Multicenter, open-label study to assess the effects of Certolizumab Pegol on the reduction of anterior uveitis flares in axial spondyloarthritis subjects with a history of anterior uveitis (C-view)

Published: 31-08-2016
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Primary objective:The primary objective of the study will be to demonstrate the effect of CZP treatment on the reduction of AU flares in subjects with both active axSpA and a documented history of AU.Secondary objective:The secondary objectives of...

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

Summary

ID

NL-OMON46252

Source
ToetsingOnline

Brief title
C-View

Condition

- Eye disorders
- Joint disorders

Synonym
anterior uveïtis flares in axial spondyloarthritis; eye inflammation in spondyloarthritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: anterior uveitis, axial spondyloarthritis

Outcome measures

Primary outcome

Primary efficacy variable:

The primary efficacy variable will be the count of distinct episodes of AU

flares during the Treatment Period.

Secondary outcome

Secondary efficacy variable:

The following secondary efficacy variables will be assessed at Week 48 and Week

96:

· Number of AU flares per 100 patient-years in subjects with active axSpA and a

history of AU

· Number of AU flares per 100 patient-years in subjects with active axSpA and

at least 1 AU episode within 12 months prior Baseline

· Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS)

· Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index

(BASDAI)

· Assessment of ASAS 20, 40, 5/6, and partial remission (PR) response rates

· Change from Baseline in tender and swollen joint count (44 joint count);

Physician*s Global Assessment of Disease Activity (PhGADA).

· Change from Baseline in the respective components of the ASAS response criteria, assessed by:

o Patient*s Global Assessment of Disease Activity (PtGADA)

o Pain assessment (total spinal pain Numerical Rating Scale [NRS])

o Function (represented by Bath Ankylosing Spondylitis Functional Index [BASFI])

o Inflammation (the mean of the BASDAI questions 5 and 6 concerning morning stiffness and duration)

The following other efficacy variables will be assessed:

· Duration of AU flares

· Severity of AU flares

· Change from Baseline in ASDAS

· Change from Baseline in BASDAI

· ASAS 20, 40, 5/6, and PR response rates

· Change from Baseline in tender and swollen joint count (44 joint count), PhGADA.

· Change from Baseline in the respective components of the ASAS criteria, assessed by:

o PtGADA

o Pain assessment (total spinal pain NRS)

o Function (represented by BASFI)

o Inflammation (the mean of the BASDAI questions 5 and 6 concerning morning stiffness and duration)

· Change from Baseline in ASDAS disease activity (clinical improvement [CI], major improvement [MI], inactive disease [ID], clinically important improvement

[CII]), and BASFI) (including Weeks 48 and 96)

· Change from Baseline in Fatigue (NRS) (from BASDAI) (including Weeks 48 and 96)

· Change from Baseline in Ankylosing Spondylitis Quality of Life (ASQoL) (including Weeks 48 and 96)

· Change from Baseline in ASAS Health Index (HI) questionnaire (including Weeks 48 and 96)

· Change from Baseline in Short-Form 36-Item Health Survey (SF-36) (including Weeks 48 and 96)

· Number of IBD exacerbations

· Number of psoriasis exacerbations (in subjects with concurrent psoriasis)

Safety variables to be assessed are:

* Adverse events (AEs)

* Blood pressure

* Physical examination

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

Study description

Background summary

The purpose of this study is to determine how effective the study drug Certolizumab Pegol (CZP) is on the reduction of anterior uveitis (AU) flares in patients with active axSpA and a documented history of AU.

Spondyloarthritis (SpA) is the name for a family of inflammatory rheumatic diseases that cause arthritides, particularly rheumatoid arthritis (RA). Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that affects mainly the spine and pelvic joints, and impacts a major part of the patients.

Uveitis is a general term describing a variety of inflammatory conditions that produce swelling and may destroy eye tissues. It is often experienced by patients with axSpA.

Certolizumab Pegol is approved for various inflammatory diseases in the USA, in the European Union, and in several other countries. UCB Pharma SPRL estimates that tens of thousands of patients have been treated worldwide with Certolizumab Pegol since approval in 2008.

