# An open label extension study of canakinumab (ACZ885) in patients with systemic juvenile idiopathic arthritis (SJIA) and active systemic manifestations who participated in studies ACZ885G2301 and ACZ885G2305; and response characterization study in canakinumab treatment-naive patients with active SJIA with and without fever.

Published: 09-06-2009
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The purpose of this open-label phase III extension study is to collect additional long term safety and efficacy data on canakinumab in the treatment of SJIA from patients who qualify to roll-over into this study from the CACZ885G2305 and...

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

## Summary

### ID

NL-OMON38236

**Source**
ToetsingOnline

**Brief title**
ß-SPECIFIC 3

## Condition

- Autoimmune disorders

**Synonym**
inflammation of the joints, rheumatism

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Novartis
**Source(s) of monetary or material Support:** Door de farmaceut zelf (Novartis Pharma)

## Intervention

**Keyword:** canakinumab (ACZ885), open-label, Systemic Juvenile Idiopathic Arthritis (SJIA)

## Outcome measures

**Primary outcome**

Study Objectives:

* To assess the long-term safety, tolerability, and immunogenicity of

canakinumab

* To assess efficacy at an exploratory level by investigating disease control

defined by

maintenance of at least an adapted ACR pediatric 30

* To perform biomarker analyses to explore the characteristics of response to

canakinumab

treatment

* To introduce Juvenile Arthritis Disease Activity Score (JADAS) and Disease

Activity Score

(DAS) as exploratory assessments of efficacy

* To assess response to canakinumab treatment based on adapted pediatric ACR30 criteria in

patients who report previous Anakinra, tocilizumab or other biologic treatment

**Secondary outcome**

Safety and efficacy will be evaluated with regards to:

* Percentage of patients who meet the adapted pediatric ACR 30/50/70/90/100

* Number of patients who are able to taper steroids

* Number of patients who reached steroid free regimen

* Number of steroid free patients who are able to reduce the canakinumab dose to 2 mg/kg every four weeks

* Percentage of patients who will meet the definition of inactive disease on medication and possible clinical remission on medication as defined by Wallace, Ruperto and Giannini (2004)

* Change in disability over time by use of the cross culturally adapted and validated version of the CHAQ©

* Change in Health-Related Quality of Life (HRQoL) over time by use of the cross culturally adapted and validated version Child Health Questionnaire (CHQ)

* Change in HRQoL over time by use of EQ-5D (for patients * 12 years of age) or EQ-5D proxy (for patients 8 - 11 years of age)

* The impact of treatment with canakinumab on sleepiness in children over time by use of the Pediatric Daytime Sleepiness Scale (PDSS)

* Progression of joint erosions in the affected hand and wrist by x-ray in a subset of volunteer patients

* Impact of treatment with canakinumab on growth velocity over time

* Impact of treatment with canakinumab on physical development in children, and

adolescents

from ages 6 * 20 by use of the Tanner stages scale over time

* Change over time in JADAS and DAS

* Progression of joint erosions in the affected hand and wrist by x-ray in a

subset of volunteer

patients

Applicable to previous canakinumab treatment-naïve patients only (Cohort 2):

* Percentage of patients, who reported previous Anakinra, tocilizumab or other

biological treatment,

who meet the adapted ACR 30/50/70/90/100

# Study description

**Background summary**

Systemic Juvenile Idiopathic Arthritis (SJIA) is a unique subset of Juvenile Idiopathic Arthritis (JIA) that occurs in children 16 years of age and younger, and accounts for approximately 4 - 17 % of JIA (Ravelli and Martini 2007). The peak age of disease onset lies between 18 months and 2 years (Symmons, et al 1996), but SJIA may occur in children of any age and, rarely, in young adults too (Woo 2006).
Canakinumab, as a potent neutralizer of IL-1*, is expected to treat the underlying structural features of arthritis (inflammation, bone and cartilage degradation), as well as providing relief of the symptoms in at least a subset of patients with these forms of arthritis.
Preliminary data from the phase II ongoing trial indicate that 13/22 patients (59%) responded to canakinumab achieving at least an adapted ACR pediatric 50 after 15 days. In 4 cases inactive disease status was reached (no joints with active arthritis, no fever, normal CRP and no disease activity according to physician*s assessment).

Based upon the encouraging preliminary results from POC/phase II, Novartis believes that it has a responsibility to evaluate canakinumab as a safe and

efficacious treatment option for children with SJIA.

