A Randomized, Double-Blind, Phase III Study of the Efficacy and Safety of Gemcitabine in Combination With TH-302 Compared With Gemcitabine in Combination With Placebo in Previously Untreated Subjects With Metastatic or Locally Advanced Unresectable Pancreatic Adenocarcinoma

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Primary objective:The primary objective of the trial is to evaluate efficacy, as measured by overall survival (OS), of gemcitabine in combination with TH-302 compared to gemcitabine in combination with placebo in subjects with previously untreated...

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

Summary

ID

NL-OMON40361

Source
ToetsingOnline

Brief title
MAESTRO study

Condition

- Other condition

Synonym
Metastatic or Locally Advanced Unresectable Pancreatic Adenocarcinoma

Health condition

adenocarcinoom van de pancreas

Research involving
Human

Sponsors and support

Primary sponsor: Merck
Source(s) of monetary or material Support: Merck KGaA;Darmstadt;Germany

Intervention

Keyword: Efficacy and Safety, Gemcitabine+TH-302 vs Gemcitabine+placebo, Metastatic or Locally Advanced Unresectable Pancreatic Adenocarcinoma

Outcome measures

Primary outcome

The primary endpoint is OS (overall survival) time.

The analysis of the primary endpoint will test the null hypothesis of equality of gemcitabine+TH-302 over gemcitabine+placebo in terms of OS time, in the Intent-to-Treat (ITT) population as randomized. A stratified, 2-sided log-rank test at a significance level of $\alpha=0.05$ will be used to compare the treatment groups. The study requires 508 events (deaths) to ensure 90% power for rejecting the null hypothesis of equal treatment effect given a hazard ratio of 0.75. Assuming a median OS time of 6.5 months for the placebo plus gemcitabine group, it is estimated that accrual will last for approximately 18 months and that the required number of events will be observed around 28 months after the first subject is randomized. A total of 660 subjects need to be randomized on a

1:1 basis taking into account a total drop-out rate of approximately 4%. Final analyses will be conducted after at least 508 deaths have been reported.

Secondary outcome

* Tumor assessment endpoints: PFS (progression free survival) and tumor response as measured by OR (objective response) and disease control, based on RECIST 1.1 criteria.

* The primary health-related quality of life (HRQoL) endpoint is based on Time to Definitive Deterioration (TUDD) assessed using EORTC QLQ-C30 (version 3). In addition, HRQoL will be evaluated using EQ-5D-5L, and TUDD of pain as measured by a NRS.

* The safety and tolerability endpoints consist of treatment-emergent adverse events (TEAE) graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v.4.03), treatment-emergent serious adverse events (SAEs), and deaths. In addition, drug exposure and standard laboratory studies (hematology, biochemistry, urinalysis, pregnancy testing in women with childbearing potential), electrocardiograms (ECGs), physical examinations, and assessments of weight and vital signs also will be performed.

* Population PK endpoints include parameters such as clearance (Cl) and volume of distribution (V) derived from plasma concentrations of TH-302 and if feasible bromo-isophosphoramide mustard (Br-IPM).

* Exploratory endpoints: CA19-9 levels; exploratory PGt endpoints including genetic markers that may be associated with the PK, efficacy, and safety of TH-302; biomarkers that may be associated with efficacy such as tumor hENT1 and hypoxia biomarkers from serum, plasma, and tumor.

Significance testing will be performed for secondary endpoints (i.e., PFS and OR). The overall significance level of 5% will be controlled by employing a hierarchical testing procedure with a 2-sided α=0.05 at each level. No interim efficacy analysis is planned. An ISMB will be established to review safety periodically. No formal statistical comparisons are planned for ISMB purposes.

