An Open-label Phase 1b/2 Study of Binimetinib Administered in Combination with Nivolumab or Nivolumab Plus Ipilimumab in Patients with Previously Treated Microsatellite-stable (MSS) Metastatic Colorectal Cancer with RAS Mutation.

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Primary:* Phase 1b:o Determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of binimetinib administered in combination with nivolumabo Determine the MTD and RP2D of binimetinib administered in combination with nivolumab plus...

Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON50266

Source
ToetsingOnline

Brief title
ARRAY-162-202

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Colorectal Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Array Biopharma, Inc.
Source(s) of monetary or material Support: Array Biopharma

Intervention

Keyword: binimetinib, colorectal cancer, phase 1b/2 trial

Outcome measures

Primary outcome

* Phase 1b:

o Incidence of dose-limiting toxicities (DLTs) resulting from binimetinib in

combination with nivolumab

o Incidence of DLTs resulting from binimetinib in combination with nivolumab

plus ipilimumab

* Phase 2: Objective response rate (ORR) per RECIST v1.1

Secondary outcome

Secondary:

* Phase 1b only: ORR per RECIST v1.1 Both Phases:

* Duration of response (DOR) per RECIST v1.1

* Rate of complete response (CR) per RECIST v1.1

* Incidence and severity of adverse events (AEs) graded according to the

National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events

(CTCAE) v4.03, and changes in clinical laboratory parameters

* Sparse plasma concentrations for binimetinib

Exploratory:

* PFS per RECIST v 1.1

* OS

* PFS per iRECIST

* ORR per iRECIST

* DOR per iRECIST

* Rate of CR per iRECIST

* Model-based correlations between binimetinib PK and measures of safety and efficacy

* Status of genomic, proteomic, and immune biomarkers in blood and tissue samples at baseline

* Change from baseline in genomic, proteomic, and immune biomarkers

Study description

Background summary

Colorectal cancer is a serious, life-threatening condition. In 2015, colorectal cancer accounted for 774,000 deaths world wide. In the US and Europe, it is the second and fourth most common cancer type, respectively. Approximately 130,000 new cases are diagnosed per year in the US and it is the second leading cause of cancer mortality). In Europe, approximately 450,000 new cases are diagnosed per year and colorectal cancer was responsible for 215,000 deaths in 2012. A quarter of patients initially present with metastases and the majority of patients will eventually develop metastatic disease. Standard systemic therapy in patients with unresectable metastatic colorectal cancer (mCRC) includes combination regimens with cytotoxic and targeted agents. In the last decade, substantial advances in the treatment of mCRC have resulted in an improvement in overall survival (OS) from 10 to 12 months to more than 20 months. This improvement has occurred with the addition of irinotecan, oxaliplatin, bevacizumab, cetuximab, and panitumumab to the standard treatment with 5-fluorouracil (5-FU)/folinic acid (leucovorin).

The proposed study will be conducted in adult patients with advanced mCRC with MSS and presence of a RAS mutation. Patients with colorectal tumors that have defects in the DNA mismatch repair system, also referred to as having a MSI, will be excluded. The central objective of the study will be to determine if nivolumab in combination with binimetinib, or nivolumab in combination with ipilimumab and binimetinib demonstrates a clinically meaningful ORR. For the doublet arm, the targeted response rate is 20%, and for the triplet arm, the targeted response rate is 30% in these patients with MSS mCRC and a RAS mutation. The addition of binimetinib to both nivolumab and nivolumab plus ipilimumab will potentially increase antigen presentation and enhance response to checkpoint inhibitors in MSS tumors.

