Safety, Pharmacokinetics, and Pharmacodynamics of Escalating Oral Doses of the Arginase Inhibitor INCB001158 (formerly known as CB-1158) as a Single Agent and in Combination with Immune Checkpoint Therapy in Patients with Advanced/Metastatic Solid Tumors

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Primary ObjectivesParts 2To evaluate the safety and tolerability of INCB001158 for patients with advanced/metastatic and/or treatment-refractory solid tumorsParts 3To evaluate the safety and tolerability of INCB001158 in combination with…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON48697

Source
ToetsingOnline

Brief title
Incyte INCB 01158-101

Condition

- Metastases

Synonym
advanced/metastatic malignant solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Incyte Corporation
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Arginase inhibitor, First in Human, INCB01158, Mono and combination therapy

Outcome measures

Primary outcome

The primary endpoint is the safety of INCB001158 as monotherapy and as combi

therapy with pembrolizumab.

The following safety analyzes will be evaluated for all patients in each

treatment combination:

Undesirable events (AEs) and changes in laboratory values, vital signs and

physical examinations.

Secondary outcome

The secondary endpoints are efficacy.

The following efficacy analyzes will be evaluated for all patients in each

treatment combination:

-On the basis of an evaluation of AEs, pharmacokinetics (PK), pharmacodynamics

and indications for clinical activity;

-Determined via standard RECIST criteria (except for pleural mesothelioma,

which will be evaluated using adjusted RECIST criteria) [total response rate

(ORR), best overall response (BOR), duration of response (duration of response,

DOR), and progression-free survival (PFS)] and immune-related RECIST (ir RECY)

criteria (irORR, irBOR, irDOR and irPFS);

-A non-compartmental analysis method will be used to analyze the plasma

concentration of INCB001158.

Study description

Background summary

INCB001158 is an experimental drug that is being studied in this study. *Experimental* means that it is currently being tested in medical scientific studies and has not been approved. Doctors cannot prescribe the study drug outside a study yet. INCB001158 has not been administered to humans before. It has been previously tested in the laboratory and on animals.

INCB001158 showed reduction of tumor growth rate in studies with animals when given alone and enhanced reduction when given in combination. The sponsor is expecting that the study drug will have benefits for patients with solid tumors. In this study will be searched for the appropriate dose to be given in order to have highest effect to slow down the tumor growth with as less as possible side effects.

INCB001158 is designed to stop cancer growth by blocking the activity of an enzyme in your body called arginase. Arginase can lower the levels of a nutrient in your body called arginine. This can make your immune system work less well. The study is intended to understand if the study drug can lower or block the activity of arginase, which allows for normal levels of arginine in the body. This may slow the growth or spread of some cancers by activating the immune system.

Pembrolizumab, also known as KEYTRUDA®, is approved in Europe, the United States, and several other countries to treat several types of cancer. In The Netherlands it has been approved to treat patients with PD-L1 positive advanced non small cell lung cancer. Pembrolizumab is a medication that strengthens the immune system. This allows the immune system kill the cancer cells better.

In this study, the combination of INCB001158 with pembrolizumab is investigational.

Study objective

Primary Objectives
Parts 2
To evaluate the safety and tolerability of INCB001158 for patients with advanced/metastatic and/or treatment-refractory solid tumors
Parts 3
To evaluate the safety and tolerability of INCB001158 in combination with pembrolizumab in patients with advanced/metastatic and/or treatment-refractory solid tumors

Secondary Objectives
Parts 2
To select the Recommended Phase 2 Dose (RP2D) of INCB001158 for patients with advanced/metastatic solid tumors
Parts 3
To select the RP2D of INCB001158 in combination with pembrolizumab for patients with advanced/metastatic solid tumors
Parts 2 and 3
To evaluate the anti-tumor effect of INCB001158 as monotherapy and in combination with pembrolizumab for patients with advanced/metastatic solid tumors
Determine PK of INCB001158 alone and in combination with pembrolizumab

Exploratory Objectives
Parts 2 and 3
To evaluate the pharmacodynamic effects of INCB001158 as monotherapy and in combination with pembrolizumab in patients with advanced/metastatic solid tumors
To investigate the relationship between PK, pharmacodynamic biomarkers and anti-tumor activity
To evaluate biomarkers that may predict the anti-tumor effect of INCB001158 in combination with pembrolizumab in patients with advanced/metastatic solid tumors
To identify potential pharmacodynamic biomarkers that may predict how advanced/metastatic solid tumors respond to either INCB001158 alone or in combination with pembrolizumab

Study design

This is an open-label, non-randomized phase 1 study in patients with advanced / metastatic solid tumors where safety, tolerability. pharmacokinetics and pharmacodynamics and anti-tumor activity arginase inhibitor INCB001158 as monotherapy and in combination with 'immune checkpoint 'inhibitor pembrolizumab, a drug against programmed cell death protein-1 (anti-PD-1),

evaluated.

