A Phase IIIb/IV Safety Trial of Flat Dose Nivolumab in Combination with Ipilimumab in Participants with Non-Small Cell Lung Cancer

Published: 26-10-2016
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To establish the efficacy and safety of nivolumab administered as a flat dose in combination with weight-based ipilimumab dosing.

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

Summary

ID

NL-OMON47686

Source
ToetsingOnline

Brief title
CA209-817

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Ipilimumab, Nivolumab, Non-small cell lung cancer, Stage IIIB/IV/Recurrent/Progressive

Outcome measures

Primary outcome

The primary objective of the study will be assessed by summarizing the number

and percentage of participants who experience high grade (Grade 3-4 and Grade

5) treatment-related select and immune-mediated adverse events.

The select adverse events of interest are the following:

- pneumonitis

- interstitial nephritis

- diarrhea/colitis

- hepatitis

- rash

- endocrinopathies

- hypersensitivity/infusion reaction events

Secondary outcome

- Progression-free survival (PFS)

- Objective Response Rate (ORR)

- Overall survival (OS)

- Duration of Response (DOR) *

- Participant reported outcomes (PROs): assessment of changes in

disease-related symptoms

Study description

Background summary

This is a clinical trial of nivolumab combined with ipilimumab in patients, with newly diagnosed stage IV or recurrent non-small cell lung cancer (NSCLC), who have not received prior systemic anticancer therapy (1st Line NSCLC), or with stage IIIB, or with recurrent or progressive disease following multimodal therapy (2nd line NSCLC), or in a special patient population (NSCLC patients with renal or hepatic dysfunction, with a controlled HIV infection, with asymptomatic brain metastases, or with a ECOG PS 2).
Lung cancer is the leading cause of cancer and cancer-related deaths globally, accounting for 1.8 million new cases and 1.6 million deaths worldwide in 2012. A significant number of patients have advanced lung cancer at diagnosis. Unfortunately with current standard of care chemotherapy, the survival rate remains poor, with less than 5% of advanced lung cancer patients alive five years on from diagnosis.
There is a clear unmet medical need for patients with advanced NSCLC. Nivolumab, is a new type of immunotherapy drug which stimulates the body*s own immune system to help attack cancer cells. It works by blocking a protein on the body*s immune cells, called PD1, so that tumours can be recognised as foreign and attacked by the immune system. Ipilimumab is already on the market for the treatment of melanoma.
Following a screening period, eligible patients will receive treatment with flat dose nivolumab combined with weight-based ipilimumab. Patients will receive study drugs until their cancer progresses or their doctor decides they should come out of the study.
Patients will undergo the following procedures during the study: tumour tissue biopsy (if no tumor tissue available at screening), CT/MRI scans, physical exams, vital signs and blood sampling for routine safety testing and study specific testing. 1000 patients will be treated in the study with approximately 22 being treated in the Netherlands.

Study objective

To establish the efficacy and safety of nivolumab administered as a flat dose in combination with weight-based ipilimumab dosing.

Study design

This is a single-arm, open-label study of nivolumab and ipilimumab in patients with newly diagnosed histologically confirmed metastatic or recurrent non small cell lung cancer (NSCLC). Subjects will receive treatment with nivolumab 240 mg as a 30 minute infusion every 2 weeks and ipilimumab 1 mg/kg as a 30 minute infusion every 6 weeks, until progression, unacceptable toxicity, withdrawal of

consent, or the study ends, whichever occurs first. After treatment, all subjects will enter the follow-up phase of the study. Subjects will have 2 visits within the first 4 months after stopping treatment. The remaining follow-up visits can be conducted over the phone and will occur every 3 months. Follow up data will be collected for up to 5 years. Subjects who are determined to be benefitting from study treatment after analysis of the primary endpoint is completed may be eligible to continue receiving study drug.

Intervention

Subjects will receive open-label treatment with nivolumab (flat dose of 240 mg every two weeks) in combination with ipilimumab (1 mg/kg every 6 weeks). Both nivolumab and ipilimumab are provided by the sponsor.

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, 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 6 until week 48) and then every 12 weeks, patients will undergo radiographic assessment of their tumors (by CT or MRI) until disease progression or treatment discontinuation whichever occurs later. Blood will also be collected at certain visits for research purposes (PK, immunogenicity and biomarker studies). The frequency of visits and number of procedures carried out during this trial would typically be considered over and above standard of care. These procedures are conducted by medically trained professionals and every effort will be made to minimise any risks or discomfort to the patient.

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

D4. Main inclusion criteria
- Male and female patients over the age of 18 with ECOG status of 0-2 - Participants with histologically confirmed Stage IV (1st line NCSLC) or IIIB/IV (2nd line NSCLC) or recurrent, progressive NSCLC squamous or non-squamous histology, with no prior systemic anticancer therapy (including EGFR and ALK inhibitors) given as primary therapy for advanced or metastatic disease (1st line NSCLC) or with recurrent or progressive disease following multimodal therapy or platinum-doublet chemotherapy (2nd line NSCLC).
Patients with untreated brain metastases, a controlled HIV infection, hepatic or renal impairment, or with a ECOG PS 2- Measurable disease by CT or MRI per RECIST 1.1.
Participants must have tissue submitted for PD-L1 IHC testing prior to the treatment assignment. If PD-L1 IHC testing has already been conducted during screening for another BMS study, it does not need to be repeated for CA209-817.
Women of childbearing potential must not be breastfeeding and must have a negative serum or urine pregnancy test within 24 hours prior to start of study treatment. This test will be repeated every 6 weeks during the study. Patients must follow the contraception requirements while enrolled in the study.

Exclusion criteria

-Patients previously treated with drugs targeting T-cell co-stimulation or checkpoint pathways.
Patients with known EGFR mutations or ALK translocations sensitive to available targeted inhibitor therapy.
Patients with an active, known or suspected autoimmune disease.
Patients with type I diabetes mellitus, hypothyroidism only requiring hormone

replacement, skin disorders (such as vitiligo, psoriasis or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enrol.
Patients with a condition requiring systemic treatment with either corticosteroids (> 10mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of treatment assignment.. Patients with interstitial lung disease or, who are incarcerated or temporarily detained for psychiatric or physical illness.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-04-2017
Enrollment:	22
Type:	Actual

Medical products/devices used

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:	26-10-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-03-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-01-2019

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-06-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-05-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-12-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2016-002621-10-NL
ClinicalTrials.gov	NCT02869789
CCMO	NL58880.042.16

Study results

Date completed: 13-05-2022

Results posted: 08-05-2023

First publication
01-01-1900