A PHASE III, OPEN-LABEL, RANDOMIZED STUDY OF ATEZOLIZUMAB AND TIRAGOLUMAB COMPARED WITH DURVALUMAB IN PATIENTS WITH LOCALLY ADVANCED, UNRESECTABLE STAGE III NON-SMALL CELL LUNG CANCER WHO HAVE NOT PROGRESSED AFTER CONCURRENT PLATINUM-BASED CHEMORADIATION.

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This study has been transitioned to CTIS with ID 2022-502480-38-00 check the CTIS register for the current data. This study will evaluate the efficacy and safety of consolidation maintenance treatment consisting of atezolizumab and tiragolumab...

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

Summary

ID

NL-OMON54439

Source
ToetsingOnline

Brief title
SKYSCRAPER-03

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
lung cancer, Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: F. Hoffman - La Roche

Intervention

Keyword: Immune therapy, Lung cancer, NSCLC

Outcome measures

Primary outcome

- To evaluate the efficacy of tiragolumab plus atezolizumab compared with

durvalumab with durvalumab in the programmed death ligand 1 positive analysis

set (PPAS) on the basis of PFS, as assessed by an IRF as assessed by an

independent review facility (IRF)

- To evaluate the efficacy of tiragolumab plus atezolizumab compared with

durvalumab in the programmed death ligand 1 positive analysis set

(PPAS) on the basis of PFS, as assessed by an IRF.

Secondary outcome

The secondary efficacy objective for this study is to evaluate the efficacy of

atezolizumab plus tiragolumab compared with durvalumab in the ITT and the

PD-L1-positive populations on the basis of the following endpoints:

- To evaluate the efficacy of tiragolumab plus atezolizumab compared with durvalumab in the FAS and PPAS on the basis of overall survival (OS), PFS as assessed by investigator, Confirmed objective response rate (ORR), as assessed by an IRF and investigator, DOR, as assessed by an IRF and investigator
- To evaluate the quality of life of patients treated with tiragolumab plus atezolizumab compared with durvalumab in the FAS and PPAS
- To evaluate the efficacy of tiragolumab plus atezolizumab compared with durvalumab on the basis of PFS rate at 12, 18, and 24 months (FAS and PPAS), OS rate at 12, 24, 36, and 48 months (FAS and PPAS), and time to distant metastasis (TTDM) (FAS and PPAS)
- To evaluate the safety and tolerability of tiragolumab plus atezolizumab compared with durvalumab.

See chapter 2 of protocol for all endpoints

Study description

Background summary

This study is designed to evaluate whether consolidation therapy with the combination of the anti-TIGIT antibody tiragolumab with atezolizumab yields improved clinical benefit compared with durvalumab monotherapy in patients with locally advanced, unresectable Stage III NSCLC who have received at least two prior cycles of platinum-based CRT and have not progressed.

The study will evaluate the efficacy in the PD-L1-positive and ITT populations given that the dependence of efficacy on PD-L1 expression with the combination in the post-CRT setting has yet to be determined.

Although the added tiragolumab plus atezolizumab benefit relative to atezolizumab alone was primarily observed in patients with PD-L1 high expression in Study GO40290 (CITYSCAPE), the dependence may be different for patients who have just received CRT.

Study objective

This study has been transitioned to CTIS with ID 2022-502480-38-00 check the CTIS register for the current data.

This study will evaluate the efficacy and safety of consolidation maintenance treatment consisting of atezolizumab and tiragolumab compared with durvalumab in patients with locally advanced, unresectable Stage III NSCLC who have received at least two cycles of concurrent platinum-based CRT and have not had radiographic disease progression.

Study design

This is a Phase III, open-label, randomized, global, multicenter study designed to evaluate the efficacy and safety of atezolizumab in combination with tiragolumab compared with durvalumab administered to patients with locally advanced, unresectable Stage III NSCLC who have not progressed following concurrent platinum-based CRT as consolidation therapy.

Eligible patients will be randomized in a 1:1 ratio to receive either atezolizumab plus tiragolumab or durvalumab.

See chapter 3 of the protocol for details.

