Phase 1/2a First-In-Human Study of BMS-986218 Monoclonal Antibody Alone & in Combination with Nivolumab in Advanced Solid Tumors

Published: 17-08-2020
Last updated: 09-04-2024

Primary Objectives: - To characterize the safety, tolerability, and DLTs and to determine the MTD/RP2D of BMS-986218 administered as monotherapy and in combination with nivolumab in participants with advanced solid tumors- To evaluate the efficacy...

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

Summary

ID

NL-OMON54185

Source
ToetsingOnline

Brief title
CA022-001

Condition

- Other condition

Synonym
Solid Tumors

Health condition

advanced solid tumour, advanced stage cutaneous melanoma and Lung/NSCLC (adenocarcinoma and squamous cell carcinoma). Other tumor histologies may also be

included by the Sponsor.

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Ipilimumab, Nivolumab, Solid Tumors

Outcome measures

Primary outcome

Safety Outcome Measures:

Safety assessments will be based on comprehensive medical review of adverse event reports, vital sign measurements, ECGs, physical examinations, oxygen saturation, and results of laboratory tests. Adverse events will be assessed continuously during the study and for 100 days after the last treatment. The incidence of observed adverse events will be tabulated and reviewed for potential significance and clinical importance.

Efficacy Measures:

Disease assessment with CT and/or MRI, as appropriate, will be performed at baseline and

Part 2A : Tumour imaging assessment to be performed at 12 weeks from the first dose, regardless of dose delays, if any (+/- 1 week), prior to initiating the next cycle of treatment.

Part 2B, 2C and 2D : Tumour imaging assessment to be performed Q8W from the

first dose (+/- 1 week), prior to initiating next cycle of treatment.

After that, subsequent tumour imaging assessments to be performed Q8W (+/- 1 week), prior to initiating the next cycle of treatment.

Participants who remain free of subsequent therapy will undergo tumour imaging assessment Q8W (+/- 1 week) until subsequent tumour-directed therapy is initiated or until 48 weeks after discontinuation of trial treatment/EOT visit, and then Q12W (+/- 2 weeks) for a total duration of 2 years.

Secondary outcome

Pharmacokinetic Measures:

Serial serum samples will be collected from all subjects at specified time points to evaluate concentrations of BMS-986218. PK parameters such as Cmax, Ctrough, Tmax, T-HALF, AUC (TAU), CLT, and accumulation index (AI) will be derived, if feasible, from serum concentration versus time data.

Parameters that May be Assessed Following the Dose Administration in Cycle 3:

CLT, Css-avg-AI and T-HALF.

Imaging Measures:

The same imaging modality is to be used for all assessments, per RECIST v1.1 (Appendix 5) or per PCWG 3 criteria for prostate (Appendix 12). Tumor assessment to be performed prior to initiating next cycle of treatment. CT and MRI scans should be acquired with slice thickness of 5 mm or less with no intervening gap (contiguous). Every attempt should be made to image each participant using an identical acquisition

protocol on the same scanner.

Immunogenicity Measures:

Serum samples for BMS-986218, ipilimumab, and nivolumab ADA and cytokines will be collected from all participants at specified timepoints.

Biomarker Measures:

Biomarker measures of baseline and on-treatment peripheral blood, serum, and tumor samples will be used to identify PD markers associated with treatment. Additional biomarkers related to mechanism of action, safety biomarkers, and associations with response to BMS-986218, alone
and in combination with nivolumab, will be explored.

Peripheral blood and tumor tissue will be collected prior to therapy and on-treatment. Biopsies must be performed at the time of progression or suspected progression for participants on study treatment for more than 4 cycles, and tumor samples (block or slides) must be submitted for analysis. If biomarker samples are drawn but study treatment(s) is not administered, samples will be retained. A detailed description of each assay system is described below and a schedule of pharmacodynamic evaluations is provided in the protocol.