All research visits are outpatient. After giving written informed consent, patients are evaluated for their eligibility for the study during a screening period within 3 weeks (21 days) prior to receiving the study medication on Day 1 of Cycle 1 (C1D1). The eligibility is examined during the screening period. Concomitant disorders / medication at the baseline are recorded and assessed. Hematology, blood chemistry, urine research, ECG; progress disorder (computed tomography [CT scan]) or magnetic resonance imaging [MRI]), and tumor assessments at the baseline (CT scan or MRI) are performed within 28 days before C1D1. Tumor biopsy will be taken within 28 days for C1D1, or an archive tumor sample is collected.All biopsies are optional.

Patients will be included in Part 2 or 3 upon proven eligibility (Part 1a and 1b are not done in the Netherlands):
Part 2 (extension cohorts for monotherapy): advanced / metastatic non-small cell lung cancer (NSCLC), advanced / metastatic colorectal cancer (CRC), advanced / metastatic tumors including gastric cancer, cancer of the gastro-esophageal junction (GEJ), urothelial cell cancer (UCC), renal cell carcinoma (RCC), melanoma, or squamous cell carcinoma of the head and neck (SCCHN) or other advanced / metastatic solid tumors (eg tumors shown or expected to show high infiltration with arginase-positive cells) may be permitted if the medical monitor is approved. (total 3 subgroups, 2a-2c)
Part 3 (extension cohorts for combi-therapy): advanced / metastatic NSCLC, melanoma, UCC, microsatellite instability-high' (MSI-H) CRC, microsatellite stable' (MSS) CRC, advanced / metastatic stomach cancer / cancer of the stomach oesophageal transition, SCCHN and malignant pleural mesothelioma. (total 8 subgroups, 3a-3h)

Visit schedule / procedures
Patients arrive on day 1 of each cycle for a planned research visit to the clinical center. During cycle 1 additional study visits will be planned to check for safety and efficacy or for PK / pharmacodynamic biomarker evaluations.
For part 2 Course 1: day 1, day 8, day 15 and day 22 (± 2 days); Course 2: day 1.
For part 3 Course 1: Day 1, day 8 and day 15 (± 2 days).
All other treatment courses: Day 1 (± 5 days).

All patients will come to the research center on C1D1 for the first dose of research medication after the following examinations have been done: measuring vital signs, safety monitoring (blood and urine tests including pregnancy tests if applicable, physical examination), an electrocardiogram (ECG)), and registration of adverse events (AEs).

On day 8 and day 15 (and day 22 for part 2) of course 1, patients will visit the research center for measuring safety and efficacy studies.

On day 1 of the next cycles, patients come to the research center for a physical examination, laboratory tests, and for the registration of side effects (AE) / concomitant medication.

Prior to C2D1, a biopsy may be taken from the patients. All biopsies are optional.

Tumor assessments (CT and / or MRI of pelvis / abdomen / head) are performed every 8 weeks (± 7 days) for part 2 and every 9 weeks (± 7 days) for part 3.

Patients can continue with the study medication after confirmed initial progressive disease, if the study doctor deems this useful. In that case relevant information is given and additional consent is requested.

End of treatment (End of Treatment, EoT): The visit EoT must take place within 28 days after the end of the research treatment and prior to the initiation of a new anti-cancer therapy / regimen.

Follow-up regarding side effects occurs 30 days (+ 7 days) and 90 days (+ 7 days) after the end of research treatment.
Follow up with regard to tumor progression: Patients who discontinue the research treatment for reasons other than tumor progression will be further assessed for their disease status during the follow-up phase and have to undergo tumor assessments every 8 weeks (monotherapy) or 9 weeks (pembrolizumab combination) until from the start of a new cancer therapy, disease progression, death or the end of the study.
Follow up with regard to alive status will occur every 3 months for the first year of follow up and after that every 6 months.

Intervention

Start dose of INCB001158 is 100 mg and can be reduced, depending on any side effects. The study medication (INCB001158) will be taken orally with a capsule formulation (25 mg or 100 mg per capsule).
Patients in part 2: INCB001158 will be taken on days 1 to 28 of each 28-day course and should be taken orally, using the number of capsules indicated in the pharmacy guide.
Patients in part 3: INCB001158 will be taken on days 1 to 21 of each 21-day course and should be taken orally, using the number of capsules indicated.