Study description

Background summary

Based on the efficacy and safety results of the randomized Phase II trial of TH-302 in pancreatic carcinoma, TH-302 will be evaluated in combination with gemcitabine, the current approved chemotherapy in subjects with locally advanced unresectable and metastatic adenocarcinoma of the pancreas. This Phase III trial will evaluate TH-302 in the same dosing regimen and schedule (340 mg/m2 TH-302 dosed on Days 1, 8 and 15 of a 28-day cycle with gemcitabine) and subject population that was assessed in the randomized Phase II trial (Trial TH* CR-404). This clinical trial will be conducted in compliance with the clinical trial protocol, current Good Clinical Practice (ICH Topic E6, GCP), and the applicable regulatory requirements. Based on the preclinical and clinical data available to date, the conduct of the trial is regarded as justifiable at the planned dose ranges.

Trial TH*CR-404 is an open-label, multicenter trial of 2 dose levels of TH-302 (T, 240 mg/m2 or 340 mg/m2) in combination with gemcitabine versus gemcitabine alone (randomized 1:1:1) was initiated in June 2010. Gemcitabine (1000 mg/m2) and TH-302 were administered via IV on Days 1, 8 and 15 of a 28-day cycle. Subjects on the gemcitabine arm could crossover after documented progression and be randomized to one of the two gemcitabine+TH-302 arms. The primary efficacy evaluation was a comparison of progression free survival (PFS) between the combination arm and gemcitabine alone (80% power to detect 50% improvement in PFS with one-sided alpha of 10%).

A total of 214 subjects with advanced pancreatic adenocarcinoma were treated as follows: 69 treated received gemcitabine (G), 71 subjects received G+TH-302 at 240 mg/m2 (G+T240), and 74 subjects received gemcitabine+TH-302 at 340 mg/m2 (G+T340). A total of 77% of subjects had distant metastases. Median PFS was 3.6 months in the G arm versus 5.5 months in the G+T240 arm with a HR of 0.64 (95%

CI: 0.43, 0.96; p = 0.031) versus 6.0 months in the G+T340 arm with a HR of 0.58 (95% CI: 0.39, 0.87; p = 0.008). Best response according to RECIST 1.1 (unconfirmed) was 12% in the G arm, 17% in the G+T240 arm, and 27% in the G+T340 arm. CA19-9 decreases were notably greater in the G+TH-302 groups and greatest in the G+T340 which had 37 of 53 (70%) subjects with a greater than 50% CA19-9 decrease. One death (suicide) was considered possibly related to study drug. The proportions of subjects with adverse events leading to discontinuation were: 16% in the G arm, 15% in the G+T240 arm and 11% in the G+T340 arm. Serious adverse events were balanced across the treatment arms. The most common non-laboratory events were similar across treatment arms; these were fatigue (50%), nausea (50%), constipation (31%), and peripheral edema (35%) in the G+T340 arm. Rash (14% G, 39% G+T240, and 45% G+T340) and stomatitis (6% G, 17% G+T240, and
36% G+T340) were notably greater with combination treatment and 4 subjects had Grade 3 rash, but there were no Grade 4 events. Grade 3/4 thrombocytopenia (11% G, 39% G+T240, and 59% G+T340) and Grade 3/4 neutropenia (28% G, 56% G+T240, and 59% G+T340) were
higher with the combination treatment.12 (Data on file, Threshold Pharmaceuticals, Inc., San Francisco, California, US).

Study objective

Primary objective:
The primary objective of the trial is to evaluate efficacy, as measured by overall survival (OS), of gemcitabine in combination with TH-302 compared to gemcitabine in combination with placebo in subjects with previously untreated locally advanced unresectable or metastatic pancreatic adenocarcinoma.

Secondary objectives:
The secondary objectives of the trial are:
* To assess the safety and tolerability of gemcitabine in combination with TH-302 compared with gemcitabine
in combination with placebo in subjects with previously untreated locally advanced unresectable or metastatic pancreatic adenocarcinoma.
* To evaluate the efficacy of gemcitabine in combination with TH-302 compared with gemcitabine in combination with placebo in subjects with
previously untreated locally advanced unresectable or metastatic pancreatic adenocarcinoma with respect to: progression free survival (PFS), and objective response (OR) and disease control.
* To assess patient reported outcomes (PROs) with respect to quality of life (QoL) measured with EORTC QLQ-C30 (Version 3) and EQ-5D-5L, and pain measured by a Numerical Rating Scale (NRS).
* To investigate levels of carbohydrate antigen 19-9 (CA19-9), a tumor marker for pancreatic carcinoma.
* To investigate the pharmacokinetics (PK) of TH-302 in plasma using a population analysis approach and to identify covariates.
* To explore the association of pharmacogenetic (PGt) markers with the PK,

efficacy, and safety of TH-302.
* To explore the association of potential predictive biomarkers such as tumor human equilibrative nucleoside transporter 1 (hENT1) and of hypoxia biomarkers from serum, plasma, and tumor with efficacy endpoints.