Study objective

Primary:
* Phase 1b:
o Determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of binimetinib administered in combination with nivolumab
o Determine the MTD and RP2D of binimetinib administered in combination with nivolumab plus ipilimumab
* Phase 2: Assess the preliminary antitumor activity of the treatment combinations based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1

Secondary:
Both Phases:
* Further assess the preliminary antitumor activity of the treatment combinations based on RECIST version 1.1
* Characterize the safety profile of the treatment combinations
* Characterize the pharmacokinetics (PK) of binimetinib in both treatment combinations

Exploratory:
* Obtain preliminary estimates of progression-free survival (PFS) and overall survival (OS)
* Assess the preliminary antitumor activity of the treatment combinations based on immune Response Evaluation Criteria in Solid Tumors (iRECIST)
* Explore binimetinib exposure-response relationships with respect to safety and efficacy
* Assess blood- and tissue-based predictive biomarkers of activity and immune effects

Study design

This is a multicenter, open-label Phase 1b/2 study to determine the MTD and RP2D and schedule of binimetinib, and to assess the safety, efficacy, and PK of

binimetinib administered in combination with nivolumab or nivolumab plus ipilimumab in patients with previously treated MSS metastatic colorectal cancer (mCRC) with documented RAS mutation. The study will include a dose-finding period in Phase 1b followed by a randomized Phase 2 period.
The total number of patients enrolled in Phase 1b of the study will depend on the number of dose levels tested and the number of patients treated in each cohort before the MTD has been determined for each arm.
Approximately 90 patients are required to complete this study. A maximum of approximately 42 patients will be enrolled in Phase 1b and a minimum of approximately 48 patients will be enrolled in Phase 2.
* Phase 1b:
o Arm 1A - binimetinib plus nivolumab (Doublet): To determine the MTD and RP2D and schedule of binimetinib in combination with nivolumab.
o Arm 1B - binimetinib with nivolumab plus ipilimumab (Triplet): To determine the MTD and RP2D and schedule of binimetinib in combination with nivolumab plus ipilimumab.
* Phase 2:
* Arm 2A - binimetinib plus nivolumab (Doublet): To determine the efficacy of binimetinib in combination with nivolumab.
o Arm 2B - binimetinib with nivolumab plus ipilimumab (Triplet): To determine the efficacy of binimetinib in combination with nivolumab plus ipilimumab.
One treatment cycle is defined as 28 days (4 weeks) for all arms. Individual treatments will be dosed on the schedules as outlined below.
Phase 1b of the study will consist of dose-finding cohorts in Arm 1A and Arm 1B. All dose-escalation decisions will be driven by the modified toxicity probability interval (mTPI-2) design.
* Patients assigned to Arm 1A (Doublet) will be dosed with 480 mg nivolumab every 4 weeks (Q4W) and 45 mg twice daily (BID) of binimetinib initially as starting Dose Level 4. In the event that this dose level is not tolerated, lower dose levels, or an intermittent binimetinib dosing schedule.
* Patients assigned to Arm 1B (Triplet) will be dosed with the RP2D of binimetinib from Arm 1A plus 480 mg nivolumab Q4W and 1 mg/kg ipilimumab Q8W. Dose de-escalation will proceed if the treatment is not tolerated..
Intra-patient dose escalation will not be permitted.

Note: In both arms, there will be flexibility to evaluate intermittent dosing schedule of binimetinib (30 or 45 mg BID; e.g., 3 weeks on/1 week off) if continuous dosing is not tolerated depending on the time of onset of DLTs.
In Phase 1b: The target DLT probability for Cycle 1 is 30%, with an equivalence interval, i.e., an acceptable interval, of 25% to 35%. Dosing in Phase 1b will continue within an arm until 9 patients (from the dose- determining set) have been treated at one dose level with a recommendation to stay (or a recommendation to escalate if there is not a higher dose level or if the tolerability of the next dose level is unacceptable), or the maximum sample size within a Phase 1b arm (n=21) has been reached. If further safety evaluations are required, additional patients may be added to a cohort.

Toxicities will only be considered DLTs if they occur in Cycle 1 although overall safety including later cycles will be considered for dose escalations and for each RP2D determination.
Patients are required to complete Cycle 1 (* 75% of the planned cumulative dose of binimetinib) to be considered evaluable for MTD determination unless discontinuation occurred due to a DLT (i.e, in the dose-determining set).
Phase 2 of the study will consist of 2 arms to investigate the safety and clinical activity of the RP2Ds established from Phase 1b: Arm 2A (nivolumab in combination with binimetinib) and Arm 2B (nivolumab plus ipilimumab in combination with binimetinib).