Study description

Background summary

This is a Phase 1/2a, first-in-human (FIH) study of BMS-986218, a non-fucosylated (NF) variant of the anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) monoclonal antibody (mAb), alone and in combination with nivolumab (anti-programmed cell death 1 [PD-1]), in humans with advanced solid tumors.
Anti-CTLA-4 (ipilimumab) and anti-PD-1 (nivolumab) are approved immunotherapies that define the field of checkpoint blockade. Ipilimumab is the first immunotherapy to show a survival advantage in late-stage metastatic melanoma and has also demonstrated a significant 25% reduction in risk of recurrence or death in the adjuvant treatment in melanoma. Blockade of CTLA-4 by ipilimumab has demonstrated anti-tumor activity in other malignancies, including lung, prostate cancer, and renal cell carcinoma (RCC). However, no significant activity was observed in bladder, colorectal, esophageal, pancreatic, gastric, hepatocellular, or breast cancer. Ipilimumab is also currently in clinical development in combination with nivolumab. The combination was associated with a greater benefit in melanoma compared to each single agent. Benefit with the combination has also been observed in non-small cell lung cancer (NSCLC) and RCC and is currently being evaluated in other tumor types. The activation of a pre-existing but attenuated immune response to cancer by checkpoint blockade is associated with an adverse event (AE) profile that is inherent to immune activation. Ipilimumab treatment-related AEs can involve multiple organ systems (digestive, skin, and endocrine) that require cessation of drug and treatment with steroids, which attenuate the AEs but do not maintain anti-tumor responses. The combination regimen is associated with an increased incidence of AEs compared to nivolumab monotherapy, but a similar overall AE profile. Developing a new anti-CTLA-4 antibody (Ab) with a more manageable AE profile and an increased depth and breadth of response would provide a significant improvement to anti-CTLA-4 therapy.

BMS-986218 (CTLA-4.4g1fa-nf) is a human mAb against CTLA-4. The sequence is derived from the original hybridoma 10D1. The amino acid sequence is exactly the same as that of ipilimumab but differs solely in its glycosylation pattern. The Ab is expressed in a fucosyltransferase-8 knockout Chinese hamster ovary cell line.
Compared to ipilimumab, the glycans attached to the heavy chain Ab do not contain fucose. As a consequence, the NF Ab harbors a higher affinity for Fc* receptors and improves antibody-dependent cellular cytotoxicity (ADCC) in addition to the CTLA-4 blocking activity of ipilimumab. T-regulatory cells (Tregs) are highly infiltrating in tumors, where they play an important role in impairing anti-tumor immune response by dampening effector cytolytic T-cell function. Tregs in tumors express higher levels of CTLA-4, and some studies have shown that part of the mechanism of action of ipilimumab is related to Treg depletion triggered by ADCC mediation once ipilimumab binds to

CTLA-4-positive Tregs, but this aspect is controversial and ipilimumab may not be a strong ADCC-mediating Ab.
Pre-clinical studies with anti-CTLA-4-NF show enhanced ADCC compared to ipilimumab, correlating with more profound Treg depletion in the tumor (but not the periphery). Therefore, it is expected that anti-CTLA-4-NF will result in a more efficacious therapy by combining CTLA-4 blocking with the depletion of Tregs expressing CTLA-4.
Based on this differentiated mechanism of action, this study will evaluate the safety and preliminary efficacy of BMS-986218 alone and in combination with nivolumab in tumors where ipilimumab did not demonstrate sufficient clinical activity and in tumors where high Treg infiltration is correlated with worse prognosis (eg, NSCLC, RCC, cutaneous melanoma), or in participants with progressive or recurrent disease after prior immunotherapy with an anti-PD-1 or anti-programmed death ligand 1 (PD-L1) containing regimen.

Study objective

Primary Objectives:
- To characterize the safety, tolerability, and DLTs and to determine the MTD/RP2D of BMS-986218 administered as monotherapy and in combination with nivolumab in participants with advanced solid tumors
- To evaluate the efficacy and safety of BMS-986218 monotherapy relative to ipilimumab in participants with advanced cutaneous melanoma previously treated with anti-PD-1/PD-L1 immunotherapy (Part 2 A only)
- To evaluate the efficacy and safety of BMS-986218 alone and in combination with nivolumab in NSCLC (Part 2B and Part 2C)
- To evaluate the efficacy and safety of BMS-986218 alone and in combination with nivolumab in MSS CRC (Part 2D)

