A Phase III Randomized, Open-Label, Multi-Center, Global Study of MEDI4736 in Combination with Tremelimumab Therapy or MEDI4736 Monotherapy Versus Standard of Care Platinum-Based Chemotherapy in First Line Treatment of Patients with Advanced or Metastatic Non Small-Cell Lung Cancer (NSCLC) (MYSTIC)

Published: 07-07-2015
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To assess the efficacy of MEDI4736 + tremelimumab combination therapy compared to SoC in terms of PFS and OS in patients with PD-L1- positieve (equal or greater than 25%) NSCLC.To assess the efficacy of MEDI4736 therapy compared to SoC in terms of...

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

Summary

ID

NL-OMON44879

Source
ToetsingOnline

Brief title
MYSTIC

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Opdrachtgever/ sponsor Astrazeneca

Intervention

Keyword: MEDI4736, non-small cell lung cancer, PD-L1, Tremelimumab

Outcome measures

Primary outcome

To assess the efficacy of MEDI4736 + tremelimumab combination therapy compared to SoC in terms of PFS and OS in patients with PD-L1- positieve (equal or greater than 25%) NSCLC.

To assess the efficacy of MEDI4736 therapy compared to SoC in terms of OS in patients with PD L1 positive (equal or greater than 25%) NSCLC

Secondary outcome

To assess the efficacy MEDI4736 + tremelimumab combination therapy compared to SoC in terms of :

-Overall Survival (OS)

-Objective Response Rate (ORR)

-Duration of Response (DoR)

-APF12

-Progressive Free Survival (PFS)

-Progressive Free Survival after subsequent anticancer therapy (PFS2)

To assess the efficacy MEDI4736 monotherapy therapy compared to SoC in terms of

:

-Overall Survival (OS)

-Objective Response Rate (ORR)

-Duration of Response (DoR)

-APF12

-Progressive Free Survival (PFS)

-Progressive Free Survival after subsequent anticancer therapy (PFS2)

To assess the efficacy MEDI4736 + tremelimumab combination therapy compared to MEDI4736 monotherapy therapy in terms of :

-Objective Response Rate (ORR)

-Overall Survival (OS)

-Progressive Free Survival (PFS)

To assess disease-related symptoms and HRQoL in patients treated with MEDI4736+ tremelimumab combination therapy and MEDI4736 monotherapy compared to SoC using the EORTC QLQ C30 v3 and the LC13 module

To assess the PK of MEDI4736 + tremelimumab combination therapy and MEDI4736

monotherapy

To investigate the immunogenicity of MEDI4736 and tremelimumab

To explore irRECIST as an assessment methodology for clinical benefit of

MEDI4736 + tremelimumab compared to SoC with assessment by BICR

Study description

Background summary

Despite the diagnosis, characterization and treatment of non-small cell lung cancer has improved in recent years, the estimated 5-year survival is only 11-17%. Patients that are diagnosed with non-small cell lung cancer have a median survival of 10 to 12 months. Platinum-based chemotherapy is currently the first-line treatment for patients with no targeted mutation in EGFR and ALK. However, disease-free survival and duration of response are limited. In this study, the new drug MEDI4736 as monotherapy or in combination with tremelimumab compared with standard chemotherapy. MEDI4736 is a monoclonal antibody (mAb) which has an influence on the binding of the Programmed Death Ligand 1 (PD-L1) and tremelimumab is a mAb which binds to the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) protein. Both PD-L1 as a CTLA-4 protein play a role in the suppression of the immune system which uses the tumor in order to escape the immune system.

Study objective

To assess the efficacy of MEDI4736 + tremelimumab combination therapy compared to SoC in terms of PFS and OS in patients with PD-L1- positieve (equal or greater than 25%) NSCLC.
To assess the efficacy of MEDI4736 therapy compared to SoC in terms of OS in patients with PD L1 positive (equal or greater than 25%) NSCLC

Study design

Phase3, open-label, randomised, multicenter, international study
Randomisation 1:1:1 stratification on PD-L1 expression and histology

* MEDI4736 + Tremelimumab
* MEDI4736 monotherapie
* Standard platimnum chemotherapy

Intervention

MEDI4736 + tremelimumab combination therapy:
MEDI4736 20 mg/kg via IV infusion q4w, starting on Week 0, for up to a total of 4 doses/cycles,
and then continue MEDI4736 20 mg/kg via IV infusion q4w, starting on Week 16, for up to a total
of 8 months (9 doses)
Tremelimumab 1 mg/kg via IV infusion q4w, starting on Week 0, for up to 4 doses/cycles

MEDI4736 monotherapy:
MEDI4736 20 mg/kg via IV infusion q4w, starting on Week 0, for up to a total 12 months
(13 doses)

Standard platunim chemotherapy

Study burden and risks

On several days during the study patients will undergo the following assessments:
-anamnesis (at screening also medical history)
-physical examination
-ECOG performance status
-vital signs (blood pressure, pulse)
-length
-CT scan
- ECG
-blood and urine assessments
-questionnaires (EORTC QLQ C-30, EORTC QLQ-LC13) (by
-pregnancy test
Adverse

