A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/adjuvant Durvalumab for the Treatment of Patients with Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)

Published: 03-03-2020
Last updated: 07-09-2024

This study has been transitioned to CTIS with ID 2023-509576-42-00 check the CTIS register for the current data. This Phase III study, the administration of durvalumab + chemotherapy prior to surgery, followed by administration of durvalumab after...

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

Summary

ID

NL-OMON52504

Source
ToetsingOnline

Brief title
AEGEAN

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
non 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, Neoadjuvant/Adjuvant, Non Small Cell Lung Cancer, Resection

Outcome measures

Primary outcome

- To compare the efficacy of durvalumab + chemotherapy administered prior to surgery followed by durvalumab post-surgery compared with placebo + chemotherapy administered prior to surgery followed by placebo post-surgery in terms of EFS (event-free survival)

- To compare the activity of durvalumab + chemotherapy administered prior to surgery compared with placebo + chemotherapy administered prior to surgery in terms of mPR(major pathologic response = 10% or less residual viable tumor tissue in lung primary tumor after neoadjuvant treatment at the time of resection)

Secondary outcome

- To compare the efficacy of perioperative durvalumab + neoadjuvant chemotherapy compared with placebo + neoadjuvant chemotherapy in terms of DFS

- To compare the efficacy of perioperative durvalumab + neoadjuvant chemotherapy compared with placebo + neoadjuvant chemotherapy in

terms of MPR

- To compare the efficacy of perioperative durvalumab + neoadjuvant

chemotherapy compared with placebo + neoadjuvant chemotherapy in

terms of OS

- To compare the efficacy of perioperative durvalumab + neoadjuvant

chemotherapy compared with placebo + neoadjuvant chemotherapy in

patients with PD-L1 TC >=1% tumors in terms of EFS, pCR, DFS, MPR and OS

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

perioperative durvalumab + neoadjuvant chemotherapy compared

with placebo + neoadjuvant chemotherapy

- To assess the PK and immunogenicity of durvalumab

Study description

Background summary

Lung cancer has been the most common cancer in the world for several decades, with an estimated 1.8 million new cases in 2012 (12.9% of all new cancers), and was also the most common cause of death from cancer in 2012, with 1.6 million deaths (19.4% of cancer deaths). NSCLC represents 80% to 85% of all lung cancers. Despite advances in the diagnosis, imaging, staging, and treatment of NSCLC, the estimated 5-year OS for patients in Europe and the United States (US) continues to be low (11% and 17%, respectively).

For early-stage NSCLC, the primary treatment is curative surgery. Only ~30% of patients present with Stages I to IIIA lung cancer; however, this percentage is expected to increase as a result of the implementation of lung cancer screening. Unfortunately, the 5-year survival for patients treated with surgery alone remains low, ranging from 67% (Stage IA) to 23% (Stage IIIA).

Studies of adjuvant chemotherapy in the NSCLC setting have demonstrated a modest but clinically meaningful improvement in OS; perioperative platinum-based chemotherapy has shown a survival rate of 5.4 percentage points higher than surgery alone, with toxicities of Grade 3 or higher observed in

more than 60% of patients.

A number of studies have demonstrated the clinical benefit of neoadjuvant chemotherapy in early-stage NSCLC; major pathologic response (mPR) was observed (improvement of the overall survival).

Despite these advances, new therapies are needed to further improve the long-term prognosis for patients with NSCLC who undergo surgical resection.

Study objective

This study has been transitioned to CTIS with ID 2023-509576-42-00 check the CTIS register for the current data.

This Phase III study, the administration of durvalumab + chemotherapy prior to surgery, followed by administration of durvalumab after surgery, will be investigated in patients with resectable Stages II and III NSCLC. The efficacy of durvalumab will be compared to a placebo group using event free survival (EFS) and major pathologic response (mPR).

Study design

Phase III, double blinded, placebo-controlled, randomized study.
Randomisation 1:1 to:

- Durvalumab (IV) + platinum-based chemotherapy (4 cycles) before surgery +12 cycles durvalumab after surgery
- Placebo (IV) + platinum-based chemotherapy (4 cycles) before surgery +12 cycles placebo after surgery

Approximately 800 patients will receive treatment upon progression, followed by FU-fase.

