A Randomized, Multicenter, Double-Blind, Phase 3 Study of Nivolumab, Nivolumab in Combination with Ipilimumab, or Placebo as Maintenance Therapy in Subjects with Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) after Completion of Platinum-based First Line Chemotherapy

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

Summary

ID

NL-OMON47067

Source
ToetsingOnline

Brief title
CheckMate 451: Nivolumab in small cell lung cancer

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Small cell lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Ipilimumab, Nivolumab, Small cell lung cancer

Outcome measures

Primary outcome

To compare OS and Blinded Independent Central Review (BICR)-assessed PFS, of nivolumab, and nivolumab in combination with ipilimumab, versus placebo in subjects with ED-SCLC after completion of platinum-based first line chemotherapy.

Secondary outcome

To evaluate (descriptively) OS and BICR-assessed PFS of nivolumab combined with ipilimumab versus nivolumab monotherapy.

Study description

Background summary

CA209-451 is a multi-centre, phase 3 study involving adult patients with Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) that have been treated with prior platinum-based chemotherapy.

The study will involve an investigational drug called Nivolumab given alone or in combination with Ipilumimab as maintenance therapy to patients who have completed a first line platinum-based chemotherapy regimen and achieved an

ongoing Complete Response (CR), Partial Response (PR) or Stable Disease (SD).

Small-cell lung cancer (SCLC) accounts for approximately 12% of all lung cancer deaths. Despite treatment with platinum-based chemotherapy, approximately 80% of all patients experience disease progression and currently the median survival rate of these patients is approximately 7 months. Patients whose disease is diagnosed in an advanced stage (so called extensive stage) undergo a platinum-based chemotherapy until the tumor size has been reduced or at least a disease stabilization has been reached. At this point the chemotherapy treatment will be stopped and patients are closely monitored to detect a recurrence or relapse of the tumor. Unfortunately, in almost all patients who were diagnosed in an advanced stage a recurrence of the tumor will occur. Therefore there is a clear need for further therapeutic options for patients who have reached at least a disease stabilization after the initial chemotherapy. In a previous clinical trial patients with advanced SCLC and recurrence of their disease after one or more chemotherapy treatments underwent treatment with Nivolumab monotherapy or Nivolumab and Ipilimumab combination therapy and tumor shrinkages were observed in these patients justifying the proposed study CA209-451.

Considering the short median overall survival for patients who have completed first line platinum based treatment, as well as the even shorter progression-free survival experienced in this disease, new treatments complementary to SCLC standard first-line platinum-base treatment are required.

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.

The aim of this study is to determine if Nivolumab or Nivolumab in combination with Ipilimumab will improve the survival time and/or prolong the time until the tumor starts to show growth again (so called Progression-Free Survival (PFS)) compared to a placebo. There is no established treatment with proven efficacy for patients who have completed the first chemotherapy, therefore treatment is not being withheld from those in the placebo group as they would not usually receive further treatment anyway.

Approximately 810 patients will take part in this study, approximately 17 of those will be from the Netherlands.

Study objective

The aim of the study is to compare overall survival (OS) and Blinded Independent Central Review (BICR)-assessed progression free survival (PFS), of nivolumab, and nivolumab in combination with ipilimumab, versus placebo in subjects with ED-SCLC after completion of platinum-based first line

chemotherapy.

Study design

This is a randomized, double-blind, three arm, multicenter, Phase 3 study in adult subjects with ED-SDLC, who achieve Stable Disease, Partial Response or Complete Response after completion of platinum based first line chemotherapy. The study will aim to treat 810 eligible male or female subjects across 30 countries, with the expected duration of treatment being up to 18 months (depending on the response to treatment).
Subjects will undergo screening tests to determine eligibility and, those eligible for the study, will be randomized to a 1:1:1 ratio across the 3 treatment arms until Progressive Disease or unacceptable toxicity:
* Arm A: Nivolumab (240mg) administered every 2 weeks.
* Arm B: Nivolumab (1mg/kg) and Ipilimumab 3mg/kg administered every 3 weeks for 4 doses, followed by Nivolumab (240mg) every 2 weeks.
* Arm C: Placebo administered according to above treatment Arms A/B to maintain a blinded study.
In order to maintain a blinded study, the schedule of investigational and placebo treatments is divided into 6 week-cycles at the start of the therapy, followed by ongoing 2-Week cycles until discontinuation criteria are met.
Randomization will be done by an automated sorting process through IVRS (a telephone based computer system) which will assign subjects to a treatment Arm based on their ECOG status, gender and whether they had prior Prophylactic Cranial Irradiation (PCI). This ensures that all Arms are equally balanced with subject numbers for comparison at time of analysis, but also ensures the integrity of the randomization itself.
Subjects must receive their treatment within 3 days of randomization. Treatment will continue until disease progression, discontinuation due to toxicity, withdrawal of consent, or the study ends. If the investigator feels it is appropriate, subjects will be permitted to continue treatment beyond initial progression per RECIST 1:1.
After treatment all subjects will be asked to continue with follow-up visits for 100 days after their last dose of study treatment. Adverse events will be collected and monitored continuously during the follow-up period. Beyond 100 days, subjects will be followed up by telephone for long term survival and subsequent anti-cancer medication information every 3 months for 5 years. For any subjects whose disease has not yet progressed, radiographic assessment (CT/MRI) will continue to be performed during the follow up period.

Intervention

Subjects will receive open-label treatment with nivolumab (Arm A); or a specific regimen of nivolumab & ipilimumab in combination (Arms B); or placebo. 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 including oxygen saturation levels, blood tests for safety assessment, pregnancy testing (for females of child bearing potential) and monitoring for adverse events. Subjects will be evaluated for presence or continued lack of tumor until distant recurrence beginning 6 weeks relative to the first dose of study treatment, and will continue to have surveillance assessment every 6 weeks for the first 36 week then every 12 weeks until disease progression.

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. The procedures are carried out by trained medical professionals and every effort will be made to minimise any risks or discomfort to the patient. Treatment for cancer often has side effects, including some that are life threatening. An independent Data Monitoring Committee (DMC) will be utilized in this trial to ensure that the safety data is reviewed during the study.

New Immune system targeted therapy (immunotherapies) such as Nivolumab and Ipilimumab could potentially provide clinical benefit and improvement in the outcome for patients with this disease (disease improvement and improvement in survival). However, 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.

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

-Subjects with histologically or cytologically confirmed extensive stage disease SCLC ;-Ongoing response of stable disease or better following 4 cycles of platinum-based first line chemotherapy;-ECOG performance status of 0 or 1

Exclusion criteria

-Subjects with untreated central nervous system metastases are excluded;-Subjects with active, known, or suspected autoimmune disease are excluded;-All side effects attributed to prior anti-cancer therapy must have resolved to Grade 1 or baseline

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-10-2016
Enrollment:	17
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:	11-02-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-07-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	18-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	06-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-10-2019

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-002441-61-NL
ClinicalTrials.gov	NCT02538666
CCMO	NL55557.078.16

Study results

Results posted: 14-11-2022

First publication
01-01-1900