A Randomized, Open-label Phase 2 Clinical Trial of BMS-986012 in Combination with Carboplatin, Etoposide, and Nivolumab as First-line Therapy in Extensive-stage Small Cell Lung Cancer

Published: 16-03-2021
Last updated: 19-09-2024

This study has been transitioned to CTIS with ID 2024-510700-36-00 check the CTIS register for the current data. Study CA001-050 is a Phase 2 randomized, open label, multicenter clinical study designed to assess the safety and tolerability, of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54331

Source
ToetsingOnline

Brief title
CA001-050

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
cancer, lung carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: anti-fucosyl GM-1, Extensive Stage Small Cell Lung Cancer, immunotherapy, Nivolumab

Outcome measures

Primary outcome

1. To assess the safety and tolerability for participants randomized to

BMS-986012 in combination with carboplatin, etoposide, and nivolumab for 4

cycles (induction) followed by BMS-986012 and nivolumab maintenance (Arm A) vs

those randomized to carboplatin, etoposide, and nivolumab for 4 cycles

(induction) followed by nivolumab maintenance (Arm B).

2. To compare the Progression Free Survival (PFS) as assessed by Blinded

Independent Central Review (BICR) of participants treated in the combination

induction and maintenance therapies of Arms A and B described above. Assessment

will be based on RECIST v1.1 criteria

Secondary outcome

1. To estimate the Progression Free Survival Rate (PFSR) at 6 and 12 months in

each treatment arm, based on Progression Free Survival (PFS) by RECIST v1.1 as

assessed by Blinded Independent Central Review (BICR)

2. To compare PFS as assessed by investigator of participants treated in the

combination induction and maintenance therapies of Arms A and B described above.

3. To estimate the PFSR at 6 and 12 months in each treatment arm based on PFS by RECIST v1.1 assessed by investigator.

4. To estimate the Objective Rate of Response (ORR), Time To Response (TTR), and Duration of Response (DOR) by RECIST v1.1 criteria by BICR and by investigator.

5. To assess Overall Survival (OS) of Arm A and Arm B and estimate Overall Survival Rate (OSR) at 12 and 24 months by treatment arm.

6. To characterize the immunogenicity of BMS-986012 in combination with carboplatin, etoposide, and nivolumab in Arm A.

Tertiary / exploratory

1. To assess disease-related symptoms measured by Lung Cancer Symptom Scale.

2. To assess the bother associated with the side effects of treatment.

3. To assess associations of fuc-GM1 expression in pretreatment tumor biopsies assessed using IHC and mass spectrometry assays with anti-tumor activity

measures.

4. To assess associations of PD-L1 expression (CPS) in pretreatment tumor biopsies with anti-tumor activity measures.

5. Fuc-GM1 expression on CTCs and associations with baseline fuc-GM1 expression measures; changes in CTC count during treatment (from baseline) and associations with response to treatment in each arm.

6. To explore associations with antitumuor activity measures in Arms A and B with changes in biomarkers during treatment such as the following:

• NK cell-mediated ADCC gene expression

• Immune cell population in blood (ie, NK cell activation)

• Shed fuc-GM1 levels in plasma

7. To explore associations with anti-tumour activity measures in Arms A and B with baseline biomarkers such as the following:

• Fuc-GM1 synthesis pathway (FUT1, FUT2, GM1 synthase, etc)

• FcγR polymorphism

• Tumour tissue-based TMB

8. To explore whether pruritus is a histamine-mediated event through a pre- and

post-dose histamine release assay.

9. To characterize PK of BMS-986012 in combination with carboplatin, etoposide, and nivolumab in Arm A.

10. To characterize PK of nivolumab in Arms A and B.

11. To characterize the immunogenicity of nivolumab in Arms A and B.

12. To explore the PK-pharmacodynamic relationship(s) of BMS-986012 with select biomarkers and anti-tumour activities.

13. To explore fuc-GM1 and PD-L1 expression in tumour tissue obtained at progression from optional biopsies.

14. Explore associations of the BMS-986279 PET tracer uptake of the biopsied lesion with fuc-GM1 expression levels by IHC and/or MS, and the heterogeneity of BMS-986279 PET tracer update in tumour lesions, in a substudy of participants at select study site(s).