Study design

This Phase III trial is a randomized, double-blind, placebo-controlled trial of gemcitabine in combination with TH-302 (gemcitabine+TH-302, investigational arm) compared to gemcitabine in combination with placebo (gemcitabine+placebo, control arm) in subjects with locally advanced unresectable or metastatic pancreatic adenocarcinoma. Randomized subjects will receive gemcitabine+TH-302 or gemcitabine+placebo in 28-day cycles until there is evidence of progressive disease (PD), intolerable toxicity, or the subject withdraws from study drug for other reasons. The primary endpoint is overall survival (OS) time. The data cut-off for statistical analyses of the primary and secondary endpoints will be reached when 508 event (deaths) are reported. No interim efficacy analysis is planned. An Independent Safety Monitoring Board (ISMB) will provide periodic evaluations of the unblinded safety data to ensure subject safety and the validity and scientific merit of the study.

Intervention

The study is made up of three parts: Screening, the Randomized Treatment Phase, and the Safety and Survival Follow-up.

After signing the informed consent form, a series of assessments (screening) will be conducted to determine if the patient qualifes for entry into the trial and to collect baseline safety information.

If the patient is eligible for participation in the trial, he/she will be randomized into one of the 2 trial groups (A or B). The patient will have an equal chance to be placed in either the TH 302 group (Group A) or to placebo group (Group B). Both groups will receive standard chemotherapy (gemcitabine).

Patients will receive gemcitabine+TH-302 or gemcitabine+placebo treatment once per week during 3 weeks from each 28-day (4 weeks) cycle (i.e. treatment during 3 weeks in a row/ 1 week no treatment). Treatment will be continued until there is evidence of progressive disease (PD), intolerable toxicity, or any other withdrawal criteria.

* TH-302 or placebo: On Days 1, 8, and 15 of each treatment cycle, the patient will receive either TH-302 (at a dose of 340 mg/m2) or placebo. TH-302 or placebo will be given to the patient by intravenous infusion over 30 minutes. Longer infusion durations are permitted. The dose of TH-302 may be adjusted based on the safety laboratory results during the treatment cycle.

* Gemcitabine: On Days 1, 8 and 15 of each treatment cycle, gemcitabine will be given to the patient at a dose of 1,000 mg/m2 by intravenous infusion over 30 minutes. This infusion will begin 2 to 2.5 hours after the completion of the TH-302 or placebo infusion. The dose of gemcitabine may be adjusted based on the safety laboratory results during the treatment cycle.

The evolution of your tumor will be evaluated according to a standard way of measuring tumors (RECIST 1.1). Tumor imaging will be conducted by CT scan (computerized tomography) or MRI (magnetic resolution imaging) every 8 weeks as calculated from your randomization date until there is evidence that the disease is no longer under control, regardless of treatment discontinuation or the start of another therapy. If the patient has bone pain, he/she may need to have a bone scan. TH-302 should not be used after the tumor is no longer under control or the trial treatment has been discontinued.

The patient will receive a care package of products to help him/her manage the skin and mucosal side effects he/she may experience from receiving study drug. The care package will include Preparation H® (phenylephrine/pramoxine hemorrhoidal cream or ointment) or equivalent, Desitin® (zinc oxide topical) or equivalent, SPF 30 Sunscreen, and petroleum jelly (Vaseline®).

During the treatment phase patients will be asked about any (serious) side effects at each visit. These will be classified according to their relationship with TH-302 treatment, severity, grade, actions taken and outcome.