Intervention

Phase 1b:

Arm Dose Level (*Starting Dose Level)
Binimetinib Nivolumab Ipilimumab

1A 4 45
mg BID 480mg Q4W N/A
(Doublet) 3 45 mg
BID 3W on / 1W off 480mg Q4W N/A
2 30
mg BID 480mg Q4W N/A
1 30
mg BID 3W on / 1W off 480mg Q4W N/A

4 45
mg BID 480mg Q4W 1mg/kg Q8W
1B (Triplet)** 3 45 mg BID
3W on / 1W off 480mg Q4W 1mg/kg Q8W
2 30
mg BID 480mg Q4W 1mg/kg Q8W
1 30
mg BID 3W on / 1W off 480mg Q4W 1mg/kg Q8W

* The starting Dose Level of Arm 1B (Triplet) will be the RP2D of binimetinib from Arm 1A. If tolerated, the RP2D from Arm 1A plus ipilimumab will be considered the RP2D for Arm 1B. If not tolerated, any dose level below the RP2D for Arm 1B may be explored.

Phase 2:
Arm 2A: Patients randomized to the nivolumab and binimetinib arm will receive nivolumab administered as 480 mg Q4W as a 30-minute intravenous (IV) infusion

on Day 1 of each treatment cycle and the recommended dose of binimetinib in Arm 1A of Phase 1b.
Arm 2B: Patients randomized to the nivolumab, ipilimumab, and binimetinib arm will receive nivolumab administered as 480 mg Q4W as a 30-minute IV infusion on Day 1 of each treatment cycle, ipilimumab IV as a dose of 1 mg/kg Q8W, and the recommended dose of binimetinib in
Arm 1B of Phase 1b.

Study burden and risks

Side Effects of Binimetinib
Because binimetinib is an investigational drug all of the side effects are not known, and serious side effects, including death, are a possibility. Long-term effects of this treatment are also unknown.

The side effects on binimetinib in combination with nivolumab (double combination) or nivolumab plus ipilumumab (triple combination) are not known. Side effects in cancer patients treated with binimetinib may include those described below.

Most likely side effects (occur in 1 in 5 people or more):
* Alteration of the light sensing part of the back of the eye that may affect your vision including blurred or impaired vision
* Rash, acne or skin irritation including redness, raised bumps, dryness or itching
* Swelling due to fluid retention or a worsening of pre-existing fluid retention in specific areas of the body. This can occur throughout your body or in specific areas such as your abdomen or arms, legs, hands, feet or face.
* Feeling weak, tired, or lacking in energy

Less likely side effects (greater than 1 in 10 people up to 1 in 5 people):
* Muscle spasms, muscle pain or inflammation

Binimetinib has caused mild to moderate visual changes in some patients (swelling and/or inflammation in and around the eyes and changes in the retina, blurred vision and, in some cases, loss of vision). While this type of visual impairment may resolve, there is a risk that the visual changes may continue.

Side Effects of Nivolumab:
Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer subjects in other clinical trials with nivolumab. In addition, there may be side effects that are not yet known that may occur.

Very common side effects of nivolumab are (greater than 1 in 10 people):
* Fatigue
* Diarrhea

* Itching
* Rash

Risks Associated with Nivolumab combined with ipilimumab
Very common side effects (greater than 1 in 10 people):
* ALT and/or ASAT increased: lab test result associated with abnormal liver function
* Decreased appetite
* Diarrhea
* Fatigue
* Fever (Temperature of 38°C or higher)
* Itching
* Lipase increased: lab result associated with pancreaqs inflammation
* Musculoskeletal pain
* Nausea
* Rash
* Thyroid function decreased

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab treatment, may lower thebody*s ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

Contacts

Public
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US
Scientific
Array Biopharma, Inc.

