A 54-week, phase II, multi-center, open-label extension study to evaluate the efficacy, safety and tolerability of ACZ885 (anti-interleukin-1beta monoclonal antibody) in patients with rheumatoid arthritis

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To assess the long-term safety and tolerability (and in particular the infection occurrence) ofACZ885 in patients with rheumatoid arthritis (RA) who participated in the core CACZ885A2204,CACZ885A2206, or CACZ885A2207 studies.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON31801

Source
ToetsingOnline

Brief title
Extension study ACZ885 in RA patients

Condition

- Autoimmune disorders

Synonym
joint pain, rheuma

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: arthritis, extension, open-label, rheuma

Outcome measures

Primary outcome

To assess the long-term safety and tolerability (and in particular the

infection occurrence) of

ACZ885 in patients with rheumatoid arthritis (RA) who participated in the core

CACZ885A2204,

CACZ885A2206, or CACZ885A2207 studies.

Secondary outcome

* To evaluate the efficacy of ACZ885 by assessing the time course of the

response to treatment

according to ACR20, ACR50, ACR70, and ACR90 criteria, and by using the

Simplified Disease

Activity Index (SDAI) and DAS28 scoring.

* To assess the effect of ACZ885 on ACR components, including a marker of

inflammation (Creactive

protein).

* To characterize the magnitude of ACZ885 joint structure preservation and/or

improvement using

magnetic resonance imaging (MRI) in RA patients who participated in the core study
CACZ885A2204 and had completed baseline and 26 weeks assessments.
* To evaluate the effect of ACZ885 treatment on radiographically detectable change in joint
structure (hands and feet) using change in modified Sharp/van der Heidje score in RA patients
who participated in the core study CACZ885A2204 and had completed baseline and 26 weeks
assessments.
* To characterize the magnitude of ACZ885 stabilization and/or improvement of the bone mineral
density (BMD) of the hand using dual-energy X-ray absorptiometry (DXA) in RA patients who
participated in the core study CACZ885A2204 and had completed baseline and 26 weeks
assessments.
* To assess the long-term immunogenicity of ACZ885.
* To evaluate the long-term pharmacokinetics (PK) of ACZ885.
* To assess the long term maintenance of health-related quality of life (HRQoL) by using the
Medical Outcome Short Form (36) Health Survey (SF-36®).

Study description

Background summary

In this trial the medication ACZ885 is being investigated. ACZ885 is possibly a new medication that is developed to treat rheumatoïd arthritis, and other inflammatory diseases. The agent has not been registered yet as medicine and does not have a name yet.
ACZ885 is a protein that binds to one of the most important inflammatory proteins which control the rheumatoïd process, interleukin-1* (IL-1*). In the rheumatoïd inflammatory process IL-1* binds to cells in the joints which are then stimulated to control the inflammatory process. This process leads to pain, swelling and limitations of the joints, and eventually also damage. ACZ885 blocks the action of IL-1* by binding to it. Hereby the inflammatory process gets the chance to rest, and could decrease the complaints of rheumatoïd arthritis.

ACZ885 has been investigated in healthy volunteers, patients with asthma, patients with rheumatoïd arthritis and patients with rare defence system such as Muckle Wells-Syndrome. Until now 133 have been treated with ACZ885 (18 healthy volunteers and 115 patients).

Study objective

To assess the long-term safety and tolerability (and in particular the infection occurrence) of
ACZ885 in patients with rheumatoid arthritis (RA) who participated in the core CACZ885A2204,
CACZ885A2206, or CACZ885A2207 studies.

Study design

This will be a multicenter, open-label, non-randomized trial without comparator which will extend active treatment by 54 weeks to those patients who completed the core CACZ885A2204, CACZ885A2206, or CACZ885A2207 study in order to collect long-term safety data.
Upon signing the informed consent, the following groups of patients will be allowed to enter the
extension study:
* Patients who were exposed to the 26-week active treatment arm, ACZ885 (+ metothrexate)
600 mg intravenous (i.v.) loading dose on Day 1 and Day 15 followed by additional i.v. infusions of 600 mg monthly, in the core CACZ885A2204 study and completed the study up to
visit 18 (Week 30) without serious or severe drug-related adverse effects.

