A Randomized, Open-Label Phase 3 Trial of BMS-936558 (Nivolumab) versus Investigator's Choice in Advanced (Unresectable or Metastatic) Melanoma Patients Progressing Post Anti-CTLA-4 Therapy.

Published: 08-11-2012
Last updated: 26-04-2024

Primary Objective* To compare the objective response rate and overall survival of BMS-936558 to investigator*s choice in subjects with advanced melanoma.Secondary Objectives* To compare the progression-free survival (PFS) of BMS-936558 to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39162

Source
ToetsingOnline

Brief title
CA209-037

Condition

- Skin neoplasms malignant and unspecified

Synonym
Advanced (Unresectable or Metastatic) Melanoma

Research involving

Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Advanced Melanoma, BMS-936558, Dacarbazine or paclitaxel/carboplatin)

Outcome measures

Primary outcome

The primary objective will be measured by the primary endpoints of OS and ORR in all randomized subjects. OS is defined as the time between the date of randomization and the date of death. For subjects without documentation of death, OS will be censored on the last date the subject was known to be alive. OS will be followed continuously while subjects are on the study drug and every 3 months via in-person or phone contact after subjects discontinue the study drug.

The ORR is defined as the number of subjects with a best overall response (BOR) of complete response (CR) or partial response (PR) divided by the number of randomized subjects. BOR is defined as the best response designation, as determined by the IRC, recorded between the date of randomization and the date of objectively documented progression per RECIST 1.1 or the date of subsequent therapy, whichever occurs first. For subjects without documented progression or subsequent therapy, all available response designations will contribute to the BOR assessment.

Secondary outcome

The first secondary objective (to compare PFS) will be measured by the endpoint PFS in all randomized subjects. It is defined as the time from randomization to the date of the first documented progression, as determined by the IRC, or death due to any cause, whichever occurs first. Subjects who die without a reported progression will be considered to have progressed on the date of their death. Subjects who did not progress or die will be censored on the date of their last evaluable tumor assessment. Subjects who did not have any on study tumor assessments and did not die will be censored on the date they were randomized. Subjects who started any subsequent anti-cancer therapy without a prior reported progression will be censored at the last evaluable tumor assessment prior to initiation of the subsequent anti-cancer therapy.
The second secondary objective will be measured by the same primary endpoints. I.e. ORR and OS in subjects within PD-L1 positive and PD-L1 negative subgroups.
The third secondary objective (to evaluate HRQoL) will be measured by mean changes from screening/baseline in the EORTC QLQ-C30 global health status/QoL composite scale and by mean changes from screening/baseline in the remaining EORTC QLQ-C30 scales in all randomized subjects.

Study description

Background summary

The lifetime risk of developing invasive melanoma has been dramatically increasing and the overall mortality from melanoma continues to rise. Although in 2011, two new agents, ipilimumab and vemurafenib, were approved for advanced melanoma there is still a large unmet need for patients who have progressed post ipilimumab and vemurafenib therapy. Ipilimumab monotherapy at 3 mg/kg has been shown to increase 2-year survival compared to a vaccine control (26% vs.

14%) in previously treated subjects with metastatic melanoma. Ipilimumab 3 mg/kg was approved for treatment of advanced melanoma without restriction to BRAF status in both the EU and US. In the US, ipilimumab was approved without restriction to line of therapy, while in the EU, ipilimumab was indicated in advanced melanoma patients who had received prior therapy.
Approximately 50% of cutaneous melanoma is BRAF mutation positive, and vemurafenib is indicated for the treatment of BRAF V600E mutation positive advanced melanoma. Vemurafenib is a potent inhibitor of mutation positive BRAF and has demonstrated an increased overall survival benefit compared to dacarbazine with a hazard ratio for death of 0.62 with a median overall survival of 13.2 months versus 9.6 months for vemurafenib and dacarbazine, respectively.
Besides these two agents, no other agent has demonstrated an overall survival benefit in a Phase 3 randomized study. Dacarbazine is approved for treatment of metastatic melanoma with a reported objective response rate of 5% to 20% by the US FDA and the EMA, but these responses are short-lived. Other drugs such as temozolomide have not resulted in significant improvement in survival when compared to dacarbazine, with a median overall survival of 7.7 months compared to 6.4 respectively. Fotemustine is approved and used in the EU and demonstrates a response rate of 15% and a median survival of 7.3 months. Finally, carboplatin and paclitaxel is another commonly used cytotoxic treatment regimen recommended by the NCCN and ESMO clinical guidelines with response rates around 11% and median overall survival around 10.5 months. The cytotoxic treatments are fairly well tolerated primarily with hematological adverse events.