15. To assess SARS-CoV-2 serologic status that will support advancing the understanding of the impact of SARS-CoV-2 on study treatments and ES-SLCLC.

PET-CT SUB STUDY Exploratory Objectives

1. Assess Safety of Fucosyl-GM1 PET tracer BMS-986279

2. Correlate BMS-986279 tracer uptake of the biopsied lesion with Fucosyl-GM1 expression levels measured by IHC and/or liquid chromatography-mass spectrometry (LC-MS) at baseline

3. Characterise the baseline heterogeneity of BMS-986279 tracer uptake in tumour lesions

4. Explore BMS-986279 uptake of tumour lesion associations with anti-tumour response to BMS-9866012 treatment.

Study description

Background summary

CA001-050 is a multicentre, phase 2, open-label study Involving patients with extensive-stage small cell lung cancer (ES-SCLC). Approximately 120 patients will take part in this study, approximately 15 will be from the Netherlands.

ES-SCLC has an impact on mortality and quality of life. The management and treatment of the disease has placed a huge demand on various healthcare services.

The standard treatment for decades is currently platinum-etoposide combination chemotherapy. Although initial response rates to platinum-etoposide chemotherapy are up to 78% most patients relapse within 6 months, and median overall survival is approximately 10 months. In recent years immunotherapy targeting immune checkpoint pathways, have shown anti-tumour response and improved overall survival for patients, across multiple cancer types, including

ES-SCLC.

2 immunotherapy treatments atezolizumab and durvalumab have been approved for use, in combination with chemotherapy. These treatment combinations have shown an improvement in overall survival timelines in phase 2 and phase 3 studies.

In a recent phase 2 study conducted in the United States, patients were treated with carboplatin or cisplatin and etoposide alone or in combination with nivolumab, an anti-PD1 monoclonal Antibody, as first-line therapy for ES-SCLC. Nivolumab in combination with platinum-etoposide significantly improved progression free survival (PFS) compared to platinum-etoposide alone. Overall survival was also improved in the nivolumab with platinum-etoposide arm. The data from this study shows comparable efficacy with current approved therapies.

Although the addition of new immune targeting therapies have shown some benefit, it has been limited. Innovative treatment combinations are needed to treat this disease.

BMS-986012 is a monoclonal antibody that binds to a specific protein of the cell membrane called fucosyl-monosialoganglioside-1 (fucosyl-GM1). Immunohistochemistry (IHC) analysis of tumour tissues samples has shown fucosyl-GM1 to be present in approximately 50 to 70% of SCLC tumours. BMS-986012 shows a high-binding affinity and dose dependent binding to fucosyl-GM1. The Fc receptor of the anitbody binds to natural Killer cells (NK), macrophages or complement resulting in tumour cell death by antibody-dependent cellular cytoxicity, antibody-dependent cellular phagocytosis or complement dependent cytoxicity, respectively.

A first in human study has shown clinical support for the combination of BMS-986012 with nivolumab. This was a phase 1/2 multicenter study in patients with relapsed / refractory SCLC. 29 participants were treated, the majority of which were in the second line setting. As 08-May-2020, clinical benefit has been observed in 13 of 29 participants across both dose levels in dose escalation and expansion, including 9 partial responses (PRs), 1 complete response (CR), and 3 stable disease (SD) responses. 1 subject achieved a PR after treatment beyond progression. Efficacy data are preliminary and subject to change. In general, pruritus was the main adverse event (AE) observed, generally Grade 1 or 2 in severity and considered an on-target treatment effect of BMS-986012. Other AEs were similar to those seen in nivolumab, again the majority of which were Grade 1 or 2 in severity. Based on the preliminary data,

BMS-986012, either administered as monotherapy or in combination with nivolumab, appears to be well tolerated with an acceptable safety profile. BMS-986012 has shown to have a tolerable safety profile both as a monotherapy and in combination with chemotherapy or nivolumab.