Secondary Objectives:
- To evaluate the preliminary efficacy of BMS-986218 alone and in combination with nivolumab in advanced solid tumors (Part 1A and Part 1B)
- To characterize the PK and immunogenicity of BMS-986218 when administered alone and in combination with nivolumab

Exploratory Objectives:
- To explore the potential associations between anti-tumor activity and select biomarker measures in the tumor and peripheral blood prior to treatment and following administration of BMS-986218 alone and in combination with nivolumab
- To explore the associations between BMS-986218 serum PK, safety, efficacy, and clinical biomarkers
- To characterize cytokines, circulating immune subsets,TILs, gene expression profile, proteomics, and Foxp3/CD8 receptor ratio and explore the association between response and pharmacodynamic markers in the tumor and peripheral blood
- To measure Tregs, and assess Treg change over time and in association with response
- To assess the preliminary efficacy of BMS-986218 alone and in combination

with nivolumab in advanced solid tumors using iRECIST
- To assess the OS in participants treated with BMS-986218 alone and in combination with nivolumab
- To characterize the PK and immunogenicity of nivolumab when administered in combination with BMS-986218
- To assess the potential effect of BMS-986218 when administered as monotherapy on the QTc interval
- To evaluate TTD in QoL and physical functioning (Part 2A)
- To evaluate changes in QoL, health status and patient reported tolerability (Part 2A, Part 2B, Part 2C,and Part 2D)

Study design

This is a Phase 1/2a, open-label study of BMS-986218, administered as a single agent and in combination with nivolumab, in participants with advanced solid tumors. The study is comprised of 2 parts: dose escalation and dose expansion.

Part 1: The Dose Escalation Phase, where the dose of BMS-986218, given alone or in combination with nivolumab, is escalated to determine the maximum tolerated dose/recommended Phase 2 dose (MTD/RP2D).
The Safety Evaluation of Combination Doses of BMS-986218 with Nivolumab (Part 1B) will evaluate the safety and tolerability of doses of BMS-986218 in combination with nivolumab. The combination of BMS-986218 with nivolumab will be evaluated using a BLRM employing the EWOC principle. Starting at least 1 dose level lower than the current monotherapy dose level of BMS-986218 demonstrating an acceptable safety
profile, BMS-986218 will be studied in combination with a 480 mg Q4W flat dose of nivolumab.
Determination of the MTD for the Safety Evaluation of Combination Doses of BMS-986218 with Nivolumab (Part 1B) will be guided by BLRM-copula.

Part 2: The Expansion Phase, where the cohort of participants is expanded to gather additional safety, tolerability, preliminary efficacy, pharmacokinetic (PK), and pharmacodynamic information in specific patient populations, regarding BMS-986218 alone and in combination with nivolumab.
- The Randomized BMS-986218 Monotherapy Cohort Expansion in Cutaneous Melanoma (Part 2A) will evaluate the preliminary efficacy of BMS-986218 monotherapy relative to ipilimumab monotherapy in a cohort of cutaneous melanoma participants who have received prior immunotherapy with an anti-PD-1 or anti-PD-L1 containing regimen and must have progressive or recurrent disease after prior PD-1/PD-L1 directed therapy. Three dose levels for BMS-986218 from the Part 1A Q4W monotherapy escalation will be evaluated that have had at least 6 DLT evaluable participants and meet safety criteria: one at 7 mg Q4W, one at 20 mg Q4W, and one at 70 mg Q4W. Evaluating multiple different doses will aid in selecting the regimen that will ultimately provide the optimal benefit-risk ratio to future study participants. Participants must not have received prior anti-CTLA-4 therapy in the advanced or metastatic setting.

