A Phase III, Randomized, Multicenter, Double-blind, Placebo-controlled Study of Durvalumab for the Treatment of Stage II-III NSCLC Patients with Minimal Residual Disease Following Surgery and Curative Intent Therapy (MERMAID-2)

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

Summary

ID

NL-OMON52301

Source
ToetsingOnline

Brief title
MeRmaiD2

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: AstraZeneca

Intervention

Keyword: Complete Resection, Durvalumab, Minimal residual disease, Non Small Cell Lung Cancer

Outcome measures

Primary outcome

To assess the efficacy of durvalumab compared to placebo as measured by DFS in

the PD-L1 TC>=1% analysis set

Secondary outcome

To assess the efficacy of durvalumab compared to placebo as measured by DFS in

all randomized patients

To assess the efficacy of durvalumab compared to placebo as measured by DFS in

the PD-L1 TC>=1% analysis set and in all randomized patients

To assess the efficacy of durvalumab compared to placebo on post-recurrence

outcomes

To assess the efficacy of durvalumab compared to placebo as measured by OS in

the PD-L1 TC>=1% analysis set and in all randomized patients

To assess patient-reported symptoms, functioning, and HRQoL in patients treated

with durvalumab compared to placebo

To investigate the relationship between a patient*s baseline PD-L1 TC

expression and efficacy of study treatments

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%. Long-term survival is improved through administration of chemotherapy in the immediate post-operative setting, yet chemotherapy in the first-line metastatic setting results in no long-term survival benefit and progression-free survival (PFS) benefits of only a small number of months.
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 earlier intervention with immunotherapy as adjuvant therapy following curative intent treatment could improve outcomes in early-stage NSCLC, prevent progression, and circumvent the need to expose patients to potentially more toxic chemotherapy regimens in the metastatic setting.

Study objective

This study is being conducted to evaluate the efficacy and safety of durvalumab adjuvant therapy compared to placebo in patients with completely resected stage II-III NSCLC who have undergone curative intent therapy (complete resection ± neoadjuvant and/or adjuvant therapy), and who become MRD+ during a 96-week surveillance period.

Study design

Phase III, double blinded, placebo-controlled, randomized study.
Randomisation 1:1 to:
- Durvalumab (IV) 26 cycles
- Placebo (IV) 26 cycles
284 patients will receive treatment once they turn MRD+ and have no evidence of recurrence according to RECIST 1.1.

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 for 26 cycles
* treatment group 2: patients receive (via IV infusion) placebo for 26 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-, stools- 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

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.
In this study certain conditions are incorporated for early signaling 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

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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 confirmed NSCLC with resectable stage II-III disease who have undergone curative intent
therapy (complete resection of the primary tumor ± neoadjuvant and/or adjuvant therapy) per SoC
• A contrast-enhanced CT/MRI scan of the chest and abdomen (including liver and adrenal glands) along with brain MRI must have been done for surgical planning prior to surgery
• Complete resection of the primary NSCLC is mandatory
• Patients should have completed curative intent therapy
• Confirmation of suitable resected tumor tissue and whole blood sample
• Post-adjuvant therapy or post-operative CT scan of the chest and abdomen and brain MRI
• Consents to be accessible for q6w plasma sample collection for MRD evaluation and for q12w CT scans during the 96-week surveillance period

Inclusion criteria for second screening period:
• CT scan of the chest and abdomen and brain MRI performed within the 28 days prior to randomization to confirm no evidence of RECIST 1.1-defined disease recurrence and/or metastasis
• Complete post-operative wound healing
• Must have recovered from all acute, reversible toxic effects from chemotherapy
• Adequate organ and marrow function
• 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.
• 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
• Received any IO therapy in the adjuvant setting or any prior exposure to durvalumab
• Received any radiotherapy in the neoadjuvant setting
• Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment (with exceptions)
• Current or prior use of immunosuppressive medication within 14 days before the first dose of IP (with exceptions)

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:	Completed
Start date (anticipated):	03-08-2021
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Imfinzi
Generic name:	Durvalumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-09-2020
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:	24-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2022

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:	20-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2022
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)

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	EUCTR74839.056.20-NL
ClinicalTrials.gov	NCT04642469
CCMO	NL74839.056.20