Given the fact that anti-PD-(L)1 therapy in combination with standard-of-care

chemotherapy has led to improved survival rates in patients with ES-SCLC in the first-line setting and the potential areas of synergy between BMS-986012 and nivolumab, the addition of targeted therapy seems a logical approach to treat patients.

This randomized study is designed to demonstrate that treatment with BMS-986012 in combination with carboplatin, etoposide, and nivolumab will have acceptable safety and tolerability and will improve PFS compared with carboplatin, etoposide, and nivolumab alone, in newly diagnosed participants with ES-SCLC.

PET-CT Sub study:
Although fucosyl-GM1 protein receptors are known to be expressed on the majority of SCLC tumours the receptor is most often lost from the biopsied tissue sample, during the process of creating a paraffin-embedded tumour block of tissue for analysis.

Therefore alternative methods for obtaining and handling tissues samples are needed.

The purpose of this study is to test the investigational imaging tracer, BMS-986279. The tracer is a slightly modified version of the main study treatment drug BMS-986012, called a tracer. The tracer attaches to a specific protein of the cell membrane called fucosyl-GM1. It is designed to be an imaging biomarker to detect fucosyl-GM1 expression.

Study objective

This study has been transitioned to CTIS with ID 2024-510700-36-00 check the CTIS register for the current data.

Study CA001-050 is a Phase 2 randomized, open label, multicenter clinical study designed to assess the safety and tolerability, of treatment with MS-986012 in combination with chemotherapy (carboplatin and etoposide) and nivolumab when administered to patients with small cell lung cancer. The study will also assess the effectiveness of this treatment combination in comparison to treatment with chemotherapy and nivolumab alone.

PET-CT Sub study:
There are no primary or secondary objectives and endpoints.

1. Assess safety of [89Zr] fuc-GM1 PET tracer BMS-986279.
2. Examine any correlation between BMS-986279 tracer uptake of the tumor lesion with fuc-GM1 expression levels measured by Immunohistochemistry (IHC) and/or liquid chromatography-mass spectroscopy (LC-MS) at baseline.
3. Review variations in baseline BMS- 986279 tracer uptake in tumor lesions.
4. Explore any associations between uptake of the tracer BMS-986279 to the

tumor lesion and anti-tumor response to BMS-986012 treatment.

Study design

Approximately 120 subjects will participate in the study. In the Netherlands it is expected that 15 subjects will take part

The study is divided into a screening period, 2 treatment periods and a follow-up period. During the first treatment period (an induction period) patients will receive chemotherapy (carboplatin and etoposide) in combination with Nivolumab and/or BMS-986012. In the second treatment period (the maintenance period) patients will receive Nivolumab in combination with BMS-986012 or Nivolumab alone. The effectiveness of the study treatment will be compared to the standard of care treatment. Patients will be assigned by chance to one of two treatment groups.

• Arm A: BMS-986012, chemotherapy and nivolumab for the first 4 cycles followed by BMS-986012 and nivolumab from cycle 5 onwards.
• Arm B: Chemotherapy and nivolumab for the first 4 cycles followed by nivolumab from cycle 5 onwards.

During the induction treatment period (cycle 1 to 4), each cycle is 3 weeks long.
During the maintenance treatment period (cycle 5 onwards), each cycle is 4 weeks long. The treatment period may continue for up to 2 years after the first dose of the study treatment.

If subjects are eligible to participate in the study after completing the screening assessments, they will be randomised. Randomisation will be done by an automated sorting process through IVRS (a telephone based computer system). This maintains the integrity of the randomisation itself. To be eligible for randomisation patients must meet the inclusion criteria and must not meet any of the exclusion criteria.

Randomisation will be stratified based on the presence of liver metastases and ECOG performance score (PS) 0 or 1. There is an 50% chance the patient will be assigned to treatment Arm A and a 50% chance that the patient will be assigned to Arm B

Patients will be treated until disease progression or unacceptable toxicity.

VISITS AND ASSESSMENTS
The screening period may consist of one or more visits to the hospital.
Patients who consent to participate in the study will undergo a physical exam, vital signs tests, ECG, and blood and urine sample rests to determine their eligibility. Patients will need to provide a tissue sample from their tumour.
The status of the patient's cancer will be assessed to establish a baseline.

