A Phase III, open-label, multicenter trial of avelumab (MSB0010718C) versus platinum-based doublet as a first-line treatment of recurrent or Stage IV PD-L1+ non*small-cell lung cancer

Published: 01-12-2015
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To demonstrate superiority with regard to Progression Free Survival based on an Independent Review Committeeassessment of avelumab versus platinum-based doublet in NSCLC subjects with PD-L1+

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

Summary

ID

NL-OMON47625

Source
ToetsingOnline

Brief title
EMR100070-005 - JAVELIN Lung 100

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Merck
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Avelumab, MSB0010718C, NSCLC, Stage IV PD-L1+

Outcome measures

Primary outcome

Progression free survival time, defined as the time from date of randomization

until date of the first documentation of PD or

death due to any cause in the absence of documented PD, whichever occurs first

Secondary outcome

- PFS time in PD L1++ ITT subjects,

- Best Overall Response according to RECIST 1.1 and as adjudicated by the IRC,

- Overall Survival time (defined as the time from randomization to the date of

death),

- Changes in Subject-reported Outcomes/Quality of life (assessed by the EQ-5D,

and the EORTC QLQ-C30, and module

QLQ-LC13 questionnaires)

Study description

Background summary

Non-small cell lung cancer is the leading cause of cancer-related death in men and women in the USA and in the EU, resulting in more cancer related deaths than breast cancer, prostate cancer, and colorectal cancer combined.
In NSCLC, results of standard therapy are poor except for the most localized cancers where surgery and / or combined modality therapy can provide a cure in

a small percentage of patients. In patients with advanced or metastatic NSCLC, chemotherapy offers modest benefit, though overall survival (OS) remains poor. Despite treatment with platinum-based regimens with third generational agents, patients with metastatic NSCLC have a median survival of approximately 10 months, and a 5-year survival rate of approximately 15%.

Study objective

To demonstrate superiority with regard to Progression Free Survival based on an Independent Review Committee
assessment of avelumab versus platinum-based doublet in NSCLC subjects with PD-L1+

Study design

This is a multicenter, international, randomized, open-label, Phase III trial in chemotherapy-naïve (first line) metastatic/recurrent NSCLC subjects comparing avelumab to first-line platinum-based chemotherapy. The trial consists of a 28-day screening period, followed by the treatment phase (4 days after randomization).

Intervention

- Avelumab at a dose of 10 mg/kg as a 1-hour intravenous (IV) infusion once every 2 weeks until disease progression or unacceptable toxicities, or
- Investigator*s choice platinum-containing chemotherapy regimen to be administered in
3-week cycles up to a maximum of 6 cycles of IV injection until disease progression or
unacceptable toxicities.

Study burden and risks

Avelumab is currently being investigated in the following ongoing clinical studies:
- Trial EMR100070-001 is a Phase I in subjects with metastatic or locally advanced solid tumors.
- Trial EMR100070-002 is a Phase I in Japanese subjects with metastatic or locally advanced solid tumors
- Trial EMR100070-003 is a Phase II in subjects with Merkel cell carcinoma
- Trial EMR100070-004 is a Phase III in subjects with non-small cell lung cancer that has progressed after a platinum-containing doublet.
Overall, the data from those studies support the development of avelumab in subjects with Stage IV NSCLC who have not yet received systemic treatment for their metastatic disease.
Based on the nonclinical and Phase I data available to date, the conduct of the

trial is considered justifiable using the dose and dose regimen of the avelumab as specified in this clinical trial protocol.
The primary known identified risks of exposure to avelumab include Infusion-related reactions.
In addition, since avelumab has been shown to induce antibody-dependent cell-mediated cytotoxicity, there is a potential risk of tumor lysis syndrome.
While on trial treatment, subjects will be asked to visit the trial site either
- once every 2 weeks up to Week 13, followed by every 6 weeks thereafter for subjects randomized to receive avelumab or
- Once every 3 weeks up to Week 13, followed by every 6 weeks thereafter for subjects randomized to receive chemotherapy.

Contacts

Public
Merck

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Darmstadt 64293
DE
Scientific
Merck

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Darmstadt 64293
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Male or female subjects * 18 years, with an ECOG PS of 0 to 1 at trial entry, with the availability of a formalinfixed, paraffin-embedded block containing tumor tissue or 7 (preferably 10) unstained tumor slides with PD-L1+, at least 1 measurable tumor lesion, and with histologically confirmed metastatic or recurrent NSCLC. Subjects must not have received any treatment for systemic lung cancer, and have an estimated life expectancy of more than 12 weeks.

Exclusion criteria

Subjects whose disease harbors an activating EGFR mutation, or with non-squamous cell NSCLC whose disease harbors and anaplastic lymphoma kinase (ALK) rearrangement are not eligible. Other exclusion criteria include prior therapy with any antibody or drug targeting T cell coregulatory proteins, concurrent anticancer treatment, or immunosuppressive agents, known severe hypersensitivity reactions to monoclonal antibodies (Grade * 3 NCI CTCAE v 4.03), history of anaphylaxis, or uncontrolled asthma (that is, 3 or more features of partially controlled asthma), and persisting toxicity related to prior therapy of Grade > 1 NCI-CTCAE v 4.03. Subjects with brain metastases are excluded, except those meeting the following criteria: brain metastases that have been treated locally and are clinically stable for at least 2 weeks prior to enrollment, subjects must be either off steroids or on a stable or decreasing dose of <10mg daily prednisone (or equivalent), do not require steroid maintenance therapy, and do
not have ongoing neurological symptoms that are related to the brain localization of the disease.
Other protocol defined criteria could apply.
All potential exceptions must be discussed with the study Medical Monitor prior to enrollment.

Study design

Design

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

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-04-2016
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avelumab
Generic name:	Bavencio
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin Hospira
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin Hospira
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine Hospira
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Paclitaxel Hospira
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-12-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-03-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-06-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Not approved Date:	10-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-03-2018
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2015-001537-24-NL
Other	IND122898; NCT02576574
CCMO	NL54926.056.15