A Phase III, Randomized, Multicenter, Double-blind, Placebo-controlled Study to Determine the Efficacy of Adjuvant Durvalumab in Combination with Platinum-based Chemotherapy in Completely Resected Stage II-III NSCLC (MeRmaiD 1)

Published: 29-04-2020
Last updated: 08-04-2024

The research hypothesis for this study is that concurrent durvalumab plus SoC chemotherapy will be more effective than placebo plus SoC chemotherapy for the treatment of MRD+ patients who have undergone complete resection of stage II-III NSCLC when…

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

Summary

ID

NL-OMON54167

Source
ToetsingOnline

Brief title
MERMAID-1

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: AstraZeneca

Intervention

Keyword: Adjuvant, Complete Resection, Durvalumab, Non Small Cell Lung Cancer

Outcome measures

Primary outcome

To assess the efficacy of durvalumab + SoC chemotherapy compared to placebo + SoC chemotherapy as measured by DFS in MRD+ patients

Secondary outcome

- To assess the efficacy of durvalumab plus SoC chemotherapy compared to placebo plus SoC chemotherapy as measured by DFS in all patients

- To assess the efficacy of durvalumab plus SoC chemotherapy compared to placebo plus SoC chemotherapy as measured by DFS in MRD+ patients and all patients

- To assess the efficacy of durvalumab plus SoC chemotherapy compared to placebo plus SoC chemotherapy as measured by OS in MRD+ patients and in all patients

- To assess patient-reported symptoms, functioning, and HRQoL in MRD+ patients treated with durvalumab plus SoC chemotherapy compared to placebo plus SoC chemotherapy

Study description

Background summary

Up to 30% of patients with NSCLC present with surgically resectable disease. For patients with stage II-IIIA and select IIIB disease, surgery and adjuvant SoC chemotherapy results in 5-year disease-free survival (DFS) rates of only ~40%. The majority of patients who remain event-free at 5 years are cured by surgery alone yet receive adjuvant treatment because there is currently no clear way to determine who will benefit from adjuvant chemotherapy.
There is evidence that identification of MRD through detection of ctDNA post-surgery can accurately predict disease recurrence. Detection of MRD at a time when there is no radiologic evidence of disease provides an opportunity for earlier therapeutic intervention. Patients with MRD (MRD-positive [MRD+]) experience inferior recurrence-free survival compared to patients without detectable MRD (MRD-negative [MRD-]). Therefore, MRD+ patients could benefit from earlier intervention and escalation of treatment; furthermore, MRD- patients (the majority of whom are cured by surgery alone) could be spared from more intensive therapy and the resulting unnecessary toxicity.
Clinical data suggest that the combination of immunotherapy and chemotherapy in the adjuvant setting, where patients have undergone a complete resection but may have residual disease, would provide additional benefits to single agent immunotherapy and improve DFS.

Study objective

The research hypothesis for this study is that concurrent durvalumab plus SoC chemotherapy will be more effective than placebo plus SoC chemotherapy for the treatment of MRD+ patients who have undergone complete resection of stage II-III NSCLC when administered in the adjuvant setting.

Study design

Phase III, double blinded, placebo-controlled, randomized study.
Randomisation 1:1 to:
- Durvalumab (IV) + platinum-based chemotherapy (4 cycles) +10 cycles durvalumab
- Placebo (IV) + platinum-based chemotherapy (4 cycles) +10 cycles placebo
323 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):
* treatment group 1: patients receive (via IV infusion) 1500 mg durvalumab + SoC chemotherapy q3w for 4 cycles + 10 cycles 1500 mg durvalumab

* treatment group 2: patients receive (via IV infusion) placebo q3w +SoC chemotherapy for 4 cycles + 10 cycles placebo.

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
- heart risk assessment
- surgery
- During screening, if there is no "tumor tissue", residual material, may be used to determine markers.

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

Contacts

Public
Astra Zeneca

Prinses Beatrixlaan 582
Den Haag 2595BM
NL
Scientific
Astra Zeneca

Prinses Beatrixlaan 582
Den Haag 2595BM
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Individuals who have diagnosis of histologically confirmed NSCLC (WHO 2015 classification) with resectable (stage II-III) disease
• A contrast-enhanced CT/MRI scan of the chest and abdomen (including liver and adrenal glands) must have been done for surgical planning prior to surgery
• Complete resection of the primary NSCLC is mandatory
• Confirmation of suitable resected tumor tissue and whole blood sample
• Post-operative CT scan of the chest and abdomen
• Adequate organ and marrow function
• Eligible to tolerate 4 cycles of platinum-based adjuvant chemotherapy
• Must have a life expectancy of at least 12 weeks

Exclusion criteria

• Unequivocal evidence of disease recurrence or tissue biopsy-proven disease recurrence
• EGFR-mutant and/or ALK-translocation
• Mixed small cell and NSCLC histology
• Require re-resection or are deemed to have unresectable NSCLC by a multidisciplinary evaluation that must include a thoracic surgeon who performs lung cancer surgery as a significant part of their practice.
• Patients who are candidates to undergo only wedge resections
• Active or prior documented autoimmune or inflammatory disorders
• Uncontrolled intercurrent illness (see protocol page 67)
• History of another primary malignancy (check for exceptions)
• History of active primary immunodeficiency
• Active infection including tuberculosis, hepatitis B, hepatitis C virus or HIV
• Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment (check for exceptions)
• Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab (check for exceptions)
• Patients who are never-smokers

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):	17-12-2020
Enrollment:	5

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:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-07-2020
Application type:	First submission

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:	06-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	02-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-10-2023
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	EUCTR2020-000556-35-NL
ClinicalTrials.gov	NCT04385368
CCMO	NL73257.056.20