**Study objective**

The purpose of this open-label phase III extension study is to collect additional long term safety and efficacy data on canakinumab in the treatment of SJIA from patients who qualify to roll-over into this study from the CACZ885G2305 and CACZ885G2301 protocols. Also canakinumab-naive patients with active SJIA will be enrolled.

**Study design**

This open-label extension study collects long-term safety and efficacy data from patients who were responsive to canakinumab in studies CACZ885G2305 and/or CACZ885G2301, or canakinumab-naive patients with active SJIA.

During this open-label, active treatment study all patients will be treated with canakinumab 4 mg/kg or 2 mg/kg s.c. every 4 weeks up until study end unless discontinuation occurs. Dosing visits and safety assessments will occur every 4 weeks. Efficacy will be assessed every 12 weeks, with the exception of CRP, which will be measured every four weeks.
Efficacy will be assessed every 12 weeks, with the exception of CRP, which will be measured
every four weeks. Efficacy will also be assessed at each visit when patient is tapering
corticosteroid, reducing canakinumab dose, or investigator is concerned regarding possible
loss of response.
All patients who do not maintain adapted ACR Pediatric 30 response or clinically deteriorate
during this study and intervention is deemed necessary by the investigator will be
discontinued unless their loss of the adapted ACR Pediatric 30 response is considered a
consequence of steroid tapering or the reduction of the canakinumab dose.

Rules for steroid tapering and canakinumab tapering can be found in the final protocol (v 5 19-jan-2010)

If patients are discontinued, they will be treated as per local standard medical practice but will
be followed-up for safety for 2 months after the last injection.

The extension study will run for a set time period, meaning all patients regardless of when they enter

the extension will have a last visit date during December 2012, unless discontinuation occurs prior to
this date.
Depending on local regulatory requirements access to canakinumab will be made available to patients
via, but not limited to, an Expanded Access program until the product is launched. Novartis will provide
the drug free of cost. Countries will ensure that, in compliance with local regulations, a simplified
access program is set up using the product monograph as a reference. Patients from countries in
whom canakinumab is not yet approved, individual arrangement in these countries for continuous care
of patients with canakinumab will be sought that may include, but not limited to, a local patient need or
compassionate use program.

**Intervention**

Patients will be dosed every 4 weeks with 4 mg/kg or 2 mg/kg of s.c. canakinumab up until October 2012 or until premature patient withdrawal (PPW). On average, patients will be followed for up to 2 years following their participation in the CACZ885G2305 or CACZ885G2301 studies. This is dependent on when last patient last visit occurs for study CACZ885G2301; because the studies run concurrently not all patients who enter the extension study will be able to receive 96 weeks of treatment.
Patients who are still receiving corticosteroid therapy (oral prednisone or equivalent) may taper their dose during this study. Guidelines for steroid tapering for patients who flared early in CACZ885G2305 or CACZ885G2301 between days 15 and 29 will be introduced.
For patients who are steroid naïve, steroid free, or who have completely tapered their corticosteroids, there is the option of decreasing the canakinumab dose to 2 mg/kg every 4 weeks.
The maximal total single dose of canakinumab allowed is 300 mg, which is administered as two s.c. 150 mg injections.
Novartis will supply investigational drug (active canakinumab) in individual 6 mL glass vials each containing either 150 mg canakinumab (to be used in patients being on canakinumab 2 mg/kg with * 15 kg BW, and all patients on canakinumab 4 mg/kg), 25 mg canakinumab (to be used in patients being on canakinumab 2 mg/kg with < 15 kg BW).

**Study burden and risks**

Risks and inconveniences
Risks are possible side effects of the study medicine or another medicine.
Risks are also possible side effects that result from taking blood. If you were

taking medication that made your symptoms of SJIA better or go away completely and you had to stop this medication to take part in the study, stopping this medication may cause these symptoms to come back. Your study doctor will discuss this more with you. The tests done at each visit are standard medical tests, however they may cause some discomfort. For example you will be asked to give some blood, which can also make you feel a bit faint or sick. It can also 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 at all. When you have your blood pressure taken, the blood pressure cuff may feel a little tight and might cause a small bruise on your arm. When you are given a dose of canakinumab or placebo this will be injected just under the skin and may cause light pain, redness, bruising or itching. The testing to see if you already have tuberculosis may cause some swelling and hardness at the injection site. You will also be asked to have an ECG. This is a test of your heart which does not hurt. However the skin may become a little itchy and red where the sticky pads are placed. There is no radiation used during the ECG procedure. If you need a chest x-ray you will be given a very small amount of radiation. This can carry very small risks but the dose of radiation in a chest x-ray is very low.
The sonography is a painless test to have a picture of your liver and spleen.
If your joints are inflamed, the assessment of your joints by your doctor may cause slight pain.

