A Phase IB, Open-Label, Multi-Center Study to Determine the Efficacy and Safety of Durvalumab in Combination With Novel Oncology Therapies, With or Without Chemotherapy, for First-Line Stage IV Non-Small Cell Lung Cancer (NSCLC) (MAGELLAN)

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To assess the safety and tolerability profile of durvalumab monotherapy, durvalumab + novel oncology therapy, durvalumab + chemotherapy, anddurvalumab + novel oncology therapy + chemotherapy combinations

Ethical review	Approved WMO
Status	Will not start
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON48202

Source
ToetsingOnline

Brief title
MAGELLAN

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: Danvatirsen, Durvalumab, Non-Small Cell Lung Cancer (NSCLC), Oleclumab

Outcome measures

Primary outcome

To assess the safety and tolerability profile of all arms.

Secondary outcome

To assess the efficacy of all durvalumab combinations in terms of ORR, PFS,

DoR, and OS

To assess the PK of durvalumab and each additional novel oncology therapy in

all treatment arms

To investigate the immunogenicity of durvalumab and each additional novel

oncology therapy in all applicable treatment arms

Study description

Background summary

NSCLC comprises 80-85% of all lung cancers and ~70% of patients with NSCLC have advanced or metastatic disease not amenable to curative resection at diagnosis. Recent studies with IO or IO+chemo represent a substantive advance; but further improvement is needed (mPFS for Phase 3 studies < 1 year

Study objective

To assess the safety and tolerability profile of durvalumab monotherapy,

durvalumab + novel oncology therapy, durvalumab + chemotherapy, and durvalumab + novel oncology therapy + chemotherapy combinations

Study design

Patients will be stratified into Cohort A (PD-L1 High) and Cohort B (PD-L1 low). Patients in Cohort A can be randomized into 3 arms: 1)Durvalumab monotherapie 2) Durvalumab + CD73 (Oleclumab) 3) Durvalumab + STAT2 (Danvatirsen). Patients in Cohort B can be randomized into 3 arms: 1)Durvalumab + Chemotherapy 2) Durvalumab + CD73 (Oleclumab)+ Chemotherapy 3) Durvalumab + STAT2 (Danvatirsen) + Chemotherapy

Intervention

1 (Cohort A) A1 Durvalumab
1 (Cohort A) A2 Durvalumab + danvatirsen
1 (Cohort A) A3 Durvalumab + oleclumab
1 (Cohort B) B1 Durvalumab + chemotherapie naar keuze
1 (Cohort B) B2 Durvalumab + chemotherapie naar keuze + danvatirsen
1 (Cohort B) B3 Durvalumab + chemotherapie naar keuze + oleclumab

Study burden and risks

On several days during the study the patients will undergo the following assessments: - tumor biopsy (during screening if <3 years 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 - pregnancy test if applicable - AE/SAE assessment

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

1) Age >=18 years at the time of screening.
2) Written informed consent.
3)Histologically or cytologically documented Stage IV NSCLC not amenable to curative surgery or radiation.
4)Tumours that lack activating EGFR mutations and ALK fusions. If a patient has squamous histology or is known to have a tumor with a KRAS mutation, then EGFR and ALK testing is not required.
5) WHO/ECOG performance status of 0 or 1 at enrolment and treatment assignment.
6) No prior chemotherapy or any other systemic therapy for metastatic NSCLC. Prior platinum-containing adjuvant, neoadjuvant, or definitive chemoradiation for non-metastatic disease is allowed, provided that progression has occurred >12 months from end of last therapy.
7) No prior exposure to immune-mediated therapy (anti-CTLA-4, anti-PD-1, anti-PD-L1, and anti-PD-L2 antibodies)
8) At least 1 lesion, not previously irradiated, that qualifies as a RECIST 1.1 target lesion at Baseline.
9) Known tumor PD-L1 status, confirmed by a central reference laboratory using a validated Ventana SP263 PD-L1 IHC assay (fresh biopsy or sample taken <=3 years prior to enrollment).
10)Adequate organ and marrow function as defined below:
- Hemoglobin >=9 g/dL
- Absolute neutrophil count >=1.5 × 109/L
- Platelet count >=100 × 109/L
- Serum bilirubin <=1.5 × the ULN, unless due to Gilbert*s syndrome, who will be allowed in consultation with their physician and AZ.
- ALT and AST <=2.5 × ULN; for patients with hepatic metastases, ALT, and AST <=5 × ULN
- Creatinine Clearance >=60 mL/min calculated by Cockcroft-Gault equation (using

actual body weight) or by measured 24-hour urine collection
Males:
Creatinine clearance (mL/min) = Weight (kg) × (140 - Age)
72 × Serum creatinine (mg/dL)
Females:
Creatinine clearance (mL/min) = Weight (kg) × (140 - Age) × 0.85
72 × Serum creatinine (mg/dL)
- Albumin >=3 g/dL
11) Life expectancy of at least 12 weeks.
12) Body weight >35kg.
13) Postmenopausal or negative pregnancy test

