A Phase III, Randomized, Multicenter, Open-Label, Comparative Study to Determine the Efficacy of Durvalumab or Durvalumab and Tremelimumab in Combination With Platinum-Based Chemotherapy for the First-Line Treatment in Patients with Extensive Disease Small-Cell Lung Cancer (SCLC)

Published: 22-02-2017
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To assess the efficacy of durvalumab +tremelimumab + EP treatment compared with EP in terms of OS and the efficacy of durvalumab + EP treatment compared with EP in terms of OS

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

Summary

ID

NL-OMON50493

Source
ToetsingOnline

Brief title
Caspian

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym

Small-Cell Lung Cancer; 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, Platinum-Based Chemotherapy, Small-Cell Lung Cancer, Tremelimumab

Outcome measures

Primary outcome

To assess the efficacy of durvalumab +tremelimumab + EP treatment compared with

EP in terms of OS and the efficacy of durvalumab + EP treatment compared with

EP in terms of OS and PFS

Secondary outcome

-To further assess the efficacy of durvalumab + tremelimumab + EP treatment

compared with EP in terms of PFS, ORR, APF6 (PFS rate at

6 months), APF12 (PFS rate at 12 months), and OS18 (OS rate at 18 months)

-To assess the efficacy of durvalumab + tremelimumab + EP treatment compared

with durvalumab + EP and the efficacy of durvalumab + EP compared with EP in

terms of PFS and OS

-To assess the PK of durvalumab and durvalumab + tremelimumab

-To investigate the immunogenicity of durvalumab and durvalumab + tremelimumab

-To assess the effect of the treatment on changes in symptoms and

health-related QoL using EORTC QLQ-C30 v3 and QLQ-LC13

Study description

Background summary

Small-cell lung cancer (SCLC) represents approximately 13% of all newly diagnosed lung cancers. SCLC is perhaps the most aggressive form of the disease, distinguishable from non-small-cell lung cancer (NSCLC) by its rapid doubling time, high growth fraction, and early dissemination. It is strongly associated with tobacco smoking and is also associated with an extremely high mutation rate.
Platinum based chemotherapy (EP) has been the standard care (SoC) for patients with extensive-stage disease (ED) SCLC for the past 25 years. Despite high initial response rates of up to 70% it is estimated that 80% of patients with limited stage and almost all patients with ED SCLC will relapse or experience disease progression. Therefore prognosis for patients with SCLC in general and particular ED SCLC is poor; the reported 2-year survival is only 5% and 5 years survival rate is less than 2%.

In this study the new investigational product Durvalumab with EP or Durvalumab + Tremelimumab + EP be compared to standard platinum chemotherapy EP treatment for small cell lung cancer. Durvalumab is a human mAb of the immunoglobulin G 1 kappa subclass that inhibits the binding of PD-L1 and tremelimumab is a mAB which binds to the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Both PD-L1 and CTLA-4 proteins play a role in the suppression on the immune system which the tumor uses in order to escape the immune system.

Study objective

To assess the efficacy of durvalumab +tremelimumab + EP treatment compared with EP in terms of OS and the efficacy of durvalumab + EP treatment compared with EP in terms of OS

Study design

Phase III, open label, Randomized, Multicenter, internation study.
Randomization 1:1:1. Stratified to choice of platinum:
• Durvalumab + Tremelimumab + EP
• Durvalumab + EP monotherapy
• Standard platinum based chemotherapy EP.

Intervention

1. Durvalumab + Tremelimumab combination therapy + EP: Durvalumab 1500mg via IV infusion q3w, start on week 0, for 4 doses/cycles, and then proceed with Durvalumab 1500mg via IV infusion q4w, start on week 12 until progression.

Tremelimumab 75mg via IV infusion q3w, start on week 0, for 4 doses/cycles, and last dose/cycle on week 16. EP (80-100 mg/m2) via IV infusion q3w, start onp Week 0, for4 doses/cycles

2. Durvalumab + EP: Durvalumab 1500mg via IV infusion q3w, start on week 0, for 4 doses/cycles, and then proceed with Durvalumab 1500 mg via IV infusion q4w, start on week 12 until progression. EP (80-100 mg/m2) via IV infusion q3w, start onp Week 0, for 4 doses/cycles

3. EP (80-100 mg/m2) via IV infusion q3w, start onp Week 0, for4 doses/cycles (can be extended with maximum of 2 doses/ cycles).

Study burden and risks

Patients will be assessed on the following assessments during the study: - Anamnesis - Physical examination - Performance status - Vital signs (BP, pulse, temperature, respiratory rate) - Height - Weight- CT/MRI - ECG - Blood and urine samples - Questionnaires (EORTC QLQ C-30, EORTC QLQ-LC1) (e-device) - Pregnancy testing (if applicable)

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

-Male or female >=18 years at the time of Screening.
-Written informed consent and any locally required authorization obtained from the patient/legal representative prior to performing any protocol-related procedures, including screening evaluations.
-Histologically or cytologically documented extensive disease (American Joint Committee on Cancer Stage (7th edition) IV SCLC [T any, N any, M1 a/b]), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan.
-Patients must be considered suitable to receive a platinum based chemotherapy regimen as 1st line treatment for the ED-SCLC. Chemotherapy must contain either cisplatin or carboplatin in combination with etoposide.
-Life expectancy >=12 weeks at Day 1.
-World Health Organization (WHO)/Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1 at enrollment
-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 computed tomography (CT) or magnetic resonance imaging (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.
- Adequate organ and marrow function

Exclusion criteria

- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site).
- Previous IP assignment in the present study.
- Concurrent enrollment in another clinical study, unless it is an observational (non-interventional) clinical study or during the follow-up period of an interventional study.
- Participation in another clinical study with an IP during the last 4 weeks.
- Medical contraindication to etoposide-platinum (carboplatin or cisplatin)-based chemotherapy

- Any history of radiotherapy to the chest prior to systemic therapy or planned consolidation chest radiation therapy.
- Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment.
- Major surgical procedure (as defined by the investigator) within 28 days prior to the first dose of IP.
- History of allogenic organ transplantation.
- Has a paraneoplastic syndrome (PNS) of autoimmune nature, requiring systemic treatment (systemic steroids or immunosuppressive agents) or has a clinical symptomatology suggesting worsening of PNS.
- Active or prior documented autoimmune or inflammatory disorders
- Uncontrolled intercurrent illness.
- History of another primary malignancy
- History of leptomeningeal carcinomatosis.
- History of active primary immunodeficiency.
- Active infection including tuberculosis, hepatitis B, hepatitis C, or human immunodeficiency virus (positive HIV 1/2 antibodies).
- Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab or tremelimumab.
- Receipt of live, attenuated vaccine within 30 days prior to the first dose of IP.
- Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ effective birth control from Screening to 90 days after the last dose of durvalumab monotherapy or 180 days after the last dose of durvalumab + tremelimumab combination therapy.
- Known allergy or hypersensitivity to durvalumab, tremelimumab, etoposide, carboplatin, cisplatin, or any of their excipients
- Prior randomization or treatment in a previous durvalumab and/or tremelimumab clinical study regardless of treatment arm assignment.

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-07-2017
Enrollment:	37
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:	22-02-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-04-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-08-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-02-2018

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Not approved Date:	23-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-05-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-08-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-01-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-11-2020

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-03-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-01-2023

Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2016-001203-23-NL
CCMO	NL59719.031.17

Study results

Date completed:	09-03-2023
Actual enrolment:	19