Side effects of study drug, canakinumab:
The study drug may involve risks that are currently unknown. 37 clinical studies with canakinumab have been started; approximately 3330 patients (including 319 children 2 years and above) have been treated with canakinumab (as of
December 2008 with several studies currently ongoing). Canakinumab was well tolerated. Canakinumab treatment discontinuations were rare. The maximum average duration patients have been on canakinumab is currently 2 1/2 years. There were serious events (or bad events). A *serious adverse event* is a side effect that may be life-threatening or may requires the study participant to be hospitalized for a time, it may or may not be related to a study drug.
Preliminary findings from an ongoing study with 23 SJIA patients show that the most common adverse events were upper respiratory tract infections. There were 8 serious adverse events where the patients were hospitalized. Five of these events were due to other underlying medical history of the patients (irritated stomach with bleeding ulcer, suspected
pericarditis, worsening of SJIA, pain and fear, and blood in the urine). Three of these events were infections leading to hospitalization (acute tonsillitis, severe sore throat and severe nail infection. All of these events resolved while continuing canakinumab treatment. In all previous and ongoing studies of approximately 670 patients without SJIA taking
canakinumab serious events occurring more than once and suspected to be related to canakinumab were included: vertigo (dizziness) (twice), nausea (twice) and vomiting (twice). You will be promptly informed should any further risks about

the study drug become known.

Allergic reactions
Sometimes people have allergic reactions to drugs. Most allergic reactions to drugs like canakinumab occurred within 2 hours after dose administration. Serious allergic reaction which may include low blood pressure, trouble breathing, seizures and death may occur. However, most reactions seen were mild to moderate. Some things that can happen during an allergic reaction are: a rash, itching, having a hard time breathing, wheezing when you breathe, sudden drop in blood pressure, swelling around the mouth, throat or eyes, fast pulse, fever, sweating, and chills. There is a risk that a rare or previously unknown side effect will occur.

It is unknown if canakinumab and other similar medications change the risk or frequency of MAS. Cases of MAS, some fatal, have been reported in SJIA patients treated with canakinumab and similar medications. The number of MAS cases reported in SJIA studies of canakinumab has been within the range of expected number of cases.
Cancer
The impact of canakinumab treatment on risk of cancer is not known. However, treatment with immunosuppressant drugs like canakinumab may result in an increase in the risk of cancer.
White blood cell count
Canakinumab treated patients may experience low white blood cell count. White blood cells are infection fighting cells in the blood stream.
Platelet count in blood
Canakinumab treated patients may experience low platelet count in blood. Platelets in blood take part in blood clotting.
Immunizations
Some vaccines should not be taken during the study It has been recommended that live and live attenuated vaccines should not be taken by patients participating in this study. These include BCG (type of tuberculosis vaccine), Ty21a (a Salmonella typhi vaccine), Measles, Mumps, Rubella, Oral Polio, Influenza, Yellow fever, Varicella, Vaccinia, and Rotavirus.
Other treatments
You do not have to be in this study to receive treatment for your SJIA. You may receive the standard therapy for SJIA which may include corticosteroids.

Benefits of treatment
You may receive no direct benefit from being in this study. However, your taking part may help patients get better care in the future.

