A randomized, double-blind, placebo controlled, single-dose study to assess the initial efficacy of canakinumab (ACZ885) with respect to the adapted ACR Pediatric 30 criteria in patients with Systemic Juvenile Idiopathic Arthritis (SJIA) and active systemic manifestations

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The primary objective of this study is:To demonstrate that the percentage of patients who meet the adapted ACR Pediatric 30 criteria at Day 15 is higher with canakinumab compared to placebo.Secondary objectives of this study are:* To evaluate the...

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

Summary

ID

NL-OMON35316

Source
ToetsingOnline

Brief title
G2305

Condition

- Autoimmune disorders

Synonym
inflammation in the joints, rheumathism

Research involving
Human

Sponsors and support

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

Intervention

Keyword: canakinumab (ACZ885), placebo-controlled, single-dose, SJIA (Systemic Juvenile Idiopatic Arthritis)

Outcome measures

Primary outcome

The primary efficacy variable is the proportion of patients who respond to

treatment at Day 15 according to the adapted ACR Pediatric 30 criteria.

Secondary outcome

The following secondary efficacy endpoints will be analyzed in the order they

are presented below:

1. Proportion of patients achieving the adapted ACR Pediatric 30 criteria at

Day 29

2. Proportion of patients achieving the adapted ACR Pediatric 50 criteria at

Day 29

3. Proportion of patients achieving the adapted ACR Pediatric 50 criteria at

Day 15

4. Patient*s pain intensity assessed on a 0-100 mm VAS by Day 29

5. Patient*s pain intensity assessed on a 0-100 mm VAS by Day 15

6. Proportion of patients who have body temperature * 38°C at Day 3

7. Proportion of patients achieving the adapted ACR Pediatric 70 criteria at

Day 29

8. Proportion of patients achieving the adapted ACR Pediatric 90 criteria at

Day 29

9. Proportion of patients achieving the adapted ACR Pediatric 100 criteria at

Day 29

10. Proportion of patients achieving the adapted ACR Pediatric 70 criteria at

Day 15

11. Proportion of patients achieving the adapted ACR Pediatric 90 criteria at

Day 15

12. Proportion of patients achieving the adapted ACR Pediatric 100 criteria at

Day 15

13. Change in HRQoL over time by use of the CHQ

14. Change in disability over time by use of the CHAQ©

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 primary objective of this study is:
To demonstrate that the percentage of patients who meet the adapted ACR Pediatric 30 criteria at Day 15 is higher with canakinumab compared to placebo.

Secondary objectives of this study are:
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 30 criteria at Day 29
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 50 criteria at Day 29
* To evaluate the efficacy (percentage of patients who meet the adapted ACR Pediatric 50
criteria) of canakinumab as compared to placebo at Day 15
* To evaluate the efficacy of canakinumab as compared to placebo with respect to overall pain
over the last week assessed on a 0-100 mm visual analog scale (VAS) in the Childhood
Health Assessment Questionnaire (CHAQ) by Day 29
* To evaluate the efficacy of canakinumab as compared to placebo with respect to overall pain
over the last week assessed on a 0-100 mm VAS in the CHAQ by Day 15
* To evaluate the efficacy of canakinumab as compared to placebo based on the percentage of
patients who have body temperature * 38°C at Day 3
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 70 criteria at Day 29
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 90 criteria at Day 29
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 100 criteria at Day 29
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 70 criteria at Day 15
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to

the adapted ACR Pediatric 90 criteria at Day 15
* To evaluate the effect of treatment with canakinumab as compared to placebo with respect to
the adapted ACR Pediatric 100 criteria at Day 15
* To evaluate the change in Health-Related Quality of Life (QoL) over time by use of the cross
culturally adapted and validated version Child Health Questionnaire (CHQ)
* To evaluate the safety, tolerability and immunogenicity of canakinumab
* To evaluate the change in disability over time by use of the cross culturally adapted and
validated version of the CHAQ

Exploratory objectives of this study are:
* To evaluate the pharmacokinetics (PK) / pharmacodynamic (PD) of canakinumab
* To explore protein, mRNA and DNA biomarkers (e.g. HLA-DQA1) in order to identify
retrospectively responder/non-responder patients at an early time point (baseline and Day 3)
* To explore the change in health-related QoL over time by use of EuroQoL Five Dimension
questionnaire (EQ-5D for patients *12 years of age and EQ-5D proxy for patients 8-11 years
of age)
* To explore the level of sleepiness in children over time by use of the Pediatric Daytime
Sleepiness Scale (PDSS)