Patients in part 3 will receive Pembrolizumab.
Pembrolizumab will be administered on day 1 of every 3-week treatment regimen after all procedures and evaluations have been completed as indicated in the evaluation schedule. A dose of 200 mg pembrolizumab will be given by IV infusion over 30 minutes. The dose of 200 mg Q3W has been approved in the United States and EU Member States. After the pembrolizumab infusion, patients will be instructed to take their morning dose of INCB001158.

Estimated duration of participation per patient is expected to last approximately 24 months per individual patient: Maximum 21 days for screening, then continuous treatment in consecutive 28-day courses for part 2 and 21-day courses for part 3 as long as a patient benefits , tolerates the regimen and does not meet criteria for discontinuation of the study treatment, and 30 and 90 days for follow-up of adverse reactions. All patients will be monitored for survival.

Study burden and risks

Patients are asked to undergo procedures as described in the research protocol. These procedures include physical examination, vital functions, ECG, CT / MRI, blood collection, keeping study medication diaries, answering questions from the researcher and
study team, administration of study medication. If no archive of tumor tissue is available, a biopsy can be taken. In addition, an additional (voluntary) tumor biopsy may be taken at cycle 2. If the patient consents an optional biopsy will be taken at PD.

In addition, patients of childbearing age, who are sexually active, must agree to total abstinence or use of
effective form of contraception with their sexual partners during participation in the study. Patients are also asked to inform their research physician about their medication use and changes in health status.

Contacts

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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. Age * 18 years
2. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1
3. Adequate organ function as indicated by the laboratory values in
* Absolute neutrophil count (ANC) *1.500/mcL
* Platelets * 100,000 / mcL
* Hemoglobin * 9 g/dL (5,59 mmol/l)
* Creatinine Clearance * 50 mL/min (calculated using the formula of Cockcroft and Gault)
* Serum total bilirubin OR Direct bilirubin (for patients with Gilbert Syndrome and total bilirubin levels >1.5 ULN) * 1.5 X ULN OR * ULN
* AST (SGOT) and ALT (SGPT) * 2.5 X ULN
* International Normalized Ratio (INR) or Prothrombin Time (PT) * 1.5 X ULN- Does not apply to patients receiving therapeutic anticoagulation
4. Measurable Disease: At least one tumor lesion/lymph node that meets the RECIST v1.1 criteria for being *measurable*.
Resolution of all treatment-related toxicities, except alopecia, anemia, or endocrinopathies managed by hormone replacement, from any previous cancer therapy to * Grade 1 or to values within those required for eligibility on this study prior to the first dose of study treatment.;Part 2 specific inclusion criteria:
Histologically or cytologically proven diagnosis of :
* advanced/metastatic NSCLC (squamous or non-squamous) in patients who have disease progression after treatment with all available therapies known to confer clinical benefit (Part 2a)
* advanced/metastatic CRC in patients who have disease progression after treatment with all available therapies known to confer clinical benefit (Part 2b)
* advanced/metastatic tumors including gastric cancer, cancer of the GEJ, UCC, RCC, melanoma, or SCCHN in patients who have disease progression after treatment with all available therapies known to confer clinical benefit. Other advanced/metastatic solid tumors (e.g., those demonstrated or expected to have high infiltration with arginase-positive cells) may be allowed based on the discretion of the Medical Monitor (Part 2c);Part 3 (pembrolizumab expansion cohorts) specific inclusion criteria:
Part 3a: Non-small cell lung cancer (NSCLC) * PD/SD on anti-PD-1/PD-L1 therapy
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic NSCLC