Study objective

Primary objective:
The primary objective of the study will be to demonstrate the effect of CZP treatment on the reduction of AU flares in subjects with both active axSpA and a documented history of AU.

Secondary objective:
The secondary objectives of the study will be to assess the effect of CZP treatment on 1) the reduction of AU flares in subjects with axSpA having at least 1 documented history of AU within 12 months prior to Baseline and 2) axSpA disease activity.

Other objectives:
Other objectives will be to assess the effect of CZP treatment on physical function, signs and symptoms of axSpA (morning stiffness, fatigue and extra-articular manifestations of axSpA), and duration and severity of AU flares. The safety objectives of the study will be to evaluate the safety and tolerability of CZP therapy.

Study design

AS0007 is a multicenter, open-label, Phase 4 study to evaluate the effects of certolizumab pegol (CZP) on the incidence of anterior uveitis (AU) flares per year in subjects with both active axial spondyloarthritis (axSpA) and a history of AU by comparing the historical AU flare rate that occurred prior to CZP treatment with the AU flare rate occurring while under CZP treatment.

The study duration from the start of treatment will be 96 weeks from Baseline onwards, and a follow-up visit will be performed at Week 104; 10 weeks after the last dose at Week 94.
The study includes 3 periods as follows:
· Period 1 (Screening Period): 1 to 5 weeks before Baseline
Subjects will be informed about the study and sign the informed consent form. Eligibility will be evaluated and assessments will be performed. The Screening Period should be kept as short as possible but can be extended to 5 weeks if certain medications need to be washed out or to allow to obtain information

from the subject*s ophthalmologist. For subjects who start a prophylactic treatment for latent tuberculosis infection the Screening Period can be extended up to 12 weeks.
· Period 2 (Treatment Period): Week 0 to Week 96
Eligible subjects will receive a dose of CZP 400mg subcutaneously (sc) at Baseline, Week 2, and Week 4 followed by CZP 200mg sc every 2 weeks (Q2W) starting at Week 6 until Week 94.
All subjects will be trained at the beginning of the study on self-administration before the subjects start self-administration with the study drug (relative or caregiver may also perform the injections). The injection schedule will provide the sequence of self-administration and site visits including injection at the site.
· Period 3 (Follow-Up [FU] Period): 10 weeks from the final dose of study medication received.
All subjects will have a FU Visit at Week 104 or earlier in case of an early withdrawal, 10 weeks after the final administration of CZP administration received within the study.
A Week 48 analysis will be performed after all subjects have either completed the Week 48 Visit or have prematurely withdrawn prior to the Week 48 Visit. The final analysis will be conducted at the end of the study after all study data is locked.

Intervention

Cimzia 200 mg solution for injection

Study burden and risks

Participation in the study could last up to a maximum of 109 weeks in total. During that time, the patient may have to attend up to 14 appointments with the study doctor.
For an overview of the risks associated with participation in this study, see also the informed consent form, paragraph 4.

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

The study population will be subjects *18 years, with a documented diagnosis of adult onset axSpA as meeting the Assessment of SpondyloArthritis International Society ([ASAS] criteria of at least 3 months* symptom duration, and with active disease defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) *4, and spinal pain *4 on a 0 to 10 Numerical Rating Scale (NRS). Nonradiographic axSpA subjects must either have C Reactive Protein > upper limit of normal (ULN) and /or current evidence of sacroiliitis on Magnetic Resonance Imaging taken within 3 months prior to Baseline (no confirmation by central reading) as defined by ASAS criteria and ankylosing spondylitis subjects must have evidence of sacroiliitis on an x-ray taken within 12 months prior to Baseline meeting modified New York criteria according to the Investigator. Subjects must have a documented history of AU diagnosed by an ophthalmologist and have at least 2 AU flares in the past, of which at least 1 AU flare was in the last 12 months prior to Baseline.
Additionally, subjects must be HLA-B27 positive (if known prior to Screening, no additional testing is to be performed; if unknown, testing is to be performed at Screening and checked at Baseline) and subjects must have been intolerant to or had an inadequate response to at least 2 Nonsteroidal Anti-inflammatory drugs (NSAIDs). Inadequate response to an NSAID is defined as lack of response to at least 14 days of continuous NSAID therapy at the highest tolerated dose of the administered NSAID.