- The Randomized BMS-986218 Monotherapy Cohort Expansion (Part 2B) will evaluate the preliminary efficacy of BMS-986218 in tumor types in which a high level of Treg infiltration correlates with poor prognosis. The tumor types to be evaluated will include NSCLC; other tumor types may be explored in the future. Participants should have received and then progressed on or relapsed/recurrence after anti-PD-1/PD-L1 directed therapy in monotherapy or in combination with chemotherapy. Prior anti-CTLA-4 therapy is allowed for no more than 20% of participants. Participants who have been intolerant to prior immunotherapy are excluded. Three dose levels or schedules for BMS-986218 from the Part 1A Q4W monotherapy escalation will be evaluated that have had at least 6 DLT evaluable participants and meet safety criteria: one at 7 mg Q4W, one at 20 mg Q4W, and one at 70 mg Q4W. The rationale for evaluating multiple dose levels is to optimize the benefit-risk ratio for the participant.
- In the BMS-986218 Combination Therapy Cohort Expansion (Part 2C) in NSCLC, the preliminary efficacy and safety of BMS-986218 in combination with nivolumab will be assessed in participants with NSCLC who have progressed or relapsed after anti-PD-1/PD-L1 therapy. Participants must not have received prior anti-CTLA-4 therapy in the advanced or metastatic setting. One or more doses to be evaluated in Part 2C will be selected from the range of doses assessed as tolerable in Part 1B, and which do not exceed the MTD or highest dose administered that has cleared safety. These dose(s) will be selected based on the totality of available safety, tolerability, efficacy, PK and PD data. The evaluation of efficacy in Part 2C will initially occur at one or more dose levels starting with up to 20 participants at each dose level. Additional participants up to 40 at a dose level may be evaluated following initial signal assessment. In Part 2C, participants will be treated Q4W for up to 2 calendar years regardless of treatment delays.
- In the BMS-986218 Combination Therapy Cohort Expansion in MSS CRC (Part 2D), the preliminary efficacy and safety of BMS-986218 in combination with nivolumab will be assessed in participants with MSS CRC who have progressed or relapsed on at least 1 prior standard therapy. Participants must not have received prior anti-CTLA-4 therapy in the advanced or metastatic setting. The dose to be evaluated in Part 2D will be selected from the range of doses assessed as tolerable in Part 1B, and which do not exceed the MTD or highest dose administered that has cleared safety. The dose will be selected based on the totality of available safety, tolerability, efficacy, PK, and PD data.
Regardless of whether or not RAS mutation status is known, all participants will be tested during screening for extended RAS (NRAS and KRAS) and BRAF mutation status. Results from this testing at screening is not required prior to receiving treatment on study. The RAS status evaluation will be conducted with the goal of enrolling approximately 20 participants each with either mutation or wild-type with respect to extended RAS status. The Sponsor may elect to prioritize enrollment of participants based on mutation status. In Part 2D, participants will be treated Q4W for up to 2 calendar years regardless of treatment delays.

The duration of the study will be approximately 5 years.

Intervention

All dosing will occur every three or four weeks as follows:
- Part 1B (BMS-986218 + Nivolumab), will be administered every 4 weeks on Day 1 of each 28 days cycle.
- Part 2A (BMS-986218 monotherapy for cutaneous melanoma subjects), will be administered every 4 weeks on Day 1 of each 28 days cycle.
- Part 2A (Ipilimumab monotherapy for cutaneous melanoma subjects) will be administered every 3 weeks on Day 1 of each 21 day cycle.
- Part 2B (BMS-986218 monotherapy for NSCLC- adenocarcinoma or squamous cell subtypes), will be administered every 4 weeks on Day 1 of each 28 days cycle.
- Part 2C (NSCLC participants) (BMS-986218 + Nivolumab), will be administered every 4 weeks on Day 1 of each 28 days cycle.
- Part 2D (MSS CRC participants) (BMS-986218 + Nivolumab), will be administered every 4 weeks on Day 1 of each 28 days cycle.

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 women of child bearing potential), and monitoring for adverse events.
In addition,patients will undergo radiographic assessment of their tumours (by CT or MRI) as per follow:
Body Imaging
Part 2A : Tumour imaging assessment to be performed at 12 weeks from the first dose, regardless of dose delays, if any (+/- 1 week), prior to initiating the next cycle of treatment.
Part 2B, 2C and 2D : Tumour imaging assessment to be performed Q8W from the first dose (+/- 1 week), prior to initiating next cycle of treatment.
After that, subsequent tumour imaging assessments to be performed Q8W (+/- 1 week), prior to initiating the next cycle of treatment.
Participants who remain free of subsequent therapy will undergo tumour imaging assessment Q8W (+/- 1 week) until subsequent tumour-directed therapy is initiated or until 48 weeks after discontinuation of trial treatment/EOT visit, and then Q12W (+/- 2 weeks) for a total duration of 2 years.