# Contacts

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Novartis

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**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

## Inclusion criteria

Inclusion * Cohort 1
1. Parent*s or legal guardian*s written informed consent and child*s assent, if appropriate, or patient*s informed consent for * 18 years of age before any study related activity is performed
2. The following patients are eligible to participate in the open label extension study (CACZ885G2301E1):
* Patients from study CACZ885G2305 or CACZ885G2301 who achieved an adapted ACR pediatric 30 response 15 days after their initial dose of canakinumab but clinically deteriorated as defined by a minimum ACR Pediatric 30 response not being

maintained after Day 15 and intervention is deemed necessary by the investigator.
* Patients in study CACZ885G2301 who are not eligible to enter Part II (withdrawal part) because they were not able to meet the corticosteroid entry criteria of 0.5 mg/kg oral prednisone (or equivalent) or were not able to taper their steroids by at least 0.3 mg/kg (please refer to CACZ885G2301 protocol for detailed rules)
* Responder patients in Part I or Part II who were maintaining their minimum ACR pediatric 30 response or had not flared when CACZ885G2301 was stopped.
* CACZ885G2301 patients who were responders in Part I (achieved and maintained a minimum adapted ACR pediatric 30) but experienced a flare in Part II.
Inclusion criteria * Cohort 2:
1. Parent*s or legal guardian*s written informed consent and child*s assent, if appropriate, or patient*s informed consent for * 18 years of age before any study related activity is performed.
2. Male and female patients aged * 2 to < 20 years at the time of the screening visit
3. Confirmed diagnosis of SJIA as per ILAR definition that must have occurred at least 2 months prior to enrollment with an onset of disease < 16 years of age:
* Arthritis in one or more joints with or preceded by fever of at least 2 weeks duration that is documented to be daily/ quotidian for at least 3 days and accompanied by one or more of the following:
* Evanescent nonfixed erythematous rash,
* Generalized lymph node enlargement,
* Hepatomegaly and/ or splenomegaly,
* Serositis
4. Active systemic disease at the time of enrollment (baseline visit) defined as having 2 or more of the followings:
* Documented spiking, intermittent fever (body temperature > 38°C) for at least 1 day during the screening period and within 1 week before first canakinumab dose
* At least 2 joints with active arthritis (using ACR definition of active joint)
* C-reactive protein (CRP) > 30 mg/L (normal range < 10 mg/L)
* Rash
* Serositis
* Lymphadenopathy
* Hepatosplenomegaly
5. Patient*s willingness to discontinue anakinra, rilonacept, tocilizumab or other experimental drug under close monitoring (Please refer to Cohort 2 exclusion criteria #3 for washout period)
6. No concomitant use of second line agents such as disease-modifying and/or immunosuppressive drugs will be allowed with the exception of:
* Stable dose of methotrexate (maximum of 20 mg/ m2/ week) for at least 1 week prior to the baseline visit, and folic/folinic acid supplementation (according to standard medical practice of the center)
* Stable dose of no more than one non-steroidal anti-inflammatory drug (NSAID) for at least 1 week prior to the baseline visit
* Stable dose of steroid treatment * 1.0 mg/kg/day (maximum 60 mg/day for children over 60 kg) in 1-2 doses per day of oral prednisone (or equivalent) for at least 3 days prior to baseline (Day 1)
7. Negative Purified Protein Derivative (PPD) test (< 5 mm induration) or negative

QuantiFERON test at screening or within 1 month prior to the screening visit, according to the national guidelines. Patients with a positive PPD test (* 5 mm induration) at screening may be enrolled only if they have either a negative chest x-ray or a negative QuantiFERON test (QFT-TB G In-Tube). If the patient has a history of Bacillus Calmette-Guérin (BCG) vaccination, then a QuantiFERON test should be performed in place of a PPD test

## Exclusion criteria

1. Pregnant or nursing (lactating) female patients, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive urine pregnancy test at screening visit
2. Female patients having reached sexual maturity (e.g. Tanner Stage 2 or above), i.e. being physiologically capable of becoming pregnant UNLESS they are:
* female patients whose career, lifestyle, or sexual orientation precludes intercourse with a male partner and/or
* using an acceptable method of contraception with a failure rate (Pearl Index (PI)) < 1. Reliable contraception should be maintained throughout the study and for 3 months after study drug discontinuation.
3. History hypersensitivity to study drug or to biologics.
4. With active or recurrent bacterial, fungal or viral infection at the time of enrollment, including patients with evidence of Human Immunodeficiency Virus (HIV) infection, Hepatitis B and Hepatitis C infection.
5. Risk factors for tuberculosis (TB) such as:
* History of any of the following: residence in a congregate setting (e.g. jail or prison, homeless shelter, or chronic care facility), substance abuse (e.g. injection or noninjection); health-care workers with unprotected exposure to patients who are at high risk of TB or patients with TB disease before the identification and correct airborne precautions of the patient, or
* Close contact (i.e. share the same air space in a household or other enclosed environment for a prolonged period (days or weeks, not minutes or hours)) with a person with active pulmonary TB disease within the last year
6. With underlying metabolic, renal, hepatic, infectious or gastrointestinal conditions which in the opinion of the investigator immunocompromises the patient and/ or places the patient at unacceptable risk for participation in an immunodulatory therapy. In particular, clinical evidence or history of multiple sclerosis or other demyelinating diseases, or Felty*s syndrome
7. With neutropenia (absolute neutrophil count < 1500/mm3) at screening
8. With significant medical conditions, which in the opinion of the Investigator will exclude the patient from the study (can be discussed on a case by case basis with Novartis)
9. History of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
10. Live vaccinations within 3 months prior to the start of the study. Killed or inactivated vaccines may be permitted according to the investigator*s discretion.