Exclusion criteria

1. The subject has previously participated in this study or has previously received CZP treatment in or outside of another clinical study. However rescreening is possible if

prophylactic treatment for latent tuberculosis infection (LTBI) was to be given but the Screening Period exceeded the 12 weeks.
2. The subject has participated in another study of an investigational medicinal product (IMP) (or a medical device) within the previous 3 months or is currently participating in another study of an IMP (or a medical device).
3. The subject has a history of chronic alcohol or drug abuse.
4. The subject has any medical or psychiatric condition that, in the opinion of the Investigator, could jeopardize or would compromise the subject*s ability to participate in this study.
5. The subject has a known hypersensitivity to any components of CZP or a history of an adverse reaction to polyethylene glycol.
Axial SpA-disease related exclusions
6. Subjects must not have any other inflammatory arthritis (eg, rheumatoid arthritis, systemic lupus erythematosus, sarcoidosis, or fibromyalgia).
7. Subjects must not have a secondary, noninflammatory condition 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 axSpA.
Ophthalmic exclusion criteria
8. Any history of uveitis (eg, posterior, panuveitis) except for AU associated with axSpA.
9. Any condition or complicating factor that may interfere with the AU assessment, for example:
a. History of cataract surgery within 6 months prior to Baseline
b. Corneal or lens opacity
c. Proliferative or severe nonproliferative diabetic retinopathy or clinically significant macular edema due to diabetic retinopathy
d. Neovascular/wet age-related macular degeneration
e. History of scleritis
f. History of intraocular surgery, with the exception of phacoemulsification
10. Subject has Retisert® or Iluvien® (glucocorticosteroid implant) within 3 years prior to the Baseline Visit or has had complications related to the device. Subject has had Retisert or Iluvien (glucocorticosteroid implant) removed within 90 days prior to the Baseline Visit or has had complications related to removal of the device.
11. Subject has received intraocular or periocular corticosteroids within 90 days prior to the Baseline visit.
12. Subject has received Ozurdex® (dexamethasone implant) within 6 months prior to the Baseline Visit.
13. Subject on cyclophosphamide within 30 days prior to the Baseline Visit.
14. Subject has received intravitreal methotrexate within 90 days prior to the Baseline Visit.
15. Subject has received intravitreal anti-vascular endothelial growth factor therapy:
a. Within 45 days of the Baseline visit for Lucentis® (ranibizumab) or Avastin® (bevacizumab)
or
b. Within 60 days of the Baseline visit for anti-VEGF Trap Zaltrap® (aflibercept)
Prior medications exclusions
16. Subjects must not have used the following medications in the manner as detailed by the exclusion criteria in Table 6-1 (protocol page 31).
Previous clinical studies and previous biological therapy exclusions