Brain Imaging: Participants with history of brain metastasis will have MRI performed as clinically indicated and at the discretion of the Investigator.

Contacts

Public
Bristol-Myers Squibb

c/o Bristol - Myers Squibb B.V. Orteliuslaan 1000
Utrecht 3528 BD
NL
Scientific
Bristol-Myers Squibb

c/o Bristol - Myers Squibb B.V. Orteliuslaan 1000
Utrecht 3528 BD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Participants must be at least 18 years old and have histologic or cytologic confirmation of
a solid tumor that is advanced (metastatic, recurrent and/or unresectable) with measurable
disease per RECIST v1.1 or per PCWG 3 criteria for prostate and have at least one soft-tissue lesion accessible for biopsy.
b) Eastern Cooperative Oncology Group Performance Status of 0 or 1
c) The Safety Evaluation of Combination Doses of BMS-986218 with Nivolumab (Part 1B):
i) Select solid tumor histologies will be permitted during dose escalation, except for
participants with CNS metastases as the only site of active disease. The

included
histologies will be NSCLC (squamous or adenocarcinoma), gastric adenocarcinoma (including GE junction), TNBC, CRC (adenocarcinoma), pancreatic adenocarcinoma, metastatic castrate resistant prostate adenocarcinoma, urothelial carcinoma or SCCHN (oral cavity, pharyngeal, oropharyngeal, hypopharynx, or laryngeal tumors only). Any other cancers of the
head and neck, including salivary gland and neuroendocrine tumors, are excluded from
enrollment. Histologically confirmed recurrent or metastatic carcinoma of the nasopharynx, SCC or other cancers of the skin of head and neck, and non-squamous histologies are not allowed. Additional tumor histologies may also be included by the Sponsor.
ii) Participants must have received, and then progressed, relapsed, or been intolerant to at
least 2 systemic therapy regimens with proven survival benefit in the advanced or
metastatic setting according to tumor type, where available. If the participant refuses
or is not eligible for these regimens, the reason must be documented in the medical record. However, if anti-PD-1 therapy is approved in a given indication, participants
are eligible to receive this treatment as part of the combination regimen in this study
prior to having completed 2 prior systemic therapy regimens after discussion and agreement with the Medical Monitor (or designee). For hormone-sensitive cancers, all
previously received and available hormonal therapies will be considered as 1 systemic
therapy regimen for the purposes of eligibility. For prostate cancer, only metastatic
castrate resistant prostate cancer is allowed.
d) The Randomized BMS-986218 Monotherapy Cohort Expansion in Cutaneous Melanoma (Part 2A):
i) Participants with advanced stage cutaneous melanoma who have received standard therapies with proven survival benefit including prior immunotherapy with an anti-PD-1 or anti-PD-L1 containing regimen and must have progressive or recurrent disease after prior PD-1/PD-L1 directed therapy. Participants must not have received prior anti-CTLA-4 therapy in the advanced or metastatic setting. Additionally, participants with cutaneous melanoma must have also been offered mutation-directed therapy, if indicated, that has proven survival benefit; if a participant refuses such
therapy, it must be documented in the medical record. No more than 1 intervening therapy is allowed but not required between prior anti-PD-1/anti-PD-L1 containing regimen and BMS-986218. No more than 70% of the randomized participants should have had progression of disease within a period of 6 months of start of therapy with anti-PD-1/PD-L1 agent. Only cutaneous melanoma is allowed. Mucosal and uveal/ocular melanomas are not allowed;