This will be achieved by using Computer Tomography (CT) scans at screening of the chest, abdomen, pelvis and any known suspected areas of disease. Patients will also receive an MRI of the brain. Patients will be asked to complete questionnaires to assess signs and symptoms of their disease and how it might be affecting their daily activities (PGIS and LCSS).

During the treatment period patients will undergo many of the same tests and procedures conducted during the screening period. In addition, patients will be asked to complete the following questionnaires to assess signs and symptoms of their disease and how it might be affecting their daily activities: PGIS, PGIC, LCSS and FACIT GP5 up to cycle 28 Day 1. Patient-reported outcome (PROs) collection has been limited to cycle 28 during treatment period (approximatively 2 years of treatment). Follow-up collection remains unchanged.

Exploratory blood samples (study drug blood levels and biomarkers [taken to measure substances in the blood such as cells, DNA and other markers]) will be collected from all patients at certain visits throughout the study. Study drug blood levels will be measured to assess study drug plasma concentration at various points. Routine blood assessments will be collected for safety tests prior to dosing.

After patients have completed the treatment period or for those who permanently discontinue the study drug before the end of the treatment period, they will enter a post treatment follow-up period. During this period, the study doctor will continue to assess their health condition. Patients will visit the hospital 3 times in the first 4 months. During the follow-up period patients will undergo a physical examination and vital signs assessment. Patients will be asked to complete questionnaires about their disease. Blood samples will also be collected for routine safety checks. The remaining follow-up visits can take place on the phone or at the hospital. These contacts will take place about every 3 months or more often.

PET-CT SUB STUDY
Patients participating in the PET-CT sub study
Approximately 15 subjects will take part in the Netherlands.

BMS-986279 PET will be performed at select, qualified site(s) in the Netherlands, participating in the main CA001-050 study.

Subjects will be asked to provide a separate consent from the main study consent, to participate in this stub-study. Screening safety blood and urine laboratory tests will be completed. The values must meet the inclusion and exclusion criteria, as defined in section 6.2 of the main study CA001-050 protocol.

If a subject is eligible, within 3 days after providing a tissue sample

(biopsy) from the tumour (ideally on the same day) they will receive 1 tracer injection. The tumour tissue sample will be collected during the screening period of the main study.

Subjects will receive either 1 or 4 PET-CT scans depending on whether they are participating in the part of the imaging study in which the optimal tracer dose and imaging time point is being evaluated (dosimetry part).

The first 4 participants will enter the dosimetry part of the study. They will have 4 PET-CT scans on Day 1, Day 6, Day 8 and Day 14 after receiving the tracer injection.

In case the first 4 dosimetry subjects are not able to complete all scheduled scans or if the dosimetry data is not sufficient to guarantee image quality, up to 4 additional subjects from the remaining 11 will be participate in the dosimetry.

Subjects not participating in the dosimetry part of the study will only have 1 PET-CT scan, typically between Day 5 and Day 8 after receiving the tracer injection.

For patients participating in dosimetry:
A blood sample will be collected before or after each PET-CT scan, to evaluate the pharmacokinetics (PK) of BMS-986279.

Intervention

Subjects will undergo screening tests and assessments to determine eligibility, and those eligible for the study will be randomised to a treatment arm in the following ratio: 1:1 Arm A: Induction period (cycle 1 - 4) Carboplatin & Etoposide (chemotherapy) Q3W (Intravenous administration) + BMS-986012 420 mg Q3W (Intravenous administration over 60 mins) + Niolvumab 360mg Q3W (Intravenous administration over 30 mins) Etoposide will also be given on Day 2 and Day 3 of each treatment cycle (cycle 1-4 only) Maintenance period (cycle 5 onwards) BMS-986012 560 mg Q4W (Intravenous administration over 60 mins) + Niolvumab 480mg Q4W (Intravenous administration over 30 min Arm B: Induction period (cycle 1 - 4) Carboplatin & Etoposide (chemotherapy) Q3W (Intravenous administration) + Nivolumab 360 mg Q3W (Intravenous administration over 30 mins) Etoposide will also be given on Day 2 and Day 3 of each treatment cycle (cycle 1-4 only) Maintenance period (cycle 5 onwards) Nivolumab 480 mg Q4W (Intravenous administration over 30 mins) The dose of carboplatin and etoposide will be based on respective product labels for the treatment of SCLC PET-CT SUB STUDY There is no intervention. The sub-study is being conducted for exploratory purposes only. Subjects will receive one intravenous injection of the radiolabelled agent or tracer BMS-986279, after a tissue sample (biopsy) is provided at screening. Approximately 37 MBq of the tracer will be injected.

