PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PARALLEL GROUP, PLACEBO CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF CERTOLIZUMAB PEGOL IN SUBJECTS WITH ADULT ONSET ACTIVE AND PROGRESSIVE PSORIATIC ARTHRITIS (PSA)

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

Summary

ID

NL-OMON36257

Source
ToetsingOnline

Brief title
PsA001

Condition

- Joint disorders

Synonym
joint inflammation with psoriasis, psoriatic arthropathy

Research involving
Human

Sponsors and support

Primary sponsor: Schwarz Biosciences
Source(s) of monetary or material Support: SCHWARZ BIOSCIENCES;GmbH (UCB Group)

Intervention

Keyword: Adult -Onset, Double-blind, Phase 3, Psoriatic Artrithis

Outcome measures

Primary outcome

The primary objectives of the study are to demonstrate the efficacy of CZP

administered sc at the dose of 200mg Q2W or 400mg Q4W after loading with 400mg

at Weeks 0, 2, and 4 on the signs and symptoms of active PsA and on the

inhibition of progression of structural damage in adults with active PsA.

Secondary outcome

The secondary objectives of the study are to assess the effects on safety and

tolerability and to demonstrate the effects of CZP on:

- Health outcomes

- Psoriatic skin disease in the subgroup of affected subjects (> 3% BSA) at

Baseline

- Dactylitis

- Enthesitis

Study description

Background summary

Psoriatic arthritis is an inflammatory arthritis that occurs in up to one-third of patients with PSO and is usually diagnosed years after, but sometimes before, the skin disease appears. More than 50% of patients with PsA experience progressive, erosive arthritis that is often accompanied by pain, fatigue, and functional impairment. The combination of joint and skin manifestations of PsA can have a profound impact on patient function, well-being, and health-related quality of life (HRQoL). The functional impairments are also associated with significant direct health care costs and substantial work-related disability, including a lower rate of employment.

Clinical manifestations of PsA include joint inflammation, enthesitis, dactylitis, and psoriatic skin lesions. Clinical features that may distinguish PsA from rheumatoid arthritis (RA) include asymmetry of joint involvement, initial oligoarticular involvement, enthesial inflammation, iritis, and infrequent presence of rheumatoid factor. Factors relevant to the assessment of disease activity and severity of peripheral arthritis in PsA patients include:

1. The extent of synovitis, with polyarticular disease (* 4 involved joints) a marker for more severe disease and impaired outcome than oligoarticular disease (< 4 involved joints)
2. The presence of joint damage, indicated by periarticular erosions, which is indicative of more severe disease and predictive of further damage
3. Impairment of functional status. The oligo- and polyarticular patterns of PsA (with or without spinal involvement) constitute the predominant forms and therefore will be the target populations for the proposed clinical study.

Therapeutic approaches for PsA have focused on a similar immunopathologic etiology underlying both RA and PsA. Treatment for PsA traditionally has included nonsteroidal anti-inflammatory drugs (NSAIDs), and data support their efficacy in the treatment of signs and symptoms of peripheral arthritis. The efficacy of oral or parenteral corticosteroids for peripheral arthritis in PsA has not been examined formally, although they are commonly used in clinical practice. Some data are available to support the use of DMARDs, ie, sulfasalazine (SSZ), leflunomide, MTX, and cyclosporine, in providing a small to medium degree of improvement in the clinical signs and symptoms, but not joint damage, of PsA. The evidence has been negative for oral and injectable gold.

Four TNF*-antagonists (infliximab [IFX], etanercept [ETN], adalimumab [ADA], and golimumab [GOL]) are currently registered in the United States (USA) and three (IFX, ETN, and ADA) are also registered in Europe for the treatment of PsA. Tumor necrosis factor-antagonists substantially improve the signs and symptoms of peripheral arthritis in PsA and accompanying psoriatic skin disease. In addition, all have demonstrated improvement in functional status and HRQoL. Moreover, the first 3 agents have demonstrated attenuation of the progression of joint damage as assessed radiographically. For reasons of loss or lack of efficacy or intolerance to currently available TNF-antagonists, there remains a need for additional TNF-antagonists as therapeutic options for patients with PsA, as observational data support that failure of an initial TNF-antagonist does not preclude the response to another one (Conti et al, 2007).