Blood Collection: Safety blood samples will be obtained as well as a blood sample for tumor markers, 2 blood samples for hypoxia biomarkers (Cycle 1 and 3 only). Total blood collected will be approximately 88 mL in Cycle 1, approximately 64 mL in Cycle 3 and approximately 48 mL for all other Cycles.

ECG: An ECG (heart tracing) will be done immediately before the end of your first infusion on Day 1. ECGs are done on Day 1 of every subsequent odd numbered cycle (e.g., Cycle 3, 5, 7 etc.) to check your heart rhythm.

Questionnaires: Validated pain and quality of life questionnaires will be completed on a regular basis as from the start of study treatment (day 1, cycle 1).

The Treatment Termination Visit will occur within 14 days after the patient receives the last dose of trial drug.

The Safety Follow-up Visit will occur approximately 30 days after the last dose of trial drug. During those calls information about further cancer therapies will be collected as well as questionnaires will be completed to evaluate the patient quality of life and eventual pain. Any side effects the patient reports

will be followed until they are resolved.

Study burden and risks

Observations from previous clinical trials:
Hematological adverse events commonly occur for both gemcitabine as well as for TH-302 in combination with gemcitabine. Thrombocytopenia (low platelets) and neutropenia (low white blood count) were the most common hematological toxicities for both gemcitabine as well as for gemcitabine + TH-302 in a trial comparing gemcitabine with gemcitabine combined with TH-302. The incidence of more severe thrombocytopenia was increased in subjects who received gemcitabine and TH-302 compared to gemcitabine alone. All subjects* platelet counts recovered. Two subjects had bleeding events associated with known bleeding sites and recovered. The incidence of severe neutropenia (low white blood count) was increased in subjects who received gemcitabine + TH-302 compared to gemcitabine alone. Because of the increased risk associated with neutropenia for infection, subjects should report any evidence of fever immediately to their doctor. In addition, because of the increased risk of bleeding associated with low platelet counts, subjects should promptly report any evidence of bleeding to their doctor.

Non-hematological adverse events that occurred in more than 20% of subjects treated with gemcitabine + TH-302 in the randomized Phase 2 trial of subjects with advanced pancreatic cancer included fatigue, nausea, constipation, peripheral edema (swelling in the legs, ankles or feet), rash, vomiting, diarrhea, abdominal pain, pyrexia (fever), decreased appetite, urinary tract infection and stomatitis (mouth sores). In subjects who received gemcitabine alone the incidence of rash and stomatitis was lower (the frequency of rash in the gemcitabine alone arm vs. gemcitabine + TH-302, rash was 14% vs. 45% of subjects, respectively while stomatitis occurred in 6% vs. 36% of subjects, respectively). The incidence of darkening of the skin in areas where trial medicines were injected was 18% in subjects who received both gemcitabine and TH-302 when TH-302 was given at the dose used in the study. Because TH-302 can cause nausea and/or vomiting, an appropriate and standard preventive treatment will be recommended by your trial doctor.

Further possible side effects: It was commonly observed that subjects have developed skin side effects (including rash, blisters, itching and sores especially in areas where skin touches skin such as the genital area) and some subjects have developed mucositis (inflammation of the lining of the mouth, vagina, urethra (tube that carries urine out from the bladder), esophagus (swallowing tube) or intestine). There may also be an increased risk of developing herpes or yeast infection in these areas. These abnormalities have improved with local treatment, delaying the dose of TH-302 or reducing the dose. Suggestions will be provided to the trial doctor for minimizing the skin and mucosal side effects that may be experienced by subjects receiving TH-302.

Other possible side effects may include: taste changes, decreased weight, hair loss, cough, decreased potassium levels, headache, dizziness, painful or bleeding hemorrhoids, loose stools and dehydration. There is a risk that the patient may experience some changes to his/her vision such as blurry vision. There may be other side effects that are not yet known. The trial doctor also will recommend medicines that should reduce symptoms associated with other side effects such as mouth sores and diarrhea. If such side effects occur, the patient must inform the trial doctor immediately. It is possible that TH-302 may cause kidney damage. Two subjects in the gemcitabine arm and one subject in the gemcitabine + TH-302 arm developed kidney failure; therefore it is important that the patient remain well hydrated. The patient kidney function will be monitored closely with blood and urine tests. It is important for the patient to tell the trial nurse or doctor about all medication that he/she is taking since some drugs are known to cause kidney damage.