This is a limited dose of radioactivity.

Study burden and risks

Several sources of clinical and preclinical research suggest that a combination of BMS-986012 with nivolumab or chemotherapy show a statistically significant improvement in antitumour activity when compared to chemotherapy alone, which may be beneficial to patients with Extensive Stage Small Cell Lung Cancer (ES-SCLC).

With all experimental drugs and clinical trials, there are known and unknown risks. Study medication and procedure related risks are outlined in the patient information sheet in detail to ensure the patients are fully informed before agreeing to take part in the study. Based on the nonclinical safety profile of BMS-986012 and the lack of unexpected toxicity observed in the program to date, the potential safety risks are expected to be minimal. BMS-986012 has been tested previously in various clinical trials where patients were treated with either BMS-986012 alone, in combination with nivolumab or in combination with chemotherapy. Given the experience with BMS-986012, a favourable benefit-risk relationship has been established, which supports further investigation of the compound. An urgent need exists for new therapies for participants with SCLC.

Therefore the study has been designed to closely monitor patients safety throughout, to assess toxicity and safety data points. Safety monitoring will occur at study sites, by the Sponsor, and also by an external, independent Data Monitoring Committee (DMC). Due to the combination of the 4 drugs, there will be additional monitoring conducted by the DMC. The DMC will assess whether the established threshold for the safety evaluable population has been met and make a benefit-risk recommendation to the study team. Evaluable patients are defined as those who have completed 8 weeks of treatment or those who have discontinued due to study drug toxicity prior to completing the evaluation period.

Medical Monitoring by the Sponsor (Safety Medical Team)
Patient safety will be monitored by the Sponsor continuously. The Sponsor will review patient-level data entered in the clinical database as well as aggregated safety data across studies. This approach facilitates close monitoring of individual safety events as well as surveillance for potential safety signals. The SMT will consist of Medical safety assessment physician, single-case review physician, the study medical monitor(s), biostatistician and epidemiologist, at minimum.

As part of the study, patients will be expected to attend multiple clinic visits where they will undergo physical examinations, vital sign measurements, biopsy, ECG, blood and urine tests for safety assessment, pregnancy testing (for females of child bearing potential) and monitoring for adverse events.

Blood will also be collected at certain visits for research purposes (PK, and

biomarker studies).

Patients will be asked to complete to complete questionnaires about their disease and quality of life and various points throughout the study.

Women of child-bearing potential must agree to follow instructions for methods of contraception for the duration of treatment with the study treatment.

Smoking can have an influence on the severity of lung cancer disease symptoms. Consequently, use of tobacco products will be assessed at each study visit. Use of a nicotine patch should be recorded as a concomitant medication.

Patients participating in the PET-CT Sub study will be required to fast for a minimum of 4 hours before the PET-CT Scans. Although this is the first study of BMS-986279 in humans, there are no known adverse effects from the administration of BMS-986279.

Patients will be asked to attend the hospital for the study procedures to be performed. Timings of these visits will be based on the protocol schedule but will be mutually agreed with both the hospital staff and the patient to avoid patient and/or staff attending hospital at unsocial hours, and to minimise any inconvenience to the patient. Patients will be reimbursed for reasonable travel expenses incurred for attending study visits.

PET-CT SUB STUDY
Patients participating in the PET-CT Sub study will be required to fast for a minimum of 4 hours before the PET-CT Scans. Although this is the first study of BMS-986279 in humans, there are no known adverse effects from the administration of BMS-986279.