Certolizumab pegol is a humanized Fab* conjugated to PEG with specificity for human TNF*. Certolizumab pegol has demonstrated efficacy in clinical studies of Crohn*s disease (CD), PSO, and RA. The objective of this study is to demonstrate the effects of CZP in the treatment of PsA in adult patients with active and progressive PsA. Certolizumab pegol has been approved by the Food and Drug Administration for reducing signs and symptoms of CD and for the treatment of moderate to severe active RA in adult patients. Two dose regimens of CZP have been selected for this study, reflecting 2 different frequencies of administration: each active group will receive 3 loading doses of CZP 400mg administered sc at Weeks 0, 2, and 4 followed by either 200mg Q2W or 400mg Q4W. Furthermore, ADA, ETN, and GOL, the 3 commercially available sc TNF-antagonists for the treatment of PsA, have identical studied and commercial dosing regimens in PsA and RA, with similar efficacy and safety profiles in both PsA and RA. Therefore, the proposed CZP dosing regimens for this study were selected on the basis that these doses of CZP were efficacious for the treatment of RA in clinical trials, are the current recommended dosing regimens for RA in the USA, and would be expected to have similar efficacy in PsA.

Study objective

Certolizumab pegol is a humanized Fab* conjugated to PEG with specificity for human TNF*. Certolizumab pegol has demonstrated efficacy in clinical studies of Crohn*s disease (CD), PSO, and RA. The objective of this study is to demonstrate the effects of CZP in the treatment of PsA in adult patients with active and progressive PsA. Certolizumab pegol has been approved by the Food and Drug Administration for reducing signs and symptoms of CD and for the treatment of moderate to severe active RA in adult patients. Two dose regimens of CZP have been selected for this study, reflecting 2 different frequencies of administration: each active group will receive 3 loading doses of CZP 400mg administered sc at Weeks 0, 2, and 4 followed by either 200mg Q2W or 400mg Q4W. Furthermore, ADA, ETN, and GOL, the 3 commercially available sc TNF-antagonists for the treatment of PsA, have identical studied and commercial dosing regimens in PsA and RA, with similar efficacy and safety profiles in both PsA and RA. Therefore, the proposed CZP dosing regimens for this study were selected on the basis that these doses of CZP were efficacious for the treatment of RA in clinical trials, are the current recommended dosing regimens for RA in the USA, and would be expected to have similar efficacy in PsA.

Study design

Study PsA001 is a multicenter, randomized, double-blind, parallel-group, placebo-controlled
clinical study to evaluate the efficacy and safety of CZP in adult subjects with active and
progressive PsA. The study includes 5 periods:

Period 1
Screening period of 1 to 5 weeks in order to obtain laboratory data, to verify that the doses of MTX, NSAIDs, and corticosteroids, if used, are stable, and to enable washout of any medications not permitted for use during the study.

Period 2 * Week 0 to Week 24: Double-blind, placebo-controlled
Eligible subjects will be allocated to the following study treatments in a 1:1:1 ratio:
- CZP administered sc at the dose of CZP 400mg Q2W at Weeks 0, 2 and 4 followed by CZP 200mg Q2W sc (starting at Week 6)
- CZP administered sc at the dose of CZP 400mg Q2W at Weeks 0, 2 and 4 followed by CZP 400mg Q4W sc (starting at Week 8)
- Placebo
Study treatments (including placebo) will be administered by dedicated unblinded trained site personnel at Weeks 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, and 22.
After the Week 24 Visit of the last subject, the database will be locked and a first interim study report will be written. Limited UCB personnel will become unblinded for the purposes of the data analysis but the Investigator and the subject will remain blind to treatment assignments. All subjects will switch to active treatment after Week 24.

Period 3 * Week 24 to Week 48: Dose-blind for the subjects and the Investigators, no placebo
Subjects originally randomized to placebo will be re-randomized in a 1:1 ratio to receive 3 loading doses of CZP sc 400mg at Weeks 24, 26, and 28 followed by either CZP 200mg Q2W or CZP 400mg Q4W from Week 30 onward.
All subjects originally randomized to CZP will continue to receive the treatment regimen they were assigned to at randomization (CZP 200mg Q2W or CZP 400mg Q4W sc).
Study treatments will be administered by dedicated unblinded trained site personnel according to the injection scheme. All subjects will be trained on self-administration at Weeks 26 and 28. Subjects will self-administer 1 injection at home Q4W starting from Week 30.
After the Week 48 Visit of the last subject, the database will be locked and a second interim study report will be written.

Period 4 * Week 48 to Week 158: Open-label
Subjects will continue to receive the same dose regimen of CZP that they received during Period 3. After Week 48, only subjects randomized to CZP 200mg Q2W will self-administer CZP 200mg (one-1mL sc injection) Q4W at home. All other injections will be administered preferably by self-administration during scheduled visits.
The last dosing visit will be at Week 156. The final study assessments are performed at Week 158.

