An open-label non-randomized extension study to evaluate the safety and tolerability of AIN457 (anti interleukin-17 monoclonal antibody) in patients with moderate to severe ankylosing spondylitis

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This study is designed as an extension study to the proof-of-concept trial CAIN457A2209 in patients with ankylosing spondylitis and aims to provide continuous treatment with AIN457 for patients in the core trial, to obtain safety and tolerability...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON36799

Source
ToetsingOnline

Brief title
A2209E1

Condition

- Autoimmune disorders

Synonym
Ankylosing spondylitis, Bechterew's disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Ankylosing spondylitis, Bechterew's disease, IL-17A, monoclonal antibody

Outcome measures

Primary outcome

To assess the safety and tolerability of AIN457 in patients with moderate to

severe ankylosing spondylitis receiving i.v. AIN457 initially up to 6 months

(Part 1) with a possible extension of a further 6 months (Part 2) in patients,

who participated in the core CAIN457A2209 phase II proof-of-concept study

Secondary outcome

* To assess the immunogenicity of AIN457

* To assess the total IL-17 concentration in blood at steady-state

* To assess the pharmacokinetics of AIN457 at steady state

Exploratory objectives

* To assess ASAS20, ASAS40 and ASAS 5/6 response and ASAS partial remission

* To assess the change in the ASAS core set (domains 1-6) as a continuous

outcome measure

(includes: BASFI, back pain & nocturnal pain, spinal mobility (measured by

chest expansion +

modified Schober test + occiput-to-wall distance)

* To evaluate BASMI scores (cervical rotation, maximal intermalleolar distance,

lumbar lateral

flexion, modified Schober index, tragus-to-wall distance)

* To evaluate BASDAI and physician global assessment

* To assess Maastricht Ankylosing Spondylitis Enthesis Score (MASES) and Leeds

enthesis index

(LEI)

* To assess the health related quality of life (HRQoL) by using SF-36 and and

the Ankylosing

Spondylitis Quality of Life Questionnaire (ASQoL)

* To evaluate patient global assessment (PGA) and pain by VAS

* To model free IL-17 levels in ankylosing spondylitis patients based on

measurements of total IL-17

* To assess MRI changes of the spine at week 28/EoS or week 56/EoS

Study description

Background summary

Ankylosing spondylitis is a frequent disease (0.1% of the population) associated with significant morbidity and disability, and thus constitutes a major socioeconomic burden. The first-line drug treatment of mild AS are non-steroidal anti-inflammatory drugs (NSAIDS).

Study objective

This study is designed as an extension study to the proof-of-concept trial CAIN457A2209 in patients with ankylosing spondylitis and aims to provide continuous treatment with AIN457 for patients in the core trial, to obtain safety and tolerability information, as well as additional PK data of AIN457.

Study design

This will be a multicenter, open-label, non-randomized trial without comparator which will provide active treatment over 24 weeks initially (Part 1), with a possible extension of a further 6 months (Part 2) to those patients who participated in the core CAIN457A2209 study and fulfill inclusion and exclusion criteria, in order to collect continuous safety data over a treatment period of up to one year. All patients will receive 3 mg/kg AIN457 every 4 weeks.

Intervention

The subjects will be treated with 3 mg/kg AIN457 every 4 weeks over a period of 24 weeks initially (Part 1), with a possible extension of a further 6 months (Part 2).

Study burden and risks

Giving blood samples can make feel a bit faint or sick, and can be uncomfortable and cause bruising. Rarely, a small blood clot or infection could occur at the site where the blood was taken. But this does not happen very often. When taking the blood pressure the blood pressure cuff may feel a little tight and might cause a small bruise on the arm.
When a dose of AIN457 is given this will be infused into the vein and may cause slight pain, redness, bruising or itching.