* Patients who were exposed to placebo (+ metothrexate) in the core CACZ885A2204 study
and completed the study up to visit 18 (Week 30) without serious or severe drug-related
adverse effects.
* Patients who were exposed to one of the four 6-week active treatment arms, ACZ885
10 mg/kg s.c., ACZ885 5 mg/kg i.v., ACZ885 2 mg/kg s.c., or ACZ885 1 mg/kg i.v.
administered as two single doses on Day 1 and Day 15, in the core CACZ885A2206 study and
completed the study up to visit 7 (Day 43 / Week 6) without serious or severe drug-related
adverse effects.
* Patients who were exposed to the 12-week active treatment arm, ACZ885 600 mg i.v. loading
dose on Day 1 and Day 15 followed by one additional i.v. infusion of 600 mg at Day 43, in the
core CACZ885A2207 study and completed the study up to visit 7 (Day 85 / Week 12) without
serious or severe drug-related adverse effects.
* Patients who were exposed to placebo in the core CACZ885A2207 study and completed the
study up to visit 7 (Day 85 / Week 12) without serious or severe drug-related adverse effects.
The assessments performed at the last visit of the core study (as specified above) will correspond to the assessment of the first visit of the extension study, i.e. baseline visit (see Figure 1). Therefore, the assessments should not be performed twice (however, the assessments will be recorded twice, i.e. in both study Case Report Forms). The baseline evaluation period before first dosing (from Day -7 to Day -1) will be used to assess eligibility. Informed consent for this study must be obtained prior to conducting any study related activities for patients entering from one of the core studies.
All patients will be administered 600 mg ACZ885 as an i.v. infusion, regardless of their treatment arm
in the core study. ACZ885 dosing will occur on Day 1 and from then on every 6 weeks (± 5 days) at
the study site.
The 54-week treatment period will be followed by a follow-up period of 3 months and a study
completion visit.
Safety, tolerability, efficacy, PK, and PD will be assessed every 6 weeks at each clinical visit.
Immunogenicity will be followed up every 3 months.

Intervention

All patients will be administered 600 mg ACZ885 as an i.v. infusion, regardless

of their treatment arm
in the core study. ACZ885 dosing will occur on Day 1 and from then on every 6 weeks (± 5 days) at
the study site.

Study burden and risks

Participation in a trial with a new medication brings a certain risk and discomfort. Until now 133 men and women have been treated with ACZ885. Most persons have received ACZ885 via an infusion. Thirty-one persons have received ACZ885 as subcutaneous injection.

No serious adverse events have occurred yet which led to discontinuation of the trial, or the use of the investigational product after the first dose. One patient stopped by himself, due to dizziness, nausea and headache after the first dose. 6 adverse events have been reported which have led to a hospitalization: a spontaneous abortion after 8 weeks pregnancy of a healthy volunteer, a broken left thigh due to a fall with the bike by a patient with rheumatoid arthritis, developing of pain on the chest (possibly angina pectoris) by a patient with rheumatoid arthritis and 3 infections, amongst which erysipelas (infection of the skin), possibly a lung infection and bronchitis, in patients with rheumatoid arthritis. All three infections responded well to a treatment of antibiotics. Whether the adverse events are correlated with ACZ885 is not clear. In none of the earlier trials, medication-related changes occurred in blood pressure, pulse, ECG and laboratory values used to determine the safety.
The preliminary conclusion is the ACZ885 is well tolerated and the there are no data which have led to worry about the safety of ACZ885.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients (male and non-pregnant, non-lactating females) who completed the core CACZ885A2204, CACZ885A2206, or CACZ885A2207 study without serious or severe drug-related adverse effects may enter the extension study upon signing informed consent. A patient is defined as completing the study if he/she completed the core CACZ885A2204 study up to and including visit 18 (Week 30), or the core CACZ885A2206 study up to and including visit 7 (Day 43 / Week 6), or the core CACZ885A2207 study up to and including visit 7 (Day 85 / Week 12).

Exclusion criteria

Patients for whom continued treatment in the extension is not considered appropriate by the treating physician. Patients who were non-compliant or who demonstrated a major protocol violation in the core study. Patients who did not complete / discontinued from the core study. Patients with drug related serious adverse events or severe adverse events.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-11-2007
Enrollment:	18
Type:	Anticipated

Ethics review

Approved WMO Date:	16-11-2007
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	03-04-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-04-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-11-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2007-001665-15-NL
CCMO	NL18959.058.07