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, Graves* disease, rheumatoid arthritis, hypophysitis, uveitis, etc).
3) Uncontrolled intercurrent illness, including but not limited to, ongoing or active infection,
symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, uncontrolled cardiac arrhythmia, active ILD, serious chronic gastrointestinal conditions associated with diarrhea, or psychiatric illness/social situations that would limit compliance with study requirement, substantially increase risk of incurring AEs or compromise the ability of the patient to give written informed consent
4) Prior history of myocardial infarction, stroke, or transient ischemic attack in the past 6 months
5) History of venous thromboembolism within the past 3 months
6) 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 treatment 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
7) History of leptomeningeal carcinomatosis
8) History of active primary immunodeficiency
9) Active infection including tuberculosis, hepatitis B, hepatitis C, or human immunodeficiency virus (positive HIV 1/2 antibodies).
10) Untreated CNS metastases identified either on the baseline brain imaging obtained during the
screening period or identified prior to signing the ICF.

11) Known allergy or hypersensitivity to any of the study treatments or any of the study treatment excipients
12) Mean QT interval corrected for heart rate using Fridericia*s formula (QTcF) >=470 ms calculated from 3 ECGs (within 15 minutes at 5 minutes apart).
13) Any clinically important abnormalities in rhythm, conduction, or morphology of resting ECG (eg, complete left bundle branch block, third-degree heart block).
14) Any factors that increase the risk of QTc prolongation or risk of arrhythmic events, such as heart failure, hypokalemia, potential for torsades de pointes, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age, or any concomitant medication known to prolong the QT interval.
15) Any prior chemotherapy or any other systemic therapy for Stage IV NSCLC
16) Any concurrent chemotherapy, study treatment, biologic, or hormonal therapy for cancer
treatment. Concurrent use of hormonal therapy for non-cancer-related conditions (eg, hormone replacement therapy) is acceptable.
17) Radiation therapy, unless it is (1) definitive radiation that had been administered at least
12 months prior to the date of progression to Stage IV disease (see also inclusion
criterion 8), (2) palliative radiation to brain, with associated criteria for stability or lack of
symptoms, at least 4 weeks prior to the first study treatment dose (see also exclusion
criterion 10), or (3) palliative radiation to painful bony lesions (this must comprise less
than 30% of the bone marrow) at least 4 weeks prior to the first study treatment dose.
18) Receipt of live attenuated vaccine within 30 days prior to the first dose of study treatment.
19) Major surgical procedure (as defined by the Investigator) within 28 days prior to the first
dose or still recovering from prior surgery. Local procedures (eg, placement of a
systemic port, core needle biopsy, and prostate biopsy) are allowed if completed at least
24 hours prior to the administration of the first dose of study treatment.
20) Current or prior use of immunosuppressive medication within 28 days before the first
dose of durvalumab.
21) Participation in another clinical study with a study treatment administered in the last 12 months
22) Previous study treatment assignment in the present study
23) 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

24) Prior randomization or treatment in a previous durvalumab clinical study regardless of
treatment arm assignment
25) Mixed SCLC and NSCLC histology, sarcomatoid variant
26) 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 180 days after the last dose of durvalumab + novel oncology therapy ± chemotherapy or 90 days after the last dose of durvalumab monotherapy, whichever is later.
27) Judgment by the Investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions, and requirements
28) Medical contraindication to platinum-based doublet chemotherapy if tumor is PD-L1 low
29) Exclusion criteria for participation in the optional (DNA) genetics research component of
the study include:
- Previous allogeneic bone marrow transplant
- Non-leukocyte-depleted whole blood transfusion in 120 days of genetic sample collection

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	17
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Brand name:	n.v.t.
Generic name:	Danvatirsen
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Durvalumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Oleclumab

Ethics review

Approved WMO Date:	19-12-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2018-001748-74-NL
ClinicalTrials.gov	NCT03819465
CCMO	NL67856.078.18

Study results

Summary results
Trial never started