A Phase III Randomized, Open-Label, Multi-Center Study of Durvalumab Versus Standard of Care Platinum-Based Chemotherapy as First Line Treatment in Patients with PD-L1-High Expression Advanced Non Small-Cell Lung Cancer (NSCLC)

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To assess the efficacy of Durvalumab monotherapy compared to SoC in terms of OS in patients with PD-L1 high expression (*25%) advanced NSCLC with wild type EGFR and ALK

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

Summary

ID

NL-OMON46307

Source
ToetsingOnline

Brief title
China PEARL

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: Durvalumab, Non-small cell lung cancer, PD-L1, Standard of Care Platinum-Based Chemotherapy

Outcome measures

Primary outcome

To assess the efficacy of Durvalumab monotherapy compared to SoC in terms of OS

in patients with PD-L1 high expression (*25%) advanced NSCLC with wild type

EGFR and ALK

Secondary outcome

- To further assess the efficacy of durvalumab compared to SoC in terms of OS,

PFS, ORR, DoR, APF12, and PFS2.

- To assess disease-related symptoms and HRQoL in patients treated with

durvalumab compared to SoC using the EORTC QLQ-C30 v3 and the LC13 module

- To investigate the immunogenicity of durvalumab

- To assess the safety and tolerability profile of durvalumab compared to SoC

Study description

Background summary

Despite advances in the diagnosis, imaging, staging and treatment of non-small cell lung cancers, the estimated 5-year survival for patients with Stage IV NSCLC is only 11-17% in Europe and US respectively. In China, the 5-year survival is less than 20%. Patients diagnosed with NSCLC with wild type EGFR and ALK status currently have an average survival of 12 months or less. First line Standard of Care treatment is with platinum based chemotherapy. However, the duration of responses are limited and toxicities can be a major limiting factor.
In this study, the new drug Durvalumab will be compared as monotherapy with the Standard of Care chemotherapy. Durvalumab is a monoclonal antibody (mAb) which has an influence on the binding of the Programmed Death Ligand 1 (PD-L1). PD-L1 plays a role in the suppression of the immune system which is used by the tumor to escape from the immune system.
Given the currently available medication in the Netherlands for patients with PD-L1 expression> 50%, it is potentially possible in this study to only include patients with a PD-L1 expression of 25-49%.

Study objective

To assess the efficacy of Durvalumab monotherapy compared to SoC in terms of OS in patients with PD-L1 high expression (*25%) advanced NSCLC with wild type EGFR and ALK

Study design

Phase 3, open label, randomized, multi center, international study

Ransomisation 1:1, stratification on PD-L1 expression and histology with smoking status:
- Durvalumab monotherapy
- Standard platinum chemotherapy

Intervention

Durvalumab monotherapy:
- 20 mg/kg durvalumab via IV infusion q4w, start on week 0 until disease progression, unacceptable toxicity or withdrawal of informed consent

Study burden and risks

On several days during the study the patients will undergo the following

assessments:
- tumor biopsy (only once during screening if <3 months biopt is unavailable)
- anamnesis (at screening also medical history)
- physical examination
- ECOG performance status
- vital signs (blood pressure, pulse, temperature and respiration rate)
- body weight
- CT or MRI scan
- ECG
- blood and urine assessments
- questionnaires (EORTC QLQ-C30, EORTC QLQ-LC13, EQ-5D-5L)
- pregnancy test if applicable
- AE/SAE assessment

Contacts

Public
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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 (according to version 7 of the International Association for the Study of Lung Cancer Staging Manual in Thoracic Oncology; IASLC Staging Manual in Thoracic Oncology);- Patients must have tumors that lack sensitizing EGFR mutation (e.g., exon 19 deletion or exon 21 L858R, exon 21 L861Q, exon 18 G719X, or exon 20 S7681 mutation) and ALK rearrangement;- Patient must have tumor cell PD-L1-high expression status, prior to randomization, defined as *25% PD-L1*membrane expression in tumoral tissue with the Ventana SP263 PD-L1 IHC assay determined by a reference laboratory;- 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;- Must have a life expectancy of at least 12 weeks

Exclusion criteria

- Prior chemotherapy or any other systemic therapy for advanced NSCLC. ;- 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;- 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;- Brain metastases or spinal cord compression unless the patient is stable (asymptomatic, no evidence of new or emerging brain metastases) and off steroids for at least 14 days prior to start of study treatment;- History of leptomeningeal carcinomatosis;- Mixed small-cell lung cancer and NSCLC histology, sarcomatoid variant;- Active or prior documented autoimmune or inflammatory disorders 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 (e.g., following Hashimoto syndrome) stable on hormone replacement or psoriasis not requiring systemic treatment, Any chronic skin condition that does not require systemic therapy, Patients without active disease in the last 5 years may be included but only after consultation with the study physician, Patients with celiac disease controlled by diet alone;- History of active primary immunodeficiency;- Active infection, including tuberculosis (clinical evaluation), hepatitis B, hepatitis C, or human immunodeficiency virus (HIV, positive HIV 1 or 2 antibodies);- Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab. 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.;- Major surgical procedure (as defined by the Investigator) within 28 days prior to the first dose of IP;- History of allogenic organ transplantation;- 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 (e.g., cervical cancer in situ);- Medical contraindication to platinum (cisplatin or carboplatin)-based doublet chemotherapy.;- Positive urinary or serum pregnancy test for female pre-menopausal patients;- Female patients who are pregnant or breast-feeding or male or female patients of reproductive potential who are not willing to employ highly effective birth control from screening to 90 days after the last dose of durvalumab.;- Known allergy or hypersensitivity to IP or any excipient or to other humanized mAbs

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):	13-09-2018
Enrollment:	18
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-05-2018
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	28-06-2018
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	17-01-2019
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2018-001375-21-NL
ClinicalTrials.gov	NCT03003962
CCMO	NL65752.096.18