Study design

Study design:
This is a randomized, double-blind, placebo controlled, single-dose study of 4 weeks duration.
Once patient eligibility is confirmed at screening, patients will be randomized at baseline to either
canakinumab or placebo in a ratio of 1:1. Patients will receive a single dose of study drug
(canakinumab 4 mg/kg or placebo) subcutaneously (s.c.) at Day 1. Randomization will be stratified by
number of active joints (* 26, > 26), non-responder to anakinra (yes or no if either responder to
anakinra or never exposed to anakinra), and level of current corticosteroid use (* 0.4 mg/kg oral
prednisone (or equivalent) or > 0.4 mg/kg oral prednisone (or equivalent).
At Day 1 (baseline), Physician*s Global Assessment of disease activity on a 0-100 mm VAS, CHAQ,
CHQ, EQ-5D, PDSS, number of joints with active arthritis using the ACR definition, number of joints

with limitation of motion, laboratory measure of inflammation (CRP) and assessment of intermittent
fever due to SJIA (oral or rectal body temperature > 38°C only for several hours during the day) during
the preceding week prior to the first dose of study medication will be assessed.
All patients with an affected hand and/or wrist who consent at baseline (volunteer patients) will be
subjected to an articular x-ray of both (left and right) hands and wrists. The x-ray film will be sent to a
Clinical Research Organization (CRO) for confirmation of the quality. Assessment of the x-ray film will
be performed by an independent x-ray reading committee.
Note: To explore the progression of joint erosion by x-ray is not an objective of this study. However,
the purpose of the x-ray in this study is to have a proper baseline x-ray for those patients who may roll
over into study CACZ885G2301 or CACZ885G2301E1 where they will have another x-ray performed
at their yearly post-baseline x-ray timepoints (e.g. 1, 2, or 3 year post-baseline x-ray timepoint) and/or
End of Study visit in CACZ885G2301 and/or CACZ885G2301E1.
At Day 3 clinical response will be assessed as per Physician*s Global Assessment of disease activity,
number of joints with active arthritis, number of joints with limitation of motion, CRP, and body
temperature.
Criteria for escape at any time between day 3 and day 15:
* Presence of fever >38°C at least 2 consecutive days not due to infection
* SJIA complications for which there is a need to increase steroid dose over baseline dose.
Complications include but are not limited to MAS and serositis.
* JIA flare according to the standard definition of flare (if at least 2 JIA core set variables cannot
worsen because they are already at the maximum limit the flare will be determined according
to the investigator*s decision)
* Any other condition, in the opinion of the investigator, that might jeopardize further
participation in the trial.
If at any time between Day 3 and Day 15, patients are * as per investigator*s discretion * not clinically
improving with study treatment, they may be unblinded.
* Those patients who are on canakinumab will complete the Premature Patient Withdrawal
(PPW) assessments, will be discontinued from the study, will be treated as per standard local
medical practice but will be followed-up for safety for 2 months after last

injection.
* Those patients who are on placebo will complete the PPW assessments, discontinue from the
study, and may roll over into Part Ia of study CACZ885G2301 where they will receive a s.c.
injection of canakinumab 4 mg/kg.
At Day 15, clinical response will be assessed as per adapted ACR Pediatric 30, i.e. improvement from
baseline of at least 30% in at least three of the six response variables and no intermittent fever in the
preceding week, with no more than one of the remaining variables worsening by more than 30%.
Patients who meet the adapted ACR Pediatric 30 criteria at Day 15 will continue in the study.
Patients who do not meet the adapted ACR Pediatric 30 criteria at Day 15 may be unblinded:
* Those patients who are on canakinumab will complete the PPW assessments, will be
discontinued from the study, will be treated as per standard local medical practice but will be
followed-up for safety for 2 months after the last injection.
* Those patients who are on placebo will complete the PPW assessments, discontinue from the
study and may roll over into Part Ia of study CACZ885G2301 where they will receive a s.c.
injection of canakinumab (4 mg/kg)..
At Day 29, clinical response as per adapted ACR Pediatric 30 and study completion assessments will
be performed. Canakinumab patients who complete the study may roll over into Part Ib of
CACZ885G2301.
PPW assessments will occur when patients discontinue from the study at any time and/or roll over to
CACZ885G2301 or CACZ885G2301E1.
In order to evaluate patients* eligibility for rolling-over into study CACZ885G2301 or
CACZ885G2301E1, patients will be unblinded as soon as they have completed PPW assessments or
complete the study on Day 29. The following rules will apply:
* Canakinumab patients who met the adapted ACR pediatric 30 criteria at Day 15 and clinically
deteriorates as defined by a minimum adapted ACR pediatric 30 response not being maintained afterwards such that the investigator feels intervention is necessary before Day 29
may be eligible to roll over into the open label extension study CACZ885G2301E1.
* Canakinumab patients who met the adapted ACR pediatric 30 criteria at Day 15 and