It is also possible that the patient could experience an allergic reaction or a reaction similar to an allergic reaction to the trial drug. Such reactions might include: itching, skin rash, hives, lip swelling, shortness of breath or wheezing, abdominal pain, and an acute or sudden drop in blood pressure with loss of consciousness and /or associated with seizures, including the possibility of death. The patient should seek immediate medical attention if he/she experiences these side effects at any time during the trial.

Other Risks: Risks from IV (intravenous) infusions and/or blood taken for laboratory testing include: discomfort, pain, redness, bleeding, bruising, itching and swelling at the site, infrequent cases of fainting, and/or inflammation/infection of the vein which could require antibiotics. Redness and increased pigmentation (darkening) of the skin have been reported at the infusion site for TH-302. Inflammation of the skin, drying and damage to the tissues may occur if TH-302 leaks out of the vein. If any signs or symptoms of leakage occur, the infusion of the trial drug should be stopped and restarted in another vein. The risk of this happening is much lower if a central line (a catheter that ends close to your heart) is used. The patient physician will monitor the site closely and recommend additional care if needed. Infusion reactions consisting of lip swelling and hives have occurred in several subjects after TH-302 infusions. These reactions reversed with steroid and anti-histamines (medicines that reduce inflammation) treatment. The patient will receive medicines to reduce the chance of having nausea and vomiting. Steroids are one of the medicines that may be given to reduce nausea and that might reduce the chance of any reactions occurring after the patient receives trial drug. Be aware that steroids can increase blood sugar levels and increase the risk of infection.

Ionizing Radiation Exposure: Risks from CT scans or other x-rays can include: exposure to radiation and serious allergic reaction to iodine containing contrast material. Radiology departments are usually well equipped to deal with these risks.

Potential Reproductive Risks:
For women:
The trial drug might harm an unborn child, such as genetic mutations or other deformities. Therefore women should not take part in the trial if they are pregnant, breast-feeding or intend to become pregnant during the trial. Also, it is unknown whether taking the trial drug can affect women ability to have children in the future. Women who are capable of becoming pregnant will be asked to have a blood pregnancy test before taking part in the trial. Women must agree to avoid becoming pregnant during the trial.

For men:
The trial drug might harm an unborn child, such as genetic mutations or other deformities. Therefore men should not take part in this trial if they intend to father a child during the trial. Also, it is unknown whether taking the trial drug can affect men ability to father children in the future.

Contacts

Public
Merck

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Darmstadt 64293
DE
Scientific
Merck

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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. At least 18 years of age.
2. Ability to understand the purposes and risks of the trial and has signed a written informed consent form approved by the investigator*s Institutional Review Board (IRB)/Independent Ethics Committee (IEC).
3. Locally advanced unresectable or metastatic pancreatic ductal adenocarcinoma proven by histology or cytology and previously untreated with chemotherapy or systemic therapy other than: radiosensitizing doses of 5-fluorouracil, radiosensitizing doses of gemcitabine if relapse occurred at least 6 months after completion of gemcitabine, neoadjuvant chemotherapy if relapse occurred at least 6 months after surgical resection or adjuvant chemotherapy if relapse occurred at least 6 months after completion of adjuvant chemotherapy.
4. Measurable disease (at least one target lesion outside of previous radiation fields) or non-measurable disease by RECIST 1.1 criteria.
5. Documentation of disease progression since any prior therapy.
6. ECOG performance status of 0 or 1. Two observers must assess performance status <=5 days prior to randomization. If discrepant, the poorer performance status is used.
7. Life expectancy of at least 3 months.
8. Acceptable liver function: bilirubin <=1.5 times upper limit of normal (ULN) (not applicable to subjects with Gilbert*s syndrome) and aspartate aminotransferase (AST [SGOT]) and alanine aminotransferase (ALT [SGPT]) <=3 times ULN (if liver metastases are present, then <=5 times ULN is allowed).
9. Acceptable renal function: serum creatinine <=1.5 times ULN or calculated creatinine clearance >=60 mL/min (Cockcroft-Gault formula).
10. Acceptable hematologic status (without growth factor support or transfusion dependency): absolute neutrophil count (ANC) >=1500 cells/µL, platelet count >=100,000/µL, hemoglobin >=9.0 g/dL.