Intervention

Patients will receive (unless there is unacceptable toxicity, withdrawal of consent, or another discontinuation criterion is met):

- before surgery
* treatment group 1: patients receive (via IV infusion) 1500 mg durvalumab q3w for up to a maximum of 4 cycles (+4 cycles platinum-based chemotherapy).
* treatment group 2: patients receive (via IV infusion) placebo q3w for up to a maximum of 4 cycles (+4 cycles platinum-based chemotherapy).

- after surgery
* treatment group 1: patients receive (via IV infusion) 1500 mg durvalumab q4w

for 12 cycles
* treatment group 2: patients receive (via IV infusion) placebo q4w for 12 cycles

Study burden and risks

Patiënts are subject to the following assessments throughout the study:
- Anamnesis (at screening, including medical history)
- Physical examination
- ECOG performance status
- Vital functions (blood pressure, heartrate, body temperature and respiratory rhythm)
- Body weight measurement
- brain MRI/CT scan with IV contrast (only at screening)
- ECG
- blood - and urine examination
- questionnaires (EORTC QLQ-C30, EORTC QLQ-LC13, EQ-5D-5L, PGIS, PRO-CTCAE)
- pregnancy test when applicable
- AE/SAE assessment
- IP administration
- CT+PET scan at screening for staging purposes and as pre-operative assessment
- pulmonary function tests and heart risk assessment
- biopsy (new biopt or <3 months old)
- surgery

Durvalumab activates the immune system of the body and this can cause adverse effects. Adverse effects can arise during or within several hours/days after the administration of the IV line. The adverse effects that are known, are obtained from previous studies. It is possible that the patient might suffer from 1 or all of the following adverse effects: fever, fatigue, rash or hives, change in blood pressure, decrease in the amount of thrombocytes, inflammation of the lungs, inflammation of the nervous system, inflammation of the pancreas, inflammation of the liver, inflammation of the intestines, changes in nodes that regulate hormone production.
Chemotherapy can also cause adverse effects.
The adverse effects can vary from mild to severe and can even be life-threatening. In this study certain conditions are incorporated for early signalling of these severe adverse effects. Moreover, the study procedures might also cause the following ailments:
- pain or bruises through collection of blood
- rash through ECG stickers
- health risks through radiation of CT-scan/MRI
- pain, scar tissue, infection, bleeding of the pneumothorax during biopsy

Contacts

Public
Astra Zeneca

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NL
Scientific
Astra Zeneca

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age >=18 years 2. Newly diagnosed and previously untreated patients with histologicallyor cytologically documented NSCLC with resectable (Stage IIA to select [ie, N2] Stage IIIB) disease 3. World Health Organization (WHO)/ECOG PS of 0 or 1 at enrollment 4. At least 1 lesion, not previously irradiated, that qualifies as a RECIST 1.1 Target Lesion (TL) at baseline 5. No prior exposure to immune-mediated therapy including, but not limited to, other anti-CTLA-4, anti-PD-1, anti-PD-L1, and anti-PD-L2 antibodies, excluding therapeutic anticancer vaccines. 6. Adequate organ and marrow function 7. Confirmation of a patients tumour PD-L1 status 8. Provision of sufficient tumour biopsy sample for evaluation and confirmation of EGFR and ALK status 9. Planned surgery to be performed need to include lobectomy, sleeve resection or bilobectomy.10. A pre-

or post-bronchodilator FEV of 1.0 L and >40% post-operative predicted value.

Exclusion criteria

1. History of allogeneic organ transplantation
2. Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease, diverticulitis, systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome).
3. History of another primary malignancy
4. History of active primary immunodeficiency
5. . Active infection including tuberculosis hepatitis B and C, or human immunodeficiency virus
6. Deemed unresectable NSCLC by multidisciplinary evaluation
7. Patients who have pre-operative radiotherapy treatment as part of their care plan
8. Patients who have brain metastases or spinal cord compression
9. Stage IIIB N3 and Stages IIIC, IVA, and IVB NSCLC
10. Known allergy or hypersensitivity to any of the study drugs or excipients11. Existence of more than one primary tumour such as mixed small cell and NSCLC histology12. Patients who are candidates to undergo only pneumonectomy, segmentectomies or wedge resections.13. Patients with a documented test result confirming the presence of EGFRm or ALK translocation.

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):	22-09-2020
Enrollment:	275
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	Pemetrexed
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Imfinzi
Generic name:	Durvalumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-03-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	09-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	21-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-03-2024
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
EU-CTR	CTIS2023-509576-42-00
EudraCT	EUCTR2018-002997-29-NL
ClinicalTrials.gov	NCT03800134
CCMO	NL72968.056.20