completed the study at Day 29 may be eligible to roll over into Part Ib of CACZ885G2301
* Canakinumab patients with no clinical improvement on Days 3-15 or who did not meet a
minimum adapted ACR pediatric 30 at Day 15 will be discontinued, treated as per standard
local medical practice and followed up for safety for 2 months after the last injection.
* Placebo patients may be eligible to roll over into Part Ia of CACZ885G2301 if further study
treatment is required (i.e. no clinical improvement on Days 3-15, a minimum adapted ACR
pediatric 30 was not met on Day 15)
* Placebo patients who met the adapted ACR pediatric 30 criteria at Day 15 and clinically
deteriorates as defined by a minimum adapted ACR pediatric 30 response not being maintained between Days 15 and 29 and intervention is deemed necessary by the investigator may be eligible to roll over into Part Ia of CACZ885G2301.
* All patients not rolling over into CACZ885G2301 or CACZ885G2301E1 will be followed-up for
safety for 2 months after the last injection.
Every effort should be made by the investigator to have all patient data as complete as possible and
entered into the eCRF before unblinding occurs.
No interim analysis is planned.

Intervention

Patients will receive a single dose of canakinumab (4 mg/kg) or placebo at Day 1. The maximal total single dose of canakinumab allowed is 300 mg. The maximal dose which can be administered per single s.c. injection is 150 mg. Therefore, some patients who require a dose greater than 150 mg (patients > 37.5 kg) will require two s.c. injections.

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. Twenty clinical studies with canakinumab have been started; approximately 700 patients (including 43 children 4 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.

In clinical trials, infections, mainly of the upper airways and in some instances serious, have been reported more frequently with patients taking canakinumab than with placebo (sugar pill). No unusual or opportunistic infections were reported and all infections that were
reported responded normally to standard therapy. The risk for the development of cancer with medications that inhibit the protein Interleukin-1, including canakinumab, is unknown, but can not be excluded entirely. A temporary spinning sensation (vertigo) has been reported in some patients soon after they begin canakinumab therapy. It usually did not require treatment and resolved without problem or interruption of their canakinumab treatment.

There were serious events (or bad events). A *serious adverse event* is a side effect that is life-threatening and requires a 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 17 serious adverse events where the patients were hospitalized. Eleven of these events were due to
other underlying medical history of the patients (irritated stomach (twice), hip arthritis, bleeding rectal skin lesion, abdominal pain from constipation with rectal bleeding, suspected pericarditis, worsening of SJIA (twice), pain and fear, tendonitis and blood in the urine). Six of these events were

infections leading to hospitalization (acute tonsillitis, severe sore throat, flu-like viral illness, stomach virus with mild bleeding abnormality, hepatitis, and severe nail infection). All of these events resolved while continuing canakinumab treatment. Serious events occurring more than once and suspected to be related to canakinumab in all previous and ongoing studies of approximately 670 patients who do not have SJIA included: vertigo (dizziness) (twice), nausea (twice) and vomiting (twice).
Mild skin inflammations at the injection site were reported by a few patients. parents and patients 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.

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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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

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 of age at the time of the screening visit
3. Confirmed diagnosis of SJIA as per ILAR definition (Petty et al, 2004) 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 disease at the time of enrollment defined as follows:
* At least 2 joints with active arthritis (using ACR definition of active joint)
* Documented spiking, intermittent fever (body temperature > 38°C) for at least 1 day during the screening period within 1 week before first canakinumab/placebo dose
* C-reactive protein > 30 mg/L (normal range < 10 mg/L)
5. Naïve to canakinumab
6. Patient*s willingness to discontinue anakinra, rilonacept, tocilizumab or other experimental drug under close monitoring (please refer to section 5.2 *Exclusion criteria #12 for washout period)
7. 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 8 weeks prior

to the screening 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 2 weeks prior to the screening 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 to randomization.
8. Negative Purified Protein Derivative (PPD) test (< 5 mm induration) or negative QuantiFERON test at screening or within 1 month prior to screening. 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 hCG laboratory test (> 5 mIU/ mL) 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 2 months after study drug discontinuation.
3. History of hypersensitivity to study drug or to biologics.
4. Diagnosis of active macrophage-activation syndrome (MAS) (Ravelli, Magni-Manzoni and Pistorio 2005) within the last 6 months
5. 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
6. 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
7. 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
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. 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)
11. Presence of moderate to severe impaired renal function as indicated by clinically significant abnormal creatinine (* 1.5 times ULN) or urea values or abnormal urinary constituents (e.g. albuminuria) at screening. Evidence of urinary obstruction or difficulty in voiding at screening.
12. Use of the following therapies prior to randomization:
* 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
* Growth hormone within 4 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) within 3 days prior to 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) 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.
13. 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.
14. Donation or loss of blood (amount depending on age and weight, 10-20% or more of total blood volume by age and weight, see Appendix 10 for approximate guidelines) within 8 weeks prior to first dosing, or longer if required by local regulation.
15. Familial and social conditions rendering regular medical assessment not possible

16. History of drug or alcohol abuse within the 12 months prior to dosing.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2009
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	canakinumab

Ethics review

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
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:	18-02-2010
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:	23-09-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-01-2011

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)

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	EUCTR2008-005476-27-NL
CCMO	NL27874.041.09