Period 5 * Week 158 to Week 166: Safety Follow-Up

All subjects, including those withdrawn from study treatment, will have a Safety Follow-Up Visit 10 weeks after their last dose of study medication.

Intervention

Subjects will receive treatment with Certolizumab by injections of 1 ml syringes.

Study burden and risks

For each subject the study will last up to the maximum of 171 weeks, consisting of the following periods:

- A screening period that lasts up to 5 weeks
- A double blind placebo controlled treatment period of 24 weeks
- A dose blind treatment period of 24 weeks
- An open label treatment period of 110 weeks
- A safety follow up visit 10 weeks after the last dose of study medication.

During these visits the subjects will undergo:

- Physical Examination
- Vital signs/function tests
- Questionnaires about general condition, disease and related problems
- Tuberculosis test
- Vena punction (max 25 ml per visit)
- Subcutaneous injection (max 1 ml per visit)
- X-ray of chest, hands and feet

Contacts

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DE
Scientific
Schwarz Biosciences

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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. Subject must be at least 18 years old at the Screening Visit.
2. An Institutional Review Board (IRB)/Independent Ethics Committee (IEC) approved written informed consent is signed and dated by the subject or designee/witness.
3. Subject is considered reliable, willing, and capable of adhering to the protocol (eg, able to understand and complete diaries), visit schedule, and medication intake according to the judgment of the Investigator.
4. Female subjects must be either postmenopausal for at least 1 year, surgically incapable of childbearing, or effectively practicing an acceptable method of contraception (either oral, parenteral, or implantable hormonal contraceptives, intrauterine device or barrier, or spermicide). Abstinence only is not an acceptable method. Subjects must agree to use adequate contraception during the study and for at least 10 weeks (or longer as per local requirement) after the last dose of study treatment. Male subjects must agree to ensure that they or their female partner(s) use adequate contraception during the study and for at least 10 weeks (or longer as per local requirement) after the subject receives their last dose of study treatment.
5. Subject must have a diagnosis of adult-onset PsA of at least 6 months* duration as defined by the CASPAR criteria (see Appendix 17.1).
6. Subject must have active psoriatic skin lesions or a documented history of PSO.
7. Subject must have active arthritis defined by:
* *3 tender joints at Screening and Baseline
* *3 swollen joints at Screening and Baseline
* And fulfilling at least 1 of the following 2 criteria during the Screening Period:
-Erythrocyte sedimentation rate (ESR) *28mm/hour (Westergren)
-CRP >upper limit of normal
8. Subjects must have failed 1 or more DMARDs.

Exclusion criteria

- The subject has previously participated in this study or has previously received CZP treatment in or outside of another clinical study.;- The subject has participated in another study of a medication or a medical device under
investigation within the last 3 months or is currently participating in another study of a medication or medical device under investigation.;- Subject has history of chronic alcohol abuse (more than 14 drinks/units per week for
women and 21 drinks/units for men [1 drink=4oz of wine, 12oz of beer, or 1oz of hard liquor] or 330mL of 5% alcohol by volume beer=2 units, 125mL of 12% wine=1.5 units, 50mL of 40% spirits=2 units) or drug abuse within the last year.;- Subject has any medical or psychiatric condition (according to the Diagnostic and
Statistical Manual of Mental Disorders [DSM] criteria) that, in the opinion of the Investigator, can jeopardize or would compromise the subject*s ability to participate in this study.;- Subject has a known hypersensitivity to any components of CZP, placebo or with a
history of an adverse reaction to polyethylene glycol (PEG).
PsA disease-related exclusions;- Subjects must not have a diagnosis of any other inflammatory arthritis, eg, RA,
sarcoidosis, systemic lupus erythematosus, or a known diagnosis of fibromyalgia.;- Subjects must not have a secondary, noninflammatory condition (eg, osteoarthritis) that
in the Investigator*s opinion is symptomatic enough to interfere with evaluation of the effect of study drug on the subject*s primary diagnosis of PsA.
Prior medications exclusion;- Subjects must not have used the following medications in the manner as detailed by the
exclusion criteria in the 2 tables described in the protocol amendment 1 page 35.;- Known TB disease, high risk of acquiring TB infection, or latent TB infection;For the rest of the exclusion criteria, please refer to Protocol Amendment 1 23 Nov 2009 page 34

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):	08-09-2010
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cimzia
Generic name:	CERTOLIZUMAB PEGOL
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	31-03-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	29-06-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	30-06-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	02-11-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	10-03-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-03-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2009-011720-59-NL
CCMO	NL31145.068.10
Other	Registratie is nog bezig. Nog niet voltooid