The highest unmet need for advanced melanoma subject is currently for those who have progressed post ipilimumab regardless of BRAF status in addition to vemurafenib if BRAF V600 mutation positive given these are the only two agents to have demonstrated overall survival benefit in a Phase 3 study. In an effort to include a homogenous population in this study, subjects will be required to have progressed post anti-CTLA-4 treatment and if BRAF V600 mutation positive, to have also progressed on a BRAF inhibitor.

Study objective

Primary Objective
* To compare the objective response rate and overall survival of BMS-936558 to investigator*s choice in subjects with advanced melanoma.

Secondary Objectives
* To compare the progression-free survival (PFS) of BMS-936558 to investigator*s choice in subjects with advanced melanoma.
* To evaluate whether PD-L1 expression is a predictive biomarker for ORR and OS.
* To evaluate Health Related Quality of Life (HRQoL) as assessed by European Organisation for Research and Treatment of Care (EORTC) QLQ-C30.

Exploratory Objectives
* To evaluate duration of and time to objective response in BMS-936558 and investigator*s choice in subjects with advanced melanoma.
* To assess the overall safety and tolerability of BMS-936558 and investigator*s choice.
* To characterize the pharmacokinetics of BMS-936558 and explore exposure-response relationships with respect to safety and efficacy.
* To characterize the immunogenicity of BMS-936558.
* To explore potential biomarkers associated with clinical response to BMS-936558 by analyzing tumor tissue specimens and serum for proteins, including but not limited to PD-1, PD-L1 and PD-L2 and lymphocytic cell populations involved in regulating immune responses in comparison to clinical outcomes.
* To assess the effects of natural genetic variation (SNPs) in select genes including but not limited to PD-1, PD-L1, PD-L2, CTLA-4 on clinical endpoints and/or on the occurrence of adverse events.
* To assess changes in health status in treatment groups by the EuroQoL EQ-5D both on treatment and during the survival follow-up period.

Study design

This is an open-label, randomized, phase 3 study in adult (* 18 years old) male and female subjects with unresectable or metastatic (advanced) melanoma who have received one and at most two prior treatment regimens in the advanced setting. Subjects will undergo screening evaluations to determine eligibility within 28 days prior to randomization. Subjects will be assigned to one of two treatment arms, BMS-936558 (3 mg/kg every 2 weeks) or investigator*s choice (dacarbazine 1000 mg/m2 or carboplatin AUC6/paclitaxel 175 mg/m2 every 3 weeks). Randomization will be stratified and balanced according to the following factors: PD-L1 expression (PD-L1 positive vs. PD-L1 negative), BRAF status (Wild type vs. Mutation positive) and prior best response to anti-CTLA-4 therapy (Prior anti-CTLA-4 therapy clinical benefit vs. No prior anti-CTLA-4 therapy clinical benefit). Treatment should be initiated within 3 days of randomization. BMS-936558 or investigator*s choice will be administered as an IV infusion on Treatment Day 1. A treatment cycle is defined as 2 weeks for BMS-936558 and 3 weeks for Investigator*s Choice. This study will consist of 3 phases: screening (up to 28 days), treatment and follow-up. Treatment will continue until documented disease progression, there is discontinuation due to toxicity, withdrawal of consent or the study ends. Subjects will be followed every 3 months for survival after completion of the follow-up visits.

Intervention

The medical interventions for this trial include both BMS-936558 and Investigator*s choice (dacarbazine and carboplatin/paclitaxel). All compounds will be supplied by the Sponsor company. BMS-936558 or Investigator*s choice

will be administered as an IV infusion on Treatment Day 1. A treatment cycle is defined as 2 weeks for BMS-936558 and 3 weeks for Investigator*s choice. BMS-936558 will be administered as an IV infusion over 60 minutes, dacarbazine over 30-60 minutes. Paclitxel wil be given as an IV infusion over 180 minutes followed by carboplatin over 30 minutes.

Study burden and risks

As part of the trial, patients will be expected to attend multiple clinic visits where they will undergo physical examinations, vital sign measurements including oxygen saturation levels, blood tests for safety assessment, pregnancy testing (for females of child bearing potential) and monitoring for adverse events. In addition, every 6 weeks (from week 9 onwards) patients will undergo radiographic assessment of their tumour(s) (by CT or MRI) until disease progression or treatment discontinuation whichever occurs later. For those patients randomized to BMS-936558, blood samples will be collected at certain visits for research purposes (PK and immunogenicity). The frequency of visits and number of procedures carried out during this trial would typically be considered over and above standard over care. These procedures are carried out by trained medical professionals and every effort will be made to minimize any risks or discomfort to the patient. Treatment for cancer often have side effects, including some that are life-threatening. An independent Data Monitoring Committee (DMC) will be utilized to monitor the activity and safety of BMS-936558 versus Investigator*s choice (dacarbazine and carboplatin/paclitaxel).

