeks 0, 2, and 4 to Placebo (PBO) in the treatment of moderate to severe chronic plaque PSO.

The secondary objectives of the study are to compare the efficacy of CZP administered subcutaneously at the doses of CZP 400mg every two weeks and CZP 200mg every two weeks after a loading dose of CZP 400mg every two weeks at

Weeks 0, 2, and 4 to ETN administered
subcutaneously bi-weekly at a cumulative weekly dose of 100mg in the treatment of moderate to severe chronic plaque PSO, to assess the optimal initial treatment dose for the treatment of moderate to severe chronic plaque PSO, to assess the optimal maintenance dose for the treatment of moderate to severe chronic plaque PSO and to assess the safety and tolerability of CZP.

Other objectives of the study are to demonstrate the effect of CZP on aspects of the disease, such as:
- Improvement of skin related quality of life (DLQI)
- Health status as measured by the EQ-5D 3L
- Productivity as measured by the WPAI-SHP
- Fatigue as measured by the FASca
- Psoriatic nail disease (target nail) as measured by mNAPSI in subjects with nail disease at Baseline
- Assess the safety and efficacy of long-term use of CZP

Study design

(Protocol v1.0 25Jul2014 p.20)
The study is a double-blind, parallel-group, randomized, placebo- and active-controlled, multicenter study with a double-blind, placebo-controlled maintenance period.
The study includes 5 periods: Screening, Initial Treatment (Double-blind, Placebo- and Activecontrolled), Maintenance Treatment (Placebo-controlled), Open-label Treatment and Post Study Safety Follow-up.

Intervention

(Protocol v1.0 25Jul2014 p.18)
Possibilities for intervention are:
- CZP 200mg: CZP administered subcutaneously at the dose of CZP 400mg once every two weeks the first three visits (loading dose) followed by CZP 200mg once every two weeks subcutaneously
- CZP 400mg: CZP administered subcutaneously at the dose of CZP 400mg once every two weeks
- ETN: ETN administered subcutaneously at 50mg twice weekly
- PBO: PBO administered subcutaneously once every two weeks

Study burden and risks

(Protocol v1.0 25Jul2014 p.14-15)
The efficacy of TNFα inhibitors in treating PSO has been attributed to their inhibition of Th17 T cells. Different from the traditional systemic drugs that impact the entire immune system, biologics target specific parts of the immune system. The efficacy and safety of these molecules is now well established and

accepted in the management of the disease, yet a recent study has shown that patients who switched to a different TNFα inhibitor as a result of secondary loss of efficacy, adverse events (AEs), or intolerance were more likely to reach a PASI75 response than those who switched as a result of primary inefficacy. Data consistently demonstrate that >50% of severely affected patients are dissatisfied with current treatments and up to 30% of severe patients are not receiving treatment in accordance with accepted therapy guidelines.
[…]
Certolizumab pegol is an inhibitor of TNFα, which is a pro-inflammatory cytokine with multiple biologic actions. A unique feature of CZP among TNF antgonists is the lack of an Fc (fragment crystallizable) region, thereby the molecule cannot initiate potential Fc-mediated effects such as complement-mediated cytotoxicity or antibody dependent, cell-mediated cytotoxicity.
Cimzia has been studied for the treatment of inflammatory diseases, such as Crohn*s disease (CD), including pediatrics; rheumatoid arthritis (RA); psoriatic arthritis (PsA); axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS); and is currently being studied in juvenile idiopathic arthritis (JIA). Certolizumab pegol has also been evaluated in two Phase 2 studies in subjects with PSO. As of 30 Apr 2013, the clinical development program for CZP includes a total of 70 completed or ongoing clinical studies, with 2 completed studies in moderate to severe chronic plaque PSO (C87040 and C87044). Various doses and regimens have been assessed in these programs.
In all studies to date, CZP has been shown to have an acceptable safety profile and was well tolerated by subjects with CD, RA, PsA, axSpA, and PSO.

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

Most important inclusion criteria (Protocol v1.0 25Jul2014, chapter 6.1, p.28): 1.Provided informed consent;2.Adult men or women >=18 years;3.Chronic plaque psoriasis for at least 6 months;4.Baseline psoriasis activity and severity index >=12 and body surface area >=10% and Physician*s Global Assessments score >=3;5.Candidate for systemic psoriasis therapy and/or phototherapy and/or chemophototherapy;6.Other protocol-defined inclusion criteria may apply

Exclusion criteria

Most important exclusion criteria (Protocol v1.0 25Jul2014, chapter 6.2, p.28-30): 1.Erythrodermic, guttate, generalized pustular form of psoriasis;2.History of current, chronic, or recurrent infections of viral, bacterial, or fungal origin as described in the protocol;3.Congestive heart failure ;4.History of a lymphoproliferative disorder including lymphoma or current signs and symptoms suggestive of lymphoproliferative disease;5.History of other malignancy concurrent malignancy as described in the protocol;6.History of, or suspected, demyelinating disease of the central nervous system (eg, multiple sclerosis or optic neuritis);7.Female subjects who are breastfeeding, pregnant, or plan to become pregnant during the study or within 3 months following last dose of study drug. Male subjects who are planning a partner pregnancy during the study or within 10 weeks following the last dose;8.Any other condition which, in the Investigator*s judgment, would make the subject unsuitable for participation in the study;9.Other protocol-defined exclusion criteria may apply ;10.Prior etanercept use

Study design

Design

Study phase:	3
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):	09-11-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cimzia
Generic name:	Certolizumab pegol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Enbrel
Generic name:	Etanercept
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	29-01-2015
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2017
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-003492-36-NL
CCMO	NL51812.018.15

Study results

Date completed:	19-11-2018
Actual enrolment:	3

Summary results
Trial is onging in other countries