The amount of BMS-986279 tracer used for the PET scan is far below the therapeutic dose of BMS-986012 that is used in clinical studies; therefore, a pharmacological effect or an impact on normal body processes is not anticipated.

The amount of radiation exposure from BMS-986279 PET is expected to be approximately 25 mSv and will be further assessed in the human dosimetry of this study.

The low-dose computed tomography (CT) scan will give an additional ~3 mSv per scan. Therefore, the total dose per participant is expected to be ~37 mSv for dosimetry (4 low-dose CTs) and ~28 mSv (1 low-dose CT) for others.

An initial radiation dose of 37 MBq will be used based on results from prior administrations of the tracer given to participants without any adverse events.

Contacts

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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. Participants must have histologically or cytologically documented Extensive Stage Small Cell Lung Cancer (ES SCLC). Participants must present with extensive stage IV disease based on the American Joint Committee on Cancer, 7th edition guidelines. The following grades will be considered: T any, N any, M1a, or M1b, or T3-4 due to multiple lung nodules that are too extensive or tumour or nodal volume that is too large to be encompassed in a tolerable radiation plan. 2. a. Archived tumor specimens, in the form of blocks or sectioned slides, are mandatory for all participants except those participating in the separate PET tracer sub-study for whom the archived tumor specimen is optional. b. Participants taking part in the separate PET tracer sub-study must provide a fresh tumor biopsy from any disease site (primary or metastatic). Mandatory minimum of 3 cores to be processed as 2 fresh frozen and the rest as formalin

fixed paraffin embedded. Refer to Section 9.8.1 and the Laboratory Manual for further details on procedures for collecting fresh tumor samples. Note: if during the attempt to collect the tumor biopsy there are safety issues and a sample may not be obtained or is not suitable for the study per protocol requirements, the participant may still be allowed to enter in the study after consultation with BMS Medical Monitor. 3. Eastern Cooperative Oncology Group (ECOG) Performance Score (PS) 0 or 1. 4. Participants must have at least 1 measurable lesion, measured by computed tomography (CT) or magnetic resonance imaging (MRI). This will be evaluated per Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST v1.1) criteria. 5. Participants must be suitable to receive a platinum-based chemotherapy regimen as per locally approved drug labels and institutional guidelines. 6. Adequate hematologic and end organ function as defined below: a. Absolute neutrophil count >= 1,500/mm3 (stable off any growth factor within 2 weeks of the first study drug administration) b. Platelets >= 100,000/mm3 (transfusion to achieve this level is not permitted within 2 weeks of the first study drug administration) c. Hemoglobin >= 9 g/dL (transfusion to achieve this level is not permitted within 2 weeks of the first study drug administration) d. White blood cells >= 2000/mm3 e. Total bilirubin <= 1.5 x upper limit of normal (ULN) f. Aspartate aminotransferase (AST; serum glutamic-oxaloacetic transaminase) and alanine aminotransferase (ALT; serum glutamic-pyruvic transaminase) <= 3 x ULN g. Serum creatinine <= 1.5 x ULN or calculated creatinine clearance > 50 mL/min (using the Cockcroft-Gault formula) 7. Males and Females aged 18 years or older a. Women who are not of childbearing potential are exempt from contraceptive requirements b. Women participants must have documented proof that they are not of childbearing potential c. Women of Childbearing Potential (WOCBP) must have a negative highly sensitive urine or serum pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin (HCG) within 24 hours prior to the start of study treatment). An extension up to 72 hours prior to the start of study treatment is permissible in situations where results cannot be obtained within the standard 24-hour window. d. WOCBP must agree to follow instructions for method(s) of contraception defined in Appendix 4 of the protocol and as described below and included in the ICF. e. Males who are sexually active with WOCBP must agree to follow instructions for method(s) of contraception defined in Appendix 4 and as described below. f. Azoospermic males are not exempt from contraceptive requirements and will be required to always use a latex or other synthetic condom during any sexual activity (eg, vaginal, anal, oral) with WOCBP even if the participant has undergone a successful vasectomy or if the partner is pregnant. g. A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least 1 of the following conditions applies: (1) Is not a WOCBP OR (2) Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), with low user dependency, as described in Appendix 4 during the intervention period and for at least 6 months and agrees not to donate eggs (ova, oocytes) for the purpose of reproduction for the same time period. h. Male participants are required to use a condom during the intervention period (ie, while receiving chemotherapy) and for at least 6 months after the last