Contacts

Public
Bristol-Myers Squibb

Vijzelmolenlaan 9
Woerden 3447 GX
NL
Scientific
Bristol-Myers Squibb

Vijzelmolenlaan 9
Woerden 3447 GX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed Written Informed Consent
2. Eastern Cooperative Oncology Group (ECOG) performance status of * 1
3. Histologically confirmed Stage III (unresectable) or Stage IV melanoma.
4. Measurable disease by CT or MRI per RECIST 1.1 criteria.
5. A pre-treatment recent core, excision or punch biopsy must be provided for PD-L1 status determination prior to randomization and for exploratory biomarker analyses. The biopsy must be from a unresectable or metastatic site, and the subject must have had no intervening systemic therapy between the time of biopsy and randomization. In order to be randomized, a subject must be classified as PD-L1 positive, PD-L1 negative or PD-L1 indeterminate. If an insufficient amount of recently acquired tumor tissue from an unresectable or metastatic site is available prior to the start of the screening phase, subjects must consent o allow the acquisition of tumor biopsy by study personnel for performance of biomarker analyses.
6. Subjects must consent to allow the acquisition of existing formalin-fixed paraffin embedded (FFPE) material (*archival*) (block or a minimum of 10 unstained slides) if available, for performance of correlative studies.
7. Subjects must have objective evidence of disease progression (eg. clinical or radiological) during or after at least 1 (V600 wildtype) or at least 2 (V600 mutation positive) prior treatment regimens for advanced melanoma.
* Subjects BRAF wildtype:
- Must have objective evidence of progression of disease (PD) post (during or following) treatment with anti-CTLA-4 containing therapy for advanced melanoma.
AND
- In addition to progression post anti-CTLA-4 therapy, subjects that have received another treatment regimen must have objective evidence of progression of disease (PD) during or following at least 1 cycle of treatment for advanced melanoma.
* Subjects BRAF V600 mutation positive:
- Must have objective evidence of progression of disease (PD) post treatment with anti-CTLA-4 containing therapy for advanced melanoma.

AND
- In addition to progressing post anti-CTLA-4 therapy, subjects must have objective evidence of progression of disease (PD) post treatment with a BRAF inhibitor.
- Subjects may have received prior anti-CTLA-4 therapy and a BRAF inhibitor in any sequence or in combination.
8. Prior chemotherapy or immunotherapy (tumor vaccine, cytokine, or growth factor given to control the cancer) must have been completed at least 4 weeks before study drug administration, and all adverse events have either returned to baseline or stabilized.
9. Prior anti-CTLA-4 therapy must have been completed at least 6 weeks before study drug administration.
10. Prior radiotherapy must have been completed at least 2 weeks prior to study drug administration.
11. Screening laboratory values must meet the following criteria and should be obtained within 14 days prior to randomization:
i. WBC * 2000/uL
ii. Neutrophils * 1500/uL
iii. Platelets * 100x10*3/uL
iv. Hemoglobin * 9.0 g/dL
v. Creatinine Serum creatinine * 1.5 x ULN or CrCl > 40 mL/min (using the Cockcroft-Gault formula)
vi. AST/ALT * 3 x ULN
vii. Bilirubin * 1.5 x ULN (except subjects with Gilbert Syndrome, who can have total bilirubin < 3.0 mg/dL).
12. Men and women aged * 18 years of age.
13. Women of childbearing potential (WOCBP) must use method(s) of contraception based on the tables in Appendix 1. Dacarbazine, carboplatin and paclitaxel are teratogenic. There is an insufficient amount of information to assess teratogenicity for BMS-936558. For a teratogenic study drug and/or when there is sufficient information to assess teratogenicity (preclinical studies have not been done), a highly effective method(s) of contraception (failure rate of less than 1% per year) is required. The individual methods of contraception and duration should be determined in consultation with the investigator. WOCBP must follow instructions for birth control when the half life of the investigational drug is greater than 24 hours, contraception should be continued for a period of 30 days plus the time required for the investigational drug to undergo five half lives. The half-life of BMS-936558 is up to 25 days; therefore, WOCBP who received BMS-936558 should use an adequate method to avoid pregnancy for 23 weeks after the last dose of BMS-936558. WOCBP must follow instructions for birth control when the half life of the investigational drug is less than 24 hours, contraception should be continued for a period of 30 days after the last dose of investigational product. The half-life of dacarbazine, carboplatin and paclitaxel is less than 24 hours, therefore WOCBP who received either dacarbazine, carboplatin or paclitaxel should use an adequate method to avoid pregnancy for 30 days after the last dose of either dacarbazine, carboplatin or paclitaxel.
14. WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of investigational product.
15. Women must not be breastfeeding
16. Men who are sexually active with WOCBP must use any contraceptive method with a failure rate of less than 1% per year (See Appendix 1). The investigator shall review

