# An open label non-randomized extension study to evaluate the safety and tolerability of AIN457 (anti interleukin-17 monoclonal antibody) in patients with psoriatic arthritis

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This study is designed as an extension study to the proof-of-concept trial CAIN457A2206 in patients with psoriatic arthritis and aims to provide continuous treatment with AIN457 for patients in the core trial, to obtain safety and tolerability…

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Autoimmune disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON34933

**Source**
ToetsingOnline

**Brief title**
A2206E1

### Condition

- Autoimmune disorders

**Synonym**
psoriatische artritis

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** IL-17A, Monoclonal antibody, Psoriatic arthritis

## Outcome measures

### Primary outcome

To assess the safety and tolerability of AIN457 administered i.v. initially up to 6 months (Part 1) with a possible extension of a further 6 months (Part 2) in patients with psoriatic arthritis who participated in the core CAIN457A2206 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 Objective(s)

* To explore the efficacy of AIN457 administered i.v. initially up to 6 months (Part 1) with a possible extension of a further 6 months (Part 2) as measured by ACR response criteria, PsARC response, DAS28, MASES, SPARCC and Leeds Dactylitis Index (LDI) basic.

* To explore the effect of AIN457 on PASI scores in patients with coexisting psoriasis.

* To explore the quality of life in psoriatic arthritis patients by using SF-36

and HAQ.

* To model concentrations of free IL-17 based on measurements of total IL-17

and to link free levels of IL-17 to DAS28 by a preliminary AIN457 dose to DAS28

response time model to allow for dose-regimen estimations.

The results from the exploratory objectives will be presented in a supplemental

report as required.

# Study description

### Background summary

PsA is a chronic debilitating disease of the joints that has a significant impact on daily life. At least 10% of patients with PsA develop severe structural joint damage (arthritis mutilans) leading to long term disability. A substantial number of patients do not respond to standard therapies. If AIN457 is efficacious in reducing symptoms of PsA, patients enrolled in this trial and receiving active drug may experience this benefit.

### Study objective

This study is designed as an extension study to the proof-of-concept trial CAIN457A2206 in patients with psoriatic arthritis 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 CAIN457A2206 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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**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

1. Patients who participate and complete the core CAIN457A2206 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 a later visit 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:
* The number of tender joints is the same or more than the core study baseline OR,
* The number of swollen joints is the same or more than the core study baseline OR,
* There is no improvement compared with the core study baseline in at least three of the following five domains: patient global assessment, physician global assessment, patient pain assessment, Health Assessment Questionnaire and CRP.
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, upto 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

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 CAIN457A2206 study.
3. Patients who discontinued from the core CAIN457A2206 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 [CAIN457A2206] 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

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-03-2010 |
| Enrollment: | 11 |
| Type: | Anticipated |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | AIN457 |
| Generic name: | Niet van toepassing |

## Ethics review

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| Approved WMO Date: | 03-12-2009 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-08-2010 |
| 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: | 16-02-2012 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-03-2012 |
| 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 | EUCTR2009-011622-34-NL |
| CCMO | NL30420.018.09 |