dose of chemotherapy (carboplatin and etoposide). i. Female partners of males participating in the study should be advised to use highly effective methods of contraception during the study intervention period (ie, while receiving chemotherapy) and for at least 6 months after the last dose of chemotherapy (carboplatin and etoposide) in the male participant. j. Male participants with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile penetration during the intervention period (ie, while receiving chemotherapy) and for at least 6 months after the last dose of chemotherapy (carboplatin and etoposide). k. Male participants must refrain from donating sperm during the intervention period (ie, while receiving chemotherapy) and for at least 6 months after the last dose of chemotherapy (carboplatin and etoposide). l. Breastfeeding partners should be advised to consult their health care provider about using appropriate highly effective contraception during the time the participant is required to use condoms. PET-CT Sub-study: Participants eligible for participation in CA001-050 at qualified sites who do not meet any imaging exclusion criteria will be eligible to participate in this PET imaging study. Participants will sign an additional PET imaging informed consent form.

Exclusion criteria

1. Medical Conditions a. Women who are pregnant or breastfeeding. b. Any significant acute or chronic medical illness that would interfere with study treatment or follow-up c. Inability to undergo venepuncture and/or tolerate venous access. d. Any other sound medical, psychiatric, and/or social reason as determined by the investigator e. Participants with symptomatic brain or other central nervous system (CNS) metastases. Participants are eligible if brain or other CNS metastases are asymptomatic and do not require immediate treatment or have been adequately treated. They must have neurologically returned to baseline (except for residual signs or symptoms related to the CNS treatment) for at least 2 weeks prior to randomization. In addition, participants must be either off corticosteroids or on a stable or decreasing dose of <= 10 mg daily prednisone (or equivalent) for at least 2 weeks prior to randomization. f. Paraneoplastic autoimmune syndrome requiring systemic treatment. g. History of idiopathic pulmonary fibrosis, drug-induced pneumonitis, idiopathic pneumonitis, organizing pneumonia, or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis is permitted. h. Grade >= 2 peripheral sensory neuropathy at study entry. i. Participant has uncontrolled or active systemic fungal, bacterial, viral, or other infection despite appropriate anti-infective treatment, within 7 days prior to the first dose of study drug. j. Known human immunodeficiency virus (HIV) positive with an acquired immunodeficiency syndrome (AIDS)-defining opportunistic infection within the past year or a current CD4 count < 350 cells/uL. Participants with known HIV are eligible if: i.) They have received antiretroviral therapy (ART) for at least 4 weeks prior to randomisation as clinically indicated while