Intervention

In the experimental arm, atezolizumab will be administered to patients by IV infusion at a fixed dose of 1680 mg, followed by tiragolumab at a fixed dose of 840 mg administered by IV infusion on Day 1 of each 28-day cycle for a maximum of 13 cycles.

The comparator arm gives 2 options:
- patients will receive the approved durvalumab dose, 10 mg/kg Q2W, administered by IV infusion on Days 1 and 15 of each 28-day cycle for a maximum of 13 cycles (not to exceed 26 doses) .
- Patients receive a fixed dose of 1500 mg, Q4W, administered by IV infusion on

Day 1 of each 28-day cycle, for a maximum of 13 cycles (not to exceed 13 doses)

Study burden and risks

The general burden for the patient consists of (a.o.) the withdrawal of blood samples, possible collection of tumor sample,
administration of investigational products (intravenously) which may lead to various adverse events.

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

Age>= 18 years

- Eastern Cooperative Oncology Group Performance Status of 0 or 1
- Histologically or cytologically documented NSCLC with locally advanced unresectable Stage III NSCLC of either squamous or non-squamous histology
- Whole-body PET-CT scan for the purposes of staging, performed prior and within 42 days of the first dose of concurrent chemoradiotherapy (CRT)
- At least two prior cycles of platinum-based chemotherapy concurrent with radio therapy (cCRT), which must be completed within 1 to 42 days prior to randomization in the study (one cycle of cCRT is defined as 21 or 28 days)
- The RT component in the CRT must have been at a total dose of radiation of 60 Gy±10% (54 Gy to 66 Gy) administered by intensity-modulated radiotherapy (preferred) or 3D-conforming technique
- No progression during or following concurrent platinum-based CRT
- Tumor PD-L1 expression, as determined by the investigational Ventana PD-L1 (SP263) CDx assay and documented by means of central testing of a representative tumor tissue, in either a previously obtained archival tumor tissue or fresh tissue obtained from a biopsy collected prior to the first dose of cCRT
- Adequate hematologic and end-organ function.

Exclusion criteria

- Any history of prior NSCLC - NSCLC known to have a mutation in the epidermal growth factor mutation and/or an anaplastic lymphoma kinase translocation - Any evidence of Stage IV disease - Treatment with sequential CRT for locally advanced NSCLC - Patients with locally advanced NSCLC who have progressed during or after the definitive concurrent CRT prior to randomization - Any Grade > 2 unresolved toxicity from previous CRT - Grade >=2 pneumonitis from prior CRT - Active or history of autoimmune disease or immune deficiency, history of idiopathic pulmonary fibrosis, organizing pneumonia - History of malignancy other than NSCLC within 5 years prior to screening - Severe infection within 4 weeks prior to initiation of study treatment, including, but not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia, or any active infection that, in the opinion of the investigator, could impact patient safety - Prior allogeneic stem cell or solid organ transplantation - Active Epstein-Barr virus (EBV) infection or known or suspected chronic active EBV infection at screening - Treatment with investigational therapy within 28 days prior to initiation of study treatment - Prior treatment with CD137 agonists or immune checkpoint blockade therapies - Any prior Grade >= 3 immune-mediated adverse event or any unresolved Grade > 1 immune-mediated adverse event while receiving any previous immunotherapy agent other than immune checkpoint blockade agents - Current treatment with anti-viral therapy for hepatitis B virus or hepatitis C virus - Prior treatment with CD137 agonists or immune checkpoint blockade therapies, including anti-cytotoxic T lymphocyte-associated protein 4, anti-T-cell immunoreceptor with Ig and ITIM domains, anti-PD-1, and anti-PD-L1 therapeutic antibodies -

Treatment with systemic immunosuppressive medication (including, but not limited to, corticosteroids, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor-[antiTNF-alpha]agents) within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressivemedication during study treatment.

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:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-01-2021
Enrollment:	21
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Imfinzi
Generic name:	durvalumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tecentriq
Generic name:	atezolizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine

Brand name:	tiragolumab
Generic name:	tiragolumab

Ethics review

Approved WMO Date:	13-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-08-2021

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-12-2021
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:	12-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2023
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
EU-CTR	CTIS2022-502480-38-00
EudraCT	EUCTR2019-004773-29-NL
CCMO	NL74054.056.20