Contacts

Public
Astra Zeneca

Louis Pasteurlaan 5

Zoetermeer 2719 EE
NL
Scientific
Astra Zeneca

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Histologically or cytologically documented Stage IV NSCLC with locally advanced disease not amendable to curative surgery or radiation. ;- Patients must have tumors that lack activating EGFR mutation and ALK rearrangement per local laboratory test.;- No prior chemotherapy or any other systemic therapy for locally advanced or metastatic NSCLC. Patients who have received prior platinum-containing adjuvant, neoadjuvant, or definitive chemoradiation for locally advanced disease are eligible, provided that progression has occurred >6 months from last therapy. ;- Able to undergo a fresh tumor biopsy during screening or to provide an available tumor sample taken <3 months prior to screening. Tumor lesions used for fresh biopsies should not be target lesions, unless there are no other lesions suitable for biopsy. Fine needle aspirate specimens are not acceptable. ;- World Health Organization (WHO)/Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 at enrolment.;- At least 1 lesion, not previously irradiated, that can be accurately measured at baseline as *10 mm in the longest diameter (except lymph nodes which must have a short axis *15 mm) with CT or MRI and that is suitable for accurate repeated measurements as per RECIST 1.1 guidelines. ;- No prior exposure to immune-mediated therapy including, but not limited to, other anti CTLA-4, anti-PD-1, anti-PD-L1, and anti-programmed cell death ligand 2 (anti-PD-L2) antibodies, excluding therapeutic anticancer vaccines.

Exclusion criteria

- Mixed small-cell lung cancer and NSCLC histology, sarcomatoid variant ;- Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment. Concurrent use of hormonal therapy for non-cancer-related conditions (eg, hormone replacement therapy) is acceptable. ;- Radiotherapy treatment to more than 30% of the bone marrow or with a wide field of radiation within 4 weeks of the first dose of study drug;- Major surgical procedure (as defined by the Investigator) within 28 days prior to the first dose of IP. ;- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [eg, colitis or Crohn*s disease], diverticulitis with the exception of diverticulosis, celiac disease or other serious gastrointestinal chronic conditions associated with diarrhea), systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome (granulomatosis with polyangiitis), Graves* disease, rheumatoid arthritis, hypophysitis, uveitis, etc) within the past 3 years prior to the start of treatment. The following are exceptions to this criterion:;* Patients with vitiligo or alopecia;* Patients with hypothyroidism (eg, following Hashimoto syndrome) stable on hormone replacement or psoriasis not requiring systemic treatment;9. Any condition that, in the opinion of the Investigator, would interfere with the evaluation of IP or interpretation of patient safety or study results, including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, interstitial lung disease, or psychiatric illness/social situations that would limit compliance with study requirement, substantially increase risk of incurring AEs from MEDI4736 or tremelimumab, or compromise the ability of the patient to give written informed consent;- No medical contraindication to platinum (cisplatin or carboplatin)-based doublet chemotherapy;- History of another primary malignancy except for ;Malignancy treated with curative intent and with no known active disease *5 years before the first dose of study drug and of low potential risk for recurrence;* Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease;* Adequately treated carcinoma in situ without evidence of disease (eg, cervical cancer in situ);- History of leptomeningeal carcinomatosis;- Brain metastases or spinal cord compression unless patient is stable (asymptomatic, no evidence of new or emerging brain metastases) and off steroids and anti-convulsants for at least 14 days prior to study treatment. - History of active primary immunodeficiency ;- Active infection including tubercolosis (clinical evaluation), hepatitis B, hepatitis C, or human immunodeficiency virus (HIV);- Current or prior use of immunosuppressive medication within 14 days before the first dose of MEDI4736 or tremelimumab. The following are exceptions to this criterion:;* Intranasal, inhaled, topical steroids, or local steroid injections (eg, intra articular injection).;* Systemic corticosteroids at physiologic doses not to exceed 10 mg/day of prednisone or its equivalent;* Steroids as premedication for hypersensitivity reactions (eg, CT scan premedication);- Receipt of live, attenuated vaccine within 30 days prior to the first dose of IP. Note: Patients, if enrolled, should not receive live vaccine during the study and up to 30 days after the last dose of IP.;- Female patients who are pregnant or breast-feeding or male or female patients of reproductive potential who are not willing to employ effective birth control from screening to 180 days after the last dose of MEDI4736 + tremelimumab combination therapy or 90 days after the last dose of MEDI4736 monotherapy.;-Known allergy or hypersensitivity to IP or any excipient

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):	15-10-2015
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Durvalumab
Product type:	Medicine
Brand name:	NA
Generic name:	Tremelimumab

Ethics review

Approved WMO

Date:	07-07-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	03-09-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-10-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-04-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-07-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-08-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-03-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-03-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-03-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-10-2017

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-02-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-03-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-04-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	05-02-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-02-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2015-001279-39-NL
ClinicalTrials.gov	NCT02453282
CCMO	NL53710.031.15