that does not harbor an activating EGFR or ALK mutation
2. Prior progression on or after platinum-based chemotherapy or refused/ineligible to receive platinum-based chemotherapy.
3. Received an anti-PD-1/PD-L1 agent in a prior line of therapy for advanced/metastatic disease and EITHER:
a. Had documented radiological disease progression (per Investigator assessment, preferably with confirmation of PD after 4 weeks) while receiving anti-PD-1/PD-L1 therapy in the most recent line of therapy, OR
b. Had documented stable disease (per Investigator assessment) for * 24 weeks while receiving pembrolizumab therapy in the most recent line of therapy;Part 3b: Melanoma * PD/SD on anti-PD-1/PD-L1 therapy
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic melanoma
2. Received an anti-PD-1/PD-L1 agent in the most recent prior line of therapy for advanced/metastatic disease and EITHER:
a. Had documented radiological disease progression (per Investigator assessment, preferably with confirmation of PD after 4 weeks) while receiving anti-PD-1/PD-L1 therapy in the most recent line of therapy, OR
b. Had documented stable disease (per Investigator assessment) for * 24 weeks while receiving pembrolizumab therapy in the most recent line of therapy;Part 3c: Urothelial cell carcinoma (UCC) * PD/SD on anti-PD-1/PD-L1 therapy
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic UCC
2. Received an anti-PD-1/PD-L1 agent in the most recent prior line of therapy for advanced/metastatic disease and EITHER:
a. Had documented radiological disease progression (per Investigator assessment, preferably with confirmation of PD after 4 weeks) while receiving anti-PD-1/PD-L1 therapy in the most recent line of therapy, OR
b. Had documented stable disease (per Investigator assessment) for * 24 weeks while receiving pembrolizumab therapy in the most recent line of therapy;Part 3d: Mismatch repair deficient and/or microsatellite instability-high (MSI-H) colorectal cancer (CRC) * PD/SD on anti-PD-1/PD-L1 therapy
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic CRC demonstrated to be mismatch repair deficient or microsatellite instability-high.
2. Received an anti-PD-1/PD-L1 agent in the most recent prior line of therapy for advanced/metastatic disease and EITHER:
a. Had documented radiological disease progression (per Investigator assessment, preferably with confirmation of PD after 4 weeks) while receiving anti-PD-1/PD-L1 therapy in the most recent line of therapy, OR
b. Had documented stable disease (per Investigator assessment) for * 24 weeks while receiving pembrolizumab therapy in the most recent line of therapy;Part 3e: Microsatellite stable (MSS) colorectal cancer (CRC) * Checkpoint inhibitor naive
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic CRC demonstrated to lack mismatch repair deficiency and microsatellite instability (low or high).
2. Received at least one prior fluoropyrimidine-containing systemic therapy for advanced/metastatic CRC
3. Has not received prior anti-PD-1/PD-L1, anti-CTLA4, or other checkpoint inhibitor or immune co-stimulator (e.g., anti-OX-40, anti-41BB, etc.);Part 3f: Gastric/gastro-esophageal

(GE) junction cancer * Checkpoint inhibitor naive
1. Histological or cytological diagnosis of locally advanced unresectable or metastatic gastric or GEJ cancer
2. Received at least two prior systemic therapies for advanced/metastatic disease; prior regimens must have included a platinum and a fluoropyrimidine
3. Human epidermal growth factor receptor 2 (HER-2/neu) negative, or, if HER2/neu positive, must have previously received treatment with trastuzumab
4. Has not received prior anti-PD-1/PD-L1, anti-CTLA4, or other checkpoint inhibitor or immune co-stimulator (e.g., anti-OX-40, anti-41BB, etc.);Part 3g: Squamous cell carcinoma of the head and neck (SCCHN) * Checkpoint inhibitor naive
1. Histological or cytological diagnosis of recurrent or metastatic SCCHN
2. Had disease progression EITHER:
a. While receiving or after platinum-containing chemotherapy administered for recurrent or metastatic SCCHN, OR
b. Following platinum-containing chemotherapy administered as part of induction, concurrent, or adjuvant therapy.
3. Has not received prior anti-PD-1/PD-L1, anti-CTLA4, or other checkpoint inhibitor or immune co-stimulator (e.g., anti-OX-40, anti-41BB, etc.).;Part 3h: Mesothelioma * Checkpoint inhibitor naive
1. Histological or cytological diagnosis of locally advanced incurable or metastatic malignant pleural mesothelioma
2. Has failed or was unable to received standard therapy for malignant pleural mesothelioma
3. Has not received prior anti-PD-1/PD-L1, anti-CTLA4, or other checkpoint inhibitor or immune co-stimulator (e.g., anti-OX-40, anti-41BB, etc.)

Exclusion criteria

1. Any other current or previous malignancy within the past three years except a) adequately treated basal cell or squamous cell skin cancer, b) carcinoma in situ of the cervix, c) prostate cancer with stable prostate specific antigen (PSA) levels for 3 years, d) or other neoplasm that, in the opinion of the Principal Investigator and with the agreement of the Medical Monitor, will not interfere with study-specific endpoints.
2. Cytotoxic chemotherapy, tyrosine kinase inhibitor (or other targeted anti-cancer agent), radiation therapy, or hormonal therapy within 14 days or 5 half-lives, whichever is longer, prior to Cycle 1 Day 1 (42 days for nitrosoureas or mitomycin C).
3. Immunotherapy or biological therapy (e.g., monoclonal antibodies) within 21 days prior to Cycle 1 Day 1
* EXCEPTION: Washout of anti-PD-1 therapy is NOT required in the Part 3 Expansion Cohorts.
4. Treatment with an unapproved investigational therapeutic agent within 21 days (or 5 half-lives for small molecule agents) prior to Cycle 1 Day 1
* EXCEPTION: Washout of anti-PD-1 therapy is NOT required in the Part 3 Expansion Cohorts.
5. Has a diagnosis of immunodeficiency or any condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other systemic immunosuppressive medications within 14 days prior to the first dose of study treatment. Inhaled steroids and adrenal replacement steroid doses < 10 mg daily prednisone equivalent