Contacts

Public
Novartis

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CH
Scientific
Novartis

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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. Patients who participate and complete the core CAIN457A2209 study up to and including the EoS i.e. Visit 16 (Week 24), may enter the extension study upon signing informed consent.
2. Patients who discontinued the core study due to unsatisfactory therapeutic effect at their Visit 14 (Week 16) or later may enter the extension study within three weeks of completing the study discontinuation visit of the core study, provided that at their discontinuation visit they meet the criteria below. Patients who do not enter the extension study within 3 weeks of completing the study discontinuation visit of the core study, will have an additional baseline visit (Visit 17) and must meet the criteria below:
a. There is no improvement (compared with the core study baseline) in two out of the following four domains: patient global assessment, pain, BASFI and the mean of the two morning stiffness questions from the BASDAI
OR
a. There is a deterioration (compared with the core study baseline) in one of the four domains (deterioration defined as ><=20% worsening and an absolute worsening of ><=1 unit)
3. Women of childbearing potential must be using simultaneously double-barrier or two highly effective methods of contraception, (e.g. intra-uterine device plus condom,diaphragm plus condom, etc; hormone replacement as either oral or implantable is acceptable as one form), from the time of screening for the duration of the entire study, up to study completion and up to 16 weeks post last drug administration. Periodic abstinence (e.g. calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
4. Male patients willing to use simultaneously two highly effective methods of contraception (e.g. intra-uterine device plus condom) for the duration of the entire study, up to study completion visit and up to 16 weeks post the last drug administration. Periodic abstinence and withdrawal are not acceptable methods of contraception.

Exclusion criteria

Patients meeting any of the following criteria will be excluded from entry into the study:

1. Patients for whom continued treatment with AIN457 in the extension is not considered appropriate by the treating physician.
2. Patients who were non-compliant or who demonstrated a major protocol deviation in the core CAIN457A2209 study.
3. Patients who discontinued from the core CAIN457A2209 study before Visit 14 (Week 16).
4. Female patients who are pregnant or lactating
5. Any active systemic infection within the past 2 weeks including a positive chest X-ray.
6. Positive human immunodeficient virus (HIV: ELISA and Western blot) test result, Hepatitis B surface antigen (HBsAg) or Hepatitis C test result, where patients have been re-tested.
The following Exclusion Criteria as defined in the core trial [CAIN457A2209] will continue to be valid with minor revisions:
7. Positive Purified Protein Derivative (PPD) tuberculin skin test of * 5 mm at baseline, (where patients have been re-tested). A positive PPD test will be defined using the MMWR 2000 guidance, summarized as criteria for tuberculin positivity by risk group.
A PPD test should not be done in subjects who had a tuberculosis vaccination in the past. These subjects will be eligible to participate if * according to local guidelines * latent tuberculosis can be excluded. For those study sites using QuantiFeron test a positive test at baseline (where patients have been re-tested) will exclude the subject from the participation in the study. If the result for either PPD or QuantiFeron test is indeterminate the subject will be excluded.
8. For previous use of immunosuppressive agents a wash-out period of at least 1 month or 5 half-lives, whatever is longer, is required. Immunosuppressive agent include but are not limited to cyclosporine, mycophenolate, tacrolimus, and 5-aminosalicylic acid (5-ASA).
If on previous treatment with anti-TNF-* therapy (or other biological therapy), the following washout periods will be required for such patients to be eligible to participate in the trial.* Six (6)-months wash out prior to dosing for alefacept, rituxan and raptiva,
* Three (3)-months washout prior to baseline for adalimumab and certolizumab,
* Two (2)-months washout prior to baseline for etanercept and infliximab,
* One (1) month washout prior to baseline for systemic immunosuppressants including, but not limited to azathioprine, cyclosporine, and leflunomide.
Patients on concomitant prednisone, methotrexate (MTX) or SSZ can be included, whereby:
* Prednisone should be kept at a stable dose 4 weeks before baseline and throughout the study and not exceed 10 mg/day.
* MTX should be kept at a stable dose 4 weeks before baseline and throughout the study and not exceed 25 mg/week.
* SSZ should be kept at a stable dose 4 weeks before baseline and throughout the study.
9. Patients who are on NSAIDS should be kept at a stable dose 4 weeks before baseline and throughout the study.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2010
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	AIN457
Generic name:	niet van toepassing

Ethics review

Approved WMO Date:	03-12-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2011

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-05-2012
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	EUCTR2009-011591-30-NL
CCMO	NL30591.018.09