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Prescreening Inclusion Criteria:, 1. Provide a signed and dated Prescreening ICF.
2. Male or female * 18 years of age at the time of signing the Screening ICF.
3. Measurable, histologically/cytologically confirmed mCRC per RECIST v1.1.
4. Have willingness and ability to participate in the study.
5. Able to provide a sufficient amount (tumor block or minimum of 6 slides) of representative tumor specimen (primary or metastatic, archival or newly obtained) for central laboratory testing of RAS mutation status and MSS.
a. If a fresh tissue sample is provided, a blood sample is required.
6. Have received no more than 2 prior lines of systematic therapy in the metastatic setting (maintenance
therapy given in the metastatic setting will not be considered a separate regimen). Generally, treatments that are separated by an event of progression are considered different regimens.
regimens.
7. Have received prior systemic treatment as recommended by National Comprehensive Cancer Network (NCCN) or European Society for Medical Oncology (ESMO) guidelines, including fluoropyrimidines, oxaliplatin, irinotecan or bevacizumab in the metastatic setting or similar treatments, as per local guidelines.
8. No known contraindications to study treatment., Screening Inclusion Criteria:, 1. Patients must meet all Prescreening inclusion criteria.
2. Provide a personally signed and dated Screening ICF.
3. mCRC categorized as MSS by immunohistochemistry (IHC) or polymerase chain reaction (PCR)-based local assay at any time prior to Screening or by the central laboratory.
4. RAS mutation per local assay at any time prior to Screening or by the central laboratory.
5. Have received at least 1 prior line of systematic therapy in the metastatic setting as recommended by National Comprehensive Cancer

Network (NCCN) or European Society for Medical Oncology (ESMO) guidelines, including fluoropyrimidines, oxaliplatin, irinotecan or bevacizumab, or similar treatments, as per local guidelines, and meets at least one of the following criteria:
a. were unable to tolerate the prior first-line regimen
b. experienced disease progression during or after prior first-line regimen for metastatic disease
c. progressed during or within 6 months of completing adjuvant chemotherapy
Note: Generally, treatments that are separated by an event of progression are considered different regimens.
6. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1.
7. Female patients are either postmenopausal for at least 1 year, are surgically sterile for at least 6 weeks; if a female patient is of childbearing potential, she must agree to follow instructions for acceptable or highly effective method(s) of contraception for the duration of study treatment and for 5 months after the last dose of study treatment with nivolumab (i.e., 30 days [duration of ovulatory cycle] plus the time required for the investigational drug to undergo approximately 5 half-lives)
8. Non-sterile male patients who are sexually active with female partners of childbearing potential must agree to follow instructions for acceptable or highly effective method(s) of contraception for the duration of study treatment and for 7 months after the last dose of study treatment with nivolumab (i.e., 90 days [duration of sperm turnover] plus the time required for the investigational drug to undergo approximately 5 half-lives) (Section 5.3).
9. Adequate renal and bone marrow function as measured by the following Screening laboratory values:
a. White blood cells (WBC) * 2000/*L
b. Neutrophils * 1500/*L
c. Platelets * 100 ×103/*L
d. Hemoglobin * 9.0 g/dL
e. Serum creatinine * 1.5 × upper limit of normal (ULN) or calculated creatinine clearance > 50 mL/min (using the Cockcroft Gault formula) or estimated glomerular filtration rate > 50 mL/min/1.73 m2 (using the Modification of Diet in Renal Disease [MDRD] Study formula)
10. Adequate hepatic function characterized by the following Screening laboratory values:
a. Serum total bilirubin * 1.5 × ULN and < 2 mg/dL Note: Patients who have a total bilirubin level > 1.5 × ULN will be allowed if their indirect bilirubin level is * 1.5 × ULN.
b. ALT and/or AST * 2.5 × ULN, or * 5 × ULN in presence of liver metastases
11. Adequate cardiac function as follows:
a. LVEF * 50% or above institutional normal value as determined by a

MUGA scan or ECHO
b. QTcF interval * 480 msec (preferably the mean from triplicate electrocardiograms (ECGs)
12. Willingness and ability to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures including computed tomography (CT)/magnetic resonance imaging (MRI) scans.