11. Donation or loss of blood (amount depending on age and weight, 10-20% or more of volume, see Appendix 3 within 8 weeks prior to first dosing, or longer if required by local regulation.
12. Familial and social conditions rendering regular medical assessment not possible
13. History of drug or alcohol abuse within the 12 months prior to dosing.
Additional exclusion criteria for Cohort 2:
1. Presence of moderate to severe impaired renal function as indicated by clinically significantly abnormal creatinine (* 1.5 x upper normal limit (ULN)) or urea values or abnormal urinary constituents (e.g., albuminuria) at screening. Evidence of urinary obstruction or difficulty in voiding at screening.;2. Clinical evidence of liver disease or liver injury as indicated by abnormal liver
function tests at screening such as AST, ALT, GGT, alkaline phosphatase, or serum bilirubin (must not exceed twice the upper limit value of the normal range for age).
3. Use of the following therapies:
* Anakinra within 24 hours prior to Baseline visit
* Rilonacept within 1 week prior to Baseline visit
* Tocilizumab within 3 weeks prior to Baseline visit
* Etanercept within 4 weeks prior to Baseline visit
* Adalimumab within 8 weeks prior to the Baseline visit
* Infliximab within 12 weeks prior to the Baseline visit
* Rituximab within 26 weeks prior to the Baseline visit
* Leflunomide within 4 weeks prior to the Baseline visit. Documentation of a completion of a full cholestyramine elimination treatment after most recent leflunomide use will be required.
* Thalidomide within 4 weeks prior to the Baseline visit
* Cyclosporine within 4 weeks prior to the Baseline visit
* Intravenous immunoglobulin (i.v. Ig) within 8 weeks prior to the Baseline visit
* 6-Merceptopurine, azathioprine, cyclophosphamide, or chlorambucil within 12 weeks prior to the Baseline visit
* Dapsone, mycophenolate mofetil within 3 weeks prior to the Baseline visit
* Corticosteroids (oral prednisone (or equivalent)) > 1.0 mg/kg/day (or greater than the maximum of 60 mg/day for children over 60 kg) for at least 3 days prior to the Baseline visit
* Intra-articular, peri-articular, or intramuscular corticosteroid injections within 4 weeks prior to the Baseline visit
* Any other investigational biologics (with the exception of the ones mentioned above or canakinumab (previous participation in studies CACZ885A2203, CACZ885G2301 or CACZ885G2305)) within 8 weeks prior to the Baseline visit
* Any other investigational drugs, other than investigational biologic treatment, within 30 days (or 3 months for investigational monoclonal antibodies) or 5 half-lives prior to the Baseline visit, whichever is longer
Wash-out period may be longer according to local requirements.

# Study design

## Design

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| Study phase: | 3 |
| 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): | 01-02-2010 |
| Enrollment: | 10 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Ilaris |
| Generic name: | canakinumab |
| Registration: | Yes - NL outside intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 09-06-2009 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 24-08-2009 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 15-10-2009 |

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|---|---|
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 05-11-2009 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 22-02-2010 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 09-03-2010 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 14-04-2010 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 07-07-2010 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 13-07-2010 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 22-03-2011 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 19-04-2011 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 16-01-2012 |

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|---|---|
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 06-02-2012 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 17-09-2012 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 20-09-2012 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 20-12-2012 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 31-05-2013 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 11-07-2013 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 29-11-2013 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 24-10-2014 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 29-10-2014 |

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|---|---|
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

# 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 | EUCTR2008-008008-42-NL |
| CCMO | NL28260.041.09 |