melanoma with unknown primary site may be enrolled if the investigator determines mucosal and uveal/ocular primary sites are unlikely.
e) The BMS-986218 Cohort Expansion - Monotherapy (Part 2B):
i) Participants must have received, and then progressed, relapsed, or been intolerant to at
least 2 standard systemic therapies with proven survival benefit according to their tumor types in the advanced or metastatic setting, if available. If the participant refuses or is not eligible for these regimens, the reason must be documented in the medical record. Additionally, participants must have progressed or have recurrent disease after prior immunotherapy with anti-PD-1/anti-PD-L1 either by itself or in combination with other systemic therapy agents. No more than 1 intervening therapy is allowed but not required between prior anti-PD-1/anti-PD-L1 containing regimen and BMS-986218. Participants who have been intolerant to prior immunotherapy are excluded. Prior anti-
CTLA4 therapy is allowed for no more than 20% of participants, and details of treatment (including dates, doses, and response) must be available.
(1) Lung/NSCLC (adenocarcinoma or squamous cell carcinoma); additionally for NSCLC, all participants with adenocarcinoma must have known EGFR, ALK, and ROS-1 status. Participants with an activating EGFR mutation, ALK translocation, or ROS-1 mutation must have received appropriate inhibitor therapy.
(2) Other tumor histologies may also be included by the Sponsor.
k) The BMS-986218 NSCLC Cohort Expansion - Combination (Part 2C):
i) Participants must have received, and then progressed, relapsed, or been intolerant to at least 2 standard systemic therapies (including anti-PD-1/anti-PD-L1 therapies) with proven survival benefit according to their tumor types in the advanced or metastatic setting, if available. If the participant refuses or is not eligible for these regimens, the reason must be documented in the medical record. Participants must have progressed or have recurrent disease after prior immunotherapy with anti-PD-1/anti-PD-L1 either by itself or in combination with other systemic therapy agents. No more than 1 intervening therapy is allowed but not required between prior anti-PD-1/anti-PD-L1 containing regimen and BMS-986218. Participants who have been intolerant to prior immunotherapy are excluded. Participants must not have received prior anti-CTLA-4 therapy in the advanced or metastatic setting.
The Sponsor may elect to prioritize enrollment of participants with best overall response (BOR) of SD, PR, or CR > than 6 months duration in response to prior anti-PD-1/anti-PD-L1 treatment.
(1) Lung/NSCLC (adenocarcinoma or squamous cell carcinoma); all participants with adenocarcinoma must have known EGFR, ALK, Kirsten rat sarcoma viral oncogene homolog (KRAS), and ROS-1 status (when testing is available as per country/region standard of care practices), participants with an activating EGFR mutation, ALK translocation, or ROS-1 mutation must have received appropriate inhibitor therapy (as available per country/region standard of care). Note: If KRAS results are not known, then a sample (tissue of microscopic slides, tissue block, or
a fresh tissue biopsy in formalin) should be sent for testing locally.

Circulating tumor DNA may be used if sequencing or polymerase chain reaction (PCR) results are not feasible, with prior Sponsor approval.
l) The BMS-986218 MSS CRC Cohort Expansion - Combination (Part 2D):
i) Participants must have received and then progressed on or after, or have been intolerant
or refractory to, at least 1 standard systemic therapy for metastatic and/or unresectable disease (or have progressed within 6 months of adjuvant therapy). If the participant refuses or is not eligible for these regimens, the reason must be documented in the medical record and participant can be enrolled.
(1) Prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan given as single regimen or over multiple regimens is required.
(2) Prior treatment with an anti-angiogenic therapy (eg, bevacizumab) is required.
ii) Participants must have known microsatellite instability (MSI) or mismatch repair status. Extended RAS (KRAS and NRAS), and BRAF status if known, should be documented.
(1) If known to be RAS wild-type, available treatments with demonstrated benefit (eg, anti-EGFR therapy) must have been received as prior treatments if consistent with approved local standard of care. The Sponsor may elect to prioritize enrollment of participants based on mutation status to ensure approximately 50 % of patients treated are RAS mutant.

Exclusion criteria

Participants with primary CNS malignancies, or tumors with CNS metastases as the only site of disease, will be excluded. Participants with controlled brain metastases; however, will be allowed to enroll. Controlled brain metastases are defined as no radiographic progression for at least 4 weeks following radiation and/or surgical treatment (or 4 weeks of observation if no intervention is clinically indicated), and no longer taking steroids for at least 2 weeks prior to first dose of study treatment, and with no new or progressive neurological signs and symptoms.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-03-2021
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	anti-CTLA4-NF mAb
Registration:	Yes - NL intended use
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:	17-08-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-01-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-04-2021
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-09-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-000597-11-NL
CCMO	NL74496.031.20
Other	U1111-1192-5477