enrolled on study ii.) They continue on ART as clinically indicated while enrolled on study iii.) CD4 counts and viral load are monitored as per standard of care by a local health care provider. NOTE: Testing for HIV must be performed at sites where mandated locally. HIV-positive participants must be excluded where mandated locally (see Appendix 8). k. Significant uncontrolled cardiovascular disease, including, but not limited to, any of the following: i.) Uncontrolled hypertension, which is defined as systolic blood pressure > 160 mm Hg or diastolic blood pressure > 100 mm Hg, despite optimal medical management. ii.) Active coronary artery disease, including unstable or newly diagnosed angina within 3 months of study enrollment. iii.) Myocardial infarction in the past 6 months. iv.) History of congenital long QT syndrome. v.) History of clinically significant arrhythmias, such as ventricular tachycardia, ventricular fibrillation, or Torsade de pointes. vi.)Uncontrolled heart failure, defined as Class 3 or 4 by New York Heart Association functional classification. vii.) History or current diagnosis of myocarditis. l. Participants with an active, known or suspected autoimmune disease or inflammatory disorder. Participants 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. m. Participants with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of randomization. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease. n. Concurrent malignancy (present during screening) requiring treatment or history of prior malignancy active within 2 years prior to randomization. Participants with a history of prior malignancy are eligible if treatment was completed at least 2 years before randomization and the participant has no evidence of disease. Participants with history of prior early stage basal/squamous cell skin cancer or non-invasive in site cancers that have undergone definitive treatment at any time are also eligible. o. Participants with history of life-threatening toxicity related to prior immune therapy (eg, anti-CTLA-4 or anti-PD-1/PD-L1 treatment or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways) except those that are unlikely to re-occur with standard countermeasures (eg, hormone replacement after adrenal crisis). p. Previous SARS-CoV-2 infection within 10 days for mild or asymptomatic infections or 20 days for severe/critical illness prior to Cycle 1 Day 1. i) Acute symptoms must have resolved and based on investigator assessment in consultation with the Medical Monitor, there are no sequelae that would place the participant at a higher risk of receiving study treatment. q. Participants cannot have had prior chemotherapy, radiation therapy, or biologic therapy for SCLC. Previously treated limited stage SCLC (LS-SCLC) participants are also excluded. 2. Prior/concomitant therapy a. Inability to comply with restrictions and prohibited treatments as listed in Section 7.7 of the protocol Concomitant Therapy. b. Treatment with complementary medications (eg, herbal supplements or

traditional Chinese medicines) to treat the disease under study within 2 weeks prior to randomization/treatment. c. Treatment with any live/attenuated vaccine within 30 days of first study treatment. d. Previous SARS-CoV-2 vaccine within 7 days of Cycle 1 Day 1. For vaccines requiring more than one dose, the full series (eg. both doses of a 2-dose series) should be completed prior to enrollment when feasible and when a delay in enrollment would not put the study participant at risk. 3. Physical and Laboratory Test Findings a. Evidence of organ dysfunction or any clinically significant deviation from normal in physical examination, vital signs, ECGs, or clinical laboratory determinations beyond what is consistent with the target population. b. Any of the following on 12-lead ECG prior to study drug administration, confirmed by repeat assessment i.) PR interval greater than or equal to 210 msec ii.) QRS complex greater than or equal to 120 msec iii.) QT interval greater than or equal to 500 msec iv.) corrected QT interval by Fredericia greater than or equal to 450 msec c. Any positive test result for hepatitis B virus or hepatitis C virus (HCV) indicating presence of virus, eg, hepatitis B surface antigen (HBsAg, Australia antigen) positive, or hepatitis C antibody (anti-HCV) positive (except if HCV- ribonucleic acid [RNA] negative). 4. Allergies and Adverse Drug Reaction a. History of allergy, hypersensitivity, or serious adverse reaction to monoclonal antibodies or related compounds. b. History of allergy or hypersensitivity to study drug components. 5. Other Exclusion Criteria a. Prisoners or participants who are involuntarily incarcerated. (Note: Under specific circumstances and only in countries where local regulations permit, a person who has been imprisoned may be included as a participant. Strict conditions apply, and BMS approval is required.) b. Participants who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness. PET-CT Sub study: Participants with the following condition(s) may be considered for participation in the main study but will not undergo the BMS-986279 PET imaging: -Participants with issues that prevent them from lying still for PET imaging procedure. -Participants who have received a therapeutic radiopharmaceutical within 7 days prior to participation in this study. -Participants who do not have adequate venous access for PET tracer injection.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-12-2021
Enrollment:	16
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	BMS-986012
Generic name:	Anti-Fucosyl-GM1 - 30 mg/ml
Product type:	Medicine
Brand name:	Carbo-cell
Generic name:	Carboplatin - 10 mg/ml
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Carboplatin Bendalis
Generic name:	Carboplatin - 10 mg/ml
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	ETO-cell
Generic name:	Etoposide - 20 mg/ml
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Opdivo
Generic name:	Nivolumab / BMS-936558 - 10 ml
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-03-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-510700-36-00
EudraCT	EUCTR2020-001863-10-NL
CCMO	NL76650.029.21