Exclusion criteria

Prescreening Exclusion Criteria:, 1. Prior treatment with any MEK inhibitor.
2. Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways.
3. Any untreated central nervous system (CNS) lesion. However, patients are eligible if: a) all known CNS lesions have been treated with radiotherapy or surgery, and b) patients remained without evidence of CNS disease progression * 4weeks after treatment, and c) patients must be off corticosteroid therapy for * 3 weeks.
4. Patients with an active, known or suspected autoimmune disease, with the following exceptions:
patients with type I diabetes mellitus, hypothyroidism only requiring hormone replacement, skin disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
5. Partial or complete bowel obstruction.
6. Impaired gastrointestinal function or disease that may significantly alter the absorption of binimetinib (e.g., ulcerative diseases, uncontrolled vomiting, malabsorption syndrome, small bowel resection with decreased intestinal absorption) or baseline diarrhea * Grade 1.
7. Known history of RVO.
8. Concurrent or previous other malignancy within 5 years of study entry, except cured basal or squamous cell skin cancer, superficial bladder cancer, prostate intraepithelial neoplasm, carcinoma in-situ of the cervix, or other noninvasive or indolent malignancy
9. Known history of Gilbert's syndrome.
10. Severe uncontrolled medical illness.
11. Psychiatric illness inhibiting informed consent or protocol compliance.
12. Pregnant or breastfeeding females.
13. History of severe hypersensitivity reactions to mAbs.
14. History of allergy or intolerance (unacceptable AEs) to study drug components or polysorbate-80-containing infusions., Screening Exclusion Criteria:, 1. Patients must not meet any of the Prescreening exclusion criteria.
2. Treatment with systemic immunosuppressive medications (including but not limited to prednisone, cyclophosphamide, azathioprine,

methotrexate, thalidomide, and anti-tumor necrosis factor [anti-TNF] agents) within 2 weeks prior to first day of study treatment:
a. The use of inhaled corticosteroids and mineralocorticoids (e.g., fludrocortisone) and topical steroids are allowed. Patients who have received acute and/or low-dose systemic immunosuppressant medications (e.g., a one-time dose of dexamethasone for nausea or chronic use of * 10 mg/day of prednisone or dose-equivalent corticosteroid) may be enrolled in the study after discussion with and approval by the Sponsor's Medical Monitor.
3. Impaired gastrointestinal function or disease that may significantly alter the absorption of binimetinib (e.g., ulcerative diseases, uncontrolled vomiting, malabsorption syndrome, small bowel resection with decreased intestinal absorption) or baseline diarrhea * Grade 1.
4. History of thromboembolic or cerebrovascular events * 6 months prior to starting study treatment, including transient ischemic attacks, cerebrovascular accidents, deep vein thrombosis or pulmonary emboli.
5. Uncontrolled hypertension defined as persistent systolic blood pressure * 150 mmHg or diastolic blood pressure * 100 mmHg despite current therapy.
6. Concurrent neuromuscular disorder that is associated with the potential of elevated CK (e.g., inflammatory myopathies, muscular dystrophy, amyotrophic lateral sclerosis, spinal muscular atrophy).
7. History or current evidence of RVO or current risk factors for RVO (e.g., uncontrolled glaucoma or ocular hypertension, history of hyperviscosity or hypercoagulability syndromes).
8. Clinically significant cardiac disease, including, but not limited to, any of the following:
a. Congestive heart failure requiring treatment (New York Heart Association Grade * 2).
b. Clinically significant and uncontrolled atrial fibrillation.
c. History of acute coronary syndromes including myocardial infarction, unstable angina, coronary artery bypass grafting, coronary angioplasty, or stenting < 6 months prior to screening.
d. Symptomatic chronic heart failure, history or current evidence of clinically significant cardiac arrhythmia and/or conduction abnormality < 6 months prior to screening except controlled atrial fibrillation and paroxysmal supraventricular tachycardia.
9. Residual CTCAE * Grade 2 toxicity from any prior anticancer therapy, with the exception of Grade 2 alopecia or Grade 2 neuropathy.
10. Known history of positive test for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
11. Any positive test for hepatitis B virus or hepatitis C virus indicating acute or chronic infection, and/or detectable virus.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-10-2018
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Binimetinib
Generic name:	Binimetinib
Product type:	Medicine
Brand name:	Opdivo
Generic name:	Nivolumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Yervoy
Generic name:	Ipilimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	24-10-2017

Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-02-2018
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-04-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-04-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	31-07-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-08-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
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Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
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Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-03-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-03-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
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Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-10-2019
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-10-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-04-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-04-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-08-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
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Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2017-003464-12-NL
ClinicalTrials.gov	NCT03271047
CCMO	NL63366.031.17

Study results

Date completed: 02-03-2021

Results posted: 24-12-2021

First publication
01-01-1900