are permitted in the absence of active autoimmune disease.;Disease-specific Exclusion Criteria:;For Part 3:
1. Intolerance to prior anti-PD-1/PD-L1 therapy including 1) discontinuation due to immune-related toxicity or, 2) immune-related toxicities that that required intensive or prolonged immunosuppression (including, high-dose IV corticosteroids, > 2 mo of immunosuppressive corticosteroids (i.e., equivalent of >10mg oral prednisone daily) or the addition of potent immunosuppression to corticosteroids (e.g., mycophenolate mofetil/CellCept or infliximab) to manage.
2. Prior severe hypersensitivity (* Grade 3) to pembrolizumab and/or any of its excipients or prior severe hypersensitivity reaction to any other monoclonal antibody (mAb).
3. Has a history of (non-infectious) pneumonitis that required steroids or current pneumonitis.
4. Has a history of interstitial lung disease.
5. Has received transfusion of blood products (including platelets or red blood cells) or administration of colony stimulating factors (including G-CSF, GM-CSF or recombinant erythropoietin) within 2 weeks prior to study Day 1.
6. Active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
7. Concomitant therapy with allopurinol and other xanthine oxidase inhibitors
8. Exclusion criterion deleted in Protocol Amendment 2-EU.
9. Patients with symptomatic ascites or pleural effusion requiring intermittent paracentesis or thoracocentesis. A patient who is clinically stable following treatment for these conditions (including therapeutic thoraco- or para-centesis) is eligible.
10. Unable to receive medications per os (PO)
11. Unstable/inadequate cardiac function:
* Myocardial infarction or symptomatic ischemia within the last 6 months
* Uncontrolled or clinically significant conduction abnormalities (e.g., ventricular tachycardia on antiarrhythmics are excluded; 1st degree AV block or asymptomatic LAFB/RBBB are eligible)
* Congestive heart failure (New York Heart Association class III to IV)
12. Known or suspected defect in the function of the urea cycle, including a known deficiency of carbamoyl phosphate synthetase I, ornithine transcarbamylase, argininosuccinate synthetase, argininosuccinate lyase, N-acetyl glutamate synthetase, or arginase.
13. Major surgery within 2 months prior to first dose of study treatment
14. Infection requiring parenteral antibiotics, antivirals, or antifungals within two weeks prior to first dose of study treatment
15. Patient is known to be positive for Human Immunodeficiency Virus (HIV), Hepatitis B or Hepatitis C.
16. Refractory nausea and vomiting, uncontrolled diarrhea, malabsorption, significant small bowel resection or gastric bypass surgery, use of feeding tubes or other situation that may preclude adequate absorption
17. Serious psychiatric or medical conditions that could interfere with treatment or protocol-related procedures
18. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis.
Note: Patients with brain metastases or CNS disease are permitted, but must have completed

treatment and either (1) have no evidence of active CNS disease for at least 4 weeks prior to the first dose OR (2) have stable CNS lesions, defined as not requiring intrathecal chemotherapy for at least 6 weeks or systemic steroid treatment to prevent CNS complications for at least 3 weeks prior to first dose. Patients with CNS disease must also have a Screening head CT or MRI demonstrating stable disease compared to their most recent CNS evaluation. This exception does not apply to patients with carcinomatous meningitis who are excluded regardless of clinical stability.
19. Patients in whom oral and/or IV fluid hydration are contraindicated
20. Patients who are pregnant or lactating
21. Has received a live-virus vaccination within 30 days of planned treatment start. Seasonal flu vaccines that do not contain live virus are permitted.
22. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the Patient*s participation for the full duration of the trial, or is not in the best interest of the Patient to participate, in the opinion of the treating investigator.
For Part 3a: NSCLC
1. Documented activating mutations in EGFR or ALK.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	INCB001158

Generic name:	(3R,4S)-3-amino-1-((S)-2-aminopropanoyl)-4-(3-boronopropyl)pyrrolidine-3-carboxylic acid
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-07-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-02-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-03-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2017-002903-82-NL
ClinicalTrials.gov	NCT02903914
CCMO	NL66339.091.18