Exclusion criteria

1. New York Heart Association (NYHA) Class III or IV congestive heart failure, myocardial infarction within 6 months prior to the date of randomization, unstable arrhythmia or symptomatic peripheral arterial vascular disease.
2. Symptomatic ischemic heart disease.
3. Known brain, leptomeningeal or epidural metastases (unless treated and well controlled for at least 3 months).
4. Previous malignancy other than pancreatic cancer in the last 5 years, except for adequately treated non-melanoma skin cancer or pre-invasive cancer of the cervix.
5. Severe chronic obstructive or other pulmonary disease with hypoxemia (requires supplementary oxygen, symptoms due to hypoxemia, or oxygen saturation <90% by pulse oximetry after a 2-minute walk) or in the opinion of the investigator any physiological state likely to cause systemic or regional hypoxemia.

6. Major surgery, other than diagnostic surgery, <=28 days prior to the date of randomization. Subject must have completely recovered from surgery.
7. Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic therapy.
8. Treatment of pancreatic cancer with radiation therapy or surgery <=28 days prior to the date of randomization.
9. Prior therapy with a hypoxic cytotoxin.
10. Subjects who participated in an investigational drug or device trial <=28 days prior to Day 1 of the first cycle.
11. Known infection with HIV, or an active infection with hepatitis B or hepatitis C.
12. Subjects who have exhibited allergic reactions to a structural compound similar to TH-302 or the drug product excipients or to gemcitabine or its excipients.
13. Subjects who are taking medications that prolong QT interval and have a risk of Torsades de Pointes.
14. Subjects with a QTc interval calculated according to Bazett*s formula (QTc=QT/RR0.5; RR=RR interval) of >450 msec based on a screening electrocardiogram (ECG).
15. Subjects with a history of long QT syndrome.
16. Subjects taking a medication that is a moderate or strong inhibitor or inducer of CYP3A4.
17. Subjects taking a medication that is a sensitive substrate or substrates with a narrow therapeutic index of CYP3A4, CYP2D6, or CYP2C9.
18. Subject is pregnant (positive serum beta human chorionic gonadotropin [β-HCG] test at screening) or is currently breast-feeding, anticipates becoming pregnant/impregnating their partner during the study or within 6 months after study participation, or subject does not agree to follow acceptable methods of birth control, such as hormonal contraception, intra-uterine pessary, condoms, or diaphragm in conjunction with spermicidal gel, or sterilization, to avoid conception during the study and for at least 6 months after receiving the last dose of study treatment.
19. Other significant concomitant disease or condition that could interfere with the conduct of the study, or that would, in the opinion of the investigator, pose an unacceptable risk to the subject in this trial.
20. Unwillingness or inability to comply with the study protocol for any reason.
21. Legal incapacity or limited legal capacity.
22. Subjects with metastatic pancreatic cancer who are, according to Investigator*s assessment, suitable for FOLFIRINOX should be excluded from the trial (in countries in which FOLFIRINOX is considered as an acceptable therapeutic option). A subject who refuses - after being informed about all therapeutic alternatives - to receive FOLFIRINOX would be considered as not suitable for this therapy (FOLFIRINOX) - even if the investigator judges him as medically suitable - and could consequently be included in the planned clinical trial.

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):	11-08-2014
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GEMZAR
Generic name:	Gemcitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Niet van toepassing
Generic name:	TH-302

Ethics review

Approved WMO Date:	04-11-2013
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-12-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-02-2014

Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-04-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-06-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-02-2016
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-02-2016
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	EUCTR2012-002957-42-NL
ClinicalTrials.gov	NCT01746979
CCMO	NL43118.058.13