contraception methods and the time period that contraception must be followed. Men that are sexually active with WOCBP must follow instructions for birth control when the half life of the investigational drug is greater than 24 hours, contraception should be continued for a period of 90 days plus the time required for the investigational drug to undergo five half lives. The half-life of BMS-936558 is up to 25 days; therefore, men who received BMS-936558 and are sexually active with WOCBP must continue contraception for 31 weeks after the last dose of BMS-936558. The half-life of dacarbazine, carboplatin and paclitaxel is less than 24 hours. However, the dacarbazine product label requires men who received dacarbazine and are sexually active with WOCBP to use an effective method of contraception for at least 6 months after the last dose of dacarbazine.

Exclusion criteria

1. Active brain metastasis or leptomeningeal metastasis. Subjects with brain metastases are eligible if these have been treated, and must be without magnetic resonance imaging (MRI) evidence of progression for at least 8 weeks and not require immunosuppressive doses of systemic corticosteroids (> 10 mg/day prednisone or equivalent) for at least 2 weeks prior to study drug administration.
2. Ocular melanoma.
3. Subjects whose melanoma is BRAF status unknown.
4. Any treatment in a BMS-936558 trial.
5. Prior systemic melanoma therapy with both dacarbazine and carboplatin and paclitaxel. Prior systemic therapy with one of the treatments is permitted.
6. Any serious or uncontrolled medical disorder or active infection that, in the opinion of the investigator, may increase the risk associated with study participation, study drug administration, or would impair the ability of the subject to receive protocol therapy.
7. Subjects with previous malignancies (except non-melanoma skin cancers, in situ bladder cancer, gastric or colon cancers, cervical cancers/dysplasia, or breast carcinoma in situ) are excluded unless a complete remission was achieved at least 2 years prior to study entry and no additional therapy is required or anticipated to be required during the study period.
8. Subjects with active, known or suspected autoimmune disease. Subjects with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
9. Subjects with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of study drug administration. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
10. Subjects who received prior therapy with an anti-PD-1, anti-PD-L1 or anti PD L2, (or any other antibody or drug specifically targeting T-cell co stimulation or checkpoint pathways except for anti-CTLA-4 therapy as described above).
11. Known drug or alcohol abuse.
12. Any positive test result for hepatitis B virus or hepatitis C virus indicating acute or chronic infection.

13. Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
14. Subjects with a known history of the following anti-CTLA-4 therapy related adverse reactions based on the CTCAE v4.0 criteria:
i) Grade * 4 anti-CTLA-4 therapy related adverse reaction except resolved nausea, fatigue, infusion reactions or endocrinopathies where clinical symptoms were able to be controlled with appropriate hormone replacement therapy. Grade 3 anti-CTLA-4 therapy related adverse reactions must have resolved or been controlled within 12 weeks.
ii) Any * Grade 2 eye pain or reduction of visual acuity that did not respond to topical therapy and did not improve to * Grade 1 severity within 2 weeks of starting topical therapy or required systemic treatment.
iii) Any * Grade 3 sensory neurologic toxicity.
iv) Any Grade 4 laboratory abnormalities, except AST, ALT or T. bilirubin;
- AST or ALT > 10 x ULN
- T. bilirubin > 5 x ULN
v) Subjects who required infliximab or other immune suppressants including mycophenolic acid for management of drug related toxicities.
vi) Any other anti-CTLA-4 therapy related adverse event requiring permanent discontinuation of anti-CTLA-4 therapy.
15. History of Grade * 3 neurologic toxicity.
16. History of Grade * 3 allergy to study drug components.
17. WOCBP who are pregnant or breastfeeding.
18. Women with a positive pregnancy test at enrollment or prior to administration of study medication.
19. Prisoners or subjects who are involuntarily incarcerated.
20. Subjects who are compulsorily detained for treatment of either a psychiatric or physical (e.g., infectious disease) illness.
21. Current participation in another clinical study involving treatment with medications, radiation or surgery.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-06-2013
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BMS-936558
Generic name:	Nivolumab
Product type:	Medicine
Brand name:	DTIC
Generic name:	Dacarbazine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paraplatin
Generic name:	Carboplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-11-2012
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-02-2013
Application type:	First submission

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-02-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	20-03-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-05-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-06-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-06-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-08-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	23-08-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-01-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-05-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-01-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-05-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-04-2017

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-05-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-09-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-02-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-01-2019
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:	11-10-2019
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	EUCTR2012-001828-35-NL
ClinicalTrials.gov	NCT01721746
CCMO	NL41284.031.12

Study results

Results posted: 22-11-2021

First publication
17-11-2021