17. Subjects must not have received any nonbiological therapy for axSpA not listed in Table 1 within or outside of a clinical study in the 3 months or within 5 half lives prior to the Baseline Visit (whichever is longer).
18. Subjects must not have received any experimental biological agents (defined as those agents unlicensed for use in axSpA in the EU or the USA).
19. Subjects must not have received previous treatment with a PEGylated compound that resulted in a severe hypersensitivity reaction or an anaphylactic reaction.
20. Subjects must not have been exposed to more than one TNF antagonist prior to the baseline visit and may not be a primary failure to any tumor necrosis factor (TNF) antagonist therapy (defined as no response within the first 12 weeks of the TNF antagonist treatment).
Medical history exclusions
21. Female subjects who are breastfeeding, pregnant, or plan to become pregnant during the study or within 5 months (or longer, if required by local regulation) following the final dose of the investigational product.
22. Subjects with a history of chronic or recurrent infections, excluding uveitis (more than 3 episodes requiring antibiotics or antivirals during the preceding year), recent serious or life*threatening infection within the 6 months prior to the Baseline Visit (including hospitalization for any infection in the last 6 months or any current sign or symptom that may indicate an infection).
23. Subjects with a history of herpes zoster infection within 6 months prior to the Baseline Visit.
24. Subjects with known tuberculosis (TB) infection, at high risk of acquiring TB infection, or LTBI.
a. Known TB infection whether present or past is defined as:
o Active TB infection or clinical signs and symptoms suspicious for TB (pulmonary or extrapulmonary)
o History of active TB infection involving any organ system or findings in other organ systems consistent with TB infection
o Any evidence by radiography or other imaging modalities consistent with previously active TB infection that is not reported in the subject*s medical history.
b. High risk of acquiring TB infection is defined as:
o Known exposure to another person with active TB infection within the 3 months prior to Screening
o Time spent in a healthcare delivery setting or institution where individuals infected with TB are housed and where the risk of transmission of infection is high.
c. Latent TB infection (unless appropriate prophylaxis is initiated prior to study treatment and continued to completion of prophylaxis) is defined as
o The absence of signs, symptoms (ie, evidence of organ-specific involvement), or physical findings suggestive of TB infection with a positive interferon-gamma release assay (IGRA; or 2 indeterminate IGRA test results) and a chest x-ray (or other imaging) without evidence of TB infection. If the result of the IGRA is indeterminate, the particular IGRA test previously performed may be repeated once; if positive or indeterminate on retest, the subject may not be randomized to study medication without further evaluation, treatment, and discussion with Study Physician, if LTBI is identified. (If active TB is identified, subject must undergo appropriate study-specified withdrawal procedures.) The retest must be done during the protocol-defined Screening window.
Note: If available, respiratory or other specimens must also be smear and culture negative for

TB (Centers for disease control diagnosis of LTBI, http://www.cdc.gov/TB/topic/testing/default.htm)
Detailed information on TB definition, clinical signs, diagnosis, documentation, and treatment will be available in this protocol.
25. Subjects with current acute or chronic viral hepatitis B or C or with human immunodeficiency virus (HIV) infection.
26. Subjects with current or a history of active infection with Histoplasma, Coccidiodes, Paracoccidioides, Pneumocystis, nontuberculous mycobacteria, Blastomyces, or Aspergillus.
27. Subjects with a history of an infected joint prosthesis at any time.
28. Subjects receiving any live (includes attenuated) vaccination within the 8 weeks prior to Baseline (eg, inactivated influenza and pneumococcal vaccines are allowed, but nasal influenza vaccination is not allowed).
29. Subjects who in the Investigator*s opinion have a high risk of infection (eg, subjects with leg ulcers, indwelling urinary catheter, persistent or recurrent chest infections, and subjects who are permanently bedridden or wheelchair bound).
30. Subjects with a history of a lymphoproliferative disorder, including lymphoma or current signs and symptoms suggestive of lymphoproliferative disease.
31. Current malignancy or a history of malignancy (although subjects with less than 3 completely excised basal cell carcinomas or with cervical carcinoma in situ successfully surgically treated more than 5 years prior to Screening may be included).
32. Subjects with Class III or IV congestive heart failure as per the New York Heart Association 1964 criteria.
33. Subjects with a history of, or suspected, demyelinating disease of the central nervous system (eg, multiple sclerosis or optic neuritis).
34. Subjects who have had major surgery (including joint surgery) within 8 weeks prior to Screening, or have planned surgery within 6 months of the Screening Visit.
35. Subjects with a history of or a current, as determined by the Investigator, severe, progressive, and/or uncontrolled renal, hepatic, hematological, endocrine, pulmonary, cardiac, or neurological disease.
36. Subjects with significant laboratory abnormalities at Screening including but not limited to:
o Liver function tests >2.0 x upper limit of normal
o Estimated Glomerular Filtration Rate<60 mL/min/1.732 as measured by Chronic Kidney Disease Epidemiology Collaboration (Levey et al, 2009)
o White blood cell count <3.0x109/L.
37. Subjects with any other condition which, in the Investigator*s judgment, would make the subject unsuitable for inclusion in the study

Study design

Design

Study phase: 4

Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-03-2017
Enrollment:	10
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:	31-08-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2017
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2018
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	EUCTR2016-000343-14-NL
CCMO	NL58170.029.16