A Phase 3, Randomized, Double-Blind Study of Ociperlimab, an Anti TIGIT Antibody, in Combination With Tislelizumab Compared to Pembrolizumab in Patients With Previously Untreated, PD L1 Selected, and Locally Advanced, Unresectable, or Metastatic Non Small Cell Lung Cancer

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This study has been transitioned to CTIS with ID 2023-507317-10-00 check the CTIS register for the current data. Primary:• To compare progression free survival (PFS) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56010

Source
ToetsingOnline

Brief title
AdvanTIG-302

Condition

- Other condition

Synonym
Lung cancer

Health condition

Locally Advanced, Unresectable, or Metastatic Non Small Cell Lung Cancer

Research involving
Human

Sponsors and support

Primary sponsor: BeiGene Switzerland GmbH
Source(s) of monetary or material Support: Ministerie van OC&W,BeiGene

Intervention

Keyword: anti TIGIT antibody, lung cancer, metastatic cancer, phase 3 study

Outcome measures

Primary outcome

Primary:

• PFS as assessed by investigators (time from the date of randomization to the date of the first objectively documented tumor progression per RECIST v1.1, or death, whichever occurs first) in the ITT Analysis Set of Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo)

• OS (time from the date of randomization to the date of death due to any cause) in the ITT Analysis Set of Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo)

Secondary outcome

Secondary:

• PFS as assessed by the BIRC in Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo)

• ORR as assessed by investigators (proportion of patients with a documented, confirmed complete response [CR] or partial response [PR] per RECIST v1.1) and DOR as assessed by investigators (time from the first determination of an objective response per RECIST v1.1 until the first documentation of progression or death, whichever occurs first) in Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo)

• HRQoL as assessed via patient reported outcomes (PRO) using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), its lung cancer module Quality of Life Questionnaire Lung Cancer 13 (QLQ-LC13), and the 5 Level EuroQol 5 Dimension (EQ-5D-5L) questionnaire in Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo). PRO endpoints include the EORTC QLQ-C30's global health status/QoL (GHS), physical function and fatigue scales, and the QLQ-LC13's index score, dyspnea, coughing, hemoptysis and pain in chest, pain in arms/shoulders and peripheral neuropathy scales.

• TTD, defined as time from randomization to the first occurence of worsening scores (10-point change, to be defined in the Statistical Analysis Plan [SAP] if otherwise) for 2 consecutive assessments or 1 assessment followed by death from any cause before the next scheduled data collection

• The incidence and severity of adverse events (AEs) according to National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) in Arm A (ociperlimab in combination with tislelizumab)

Study description

Background summary

Ociperlimab and tislelizumab are experimental drugs. This means they have not been approved for non-small cell lung cancer by the regulatory agencies in your country. As of 20 July 2022, tislelizumab has been given to approximately 2173 participants taking part in other research studies as a single drug. As of 28 July 2022, ociperlimab has been given to approximately 277 participants involving ociperlimab as a single drug (9 patients) or in combination with tislelizumab (268 patients).

Ociperlimab and tislelizumab are both antibodies. An antibody is a common type of protein found in your body, through which the immune system finds and destroys bacteria, viruses, and other foreign substances that enter your body. Antibodies can also be produced in the laboratory and used for treating subjects. Currently, several antibodies have been approved for the treatment of cancer and other diseases.

Tislelizumab and pembrolizumab bind to PD-1, which is a protein present on the surface of immune cells. The PD-1 protein becomes active when its partner (PD-L1) binds to it like a handshake and prevents your body*s immune cells from killing tumor cells. The result of this binding is like stepping on a car brake, but this brake stops your immune cells. Tislelizumab can block PD-1 and its partner PD-L1 from binding to each other, thereby releasing the *brake* and restoring the tumor-killing function of immune cells.

Your body*s immune cells have another protein present on their surface, which is referred to as TIGIT (or T-cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain). The TIGIT protein functions similarly to PD-1 and works together with PD-1 to stop your body*s immune cells from killing tumor cells. Like PD-1, TIGIT becomes active when it binds to one of its ligands (partners). The ociperlimab antibody blocks the interaction between TIGIT and its ligands to further release the *brake* on your immune cells, which may increase the tumor killing capacity of your immune cells.

Study objective

This study has been transitioned to CTIS with ID 2023-507317-10-00 check the CTIS register for the current data.

Primary:
• To compare progression free survival (PFS) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the Intent to Treat (ITT) Analysis Set as assessed by investigators according to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

• To compare overall survival (OS) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set

Secondary:
• To compare PFS between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set as assessed by the Blinded Independent Review Committee (BIRC) according to RECIST v1.1
• To compare the overall response rate (ORR) and duration of response (DOR) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set as assessed by investigators according to RECIST v1.1
• To compare health-related quality of life (HRQoL) and time to deterioration (TTD) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set
• To further investigate the safety and tolerability of ociperlimab in combination with tislelizumab

Exploratory:
• To compare the disease control rate (DCR), clinical benefit rate (CBR), and time to response (TTR) between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set as assessed by investigators according to RECIST v1.1
• To compare ORR, DOR, DCR, CBR, and TTR between Arm A (ociperlimab in combination with tislelizumab) and Arm B (pembrolizumab followed by placebo) in the ITT Analysis Set as assessed by the BIRC according to RECIST v1.1
• To evaluate OS, as well as ORR, DOR, PFS, DCR, CBR, and TTR as assessed by the BIRC and investigators according to RECIST v1.1, in the ITT Analysis Set of Arm C (tislelizumab followed by placebo)
• To evaluate PFS after next line of treatment (PFS2)
• To characterize the pharmacokinetics (PK) of ociperlimab and tislelizumab
• To evaluate the potential association of exploratory biomarkers with response or resistance to treatment with ociperlimab and tislelizumab and with patient prognosis.
• To determine host immunogenicity to ociperlimab and tislelizumab
• To further investigate the safety and tolerability of tislelizumab
• Patient-reported changes in non-small cell lung cancer (NSCLC) symptom severity from baseline via the PGI-S questionnaire and patient reported treatment-related side effect burden via the PRTSE questionnaire in Arms A, B, and C
• To measure HRQoL in Arm C in the ITT Analysis Set

Study design

This is a randomized, double-blind, multicenter, Phase 3 study designed to evaluate the efficacy and safety of ociperlimab + tislelizumab compared with

that of pembrolizumab in patients with PD-L1-selected non-small cell lung cancer (NSCLC) who have locally advanced or recurrent disease that is unresectable or not amenable to radiotherapy, with or without chemoradiotherapy, or previously untreated metastatic disease, and whose tumors do not harbor epidermal growth factor receptor (EGFR)-sensitizing mutations, anaplastic lymphoma kinase (ALK) translocations, BRAF V600E mutations, or ROS1 mutations. The efficacy and safety of tislelizumab alone will be explored in a cohort of the same patient population.

A safety run-in substudy investigating the safety, tolerability, PK, and preliminary efficacy of ociperlimab in combination with tislelizumab in Japanese patients is planned; preliminary safety and tolerability will be evaluated before Japanese patients are randomized in this Phase 3 study. Patients will be required to sign a prescreening informed consent form (ICF) to undergo prescreening collection of tissue samples (archival tissue or fresh biopsy) for central evaluation of PD-L1 status. Patients will be required to sign the main ICF to undergo screening procedures. Approximately 660 patients will be enrolled in the main study.

Blinding will be accomplished using placebo infusions of normal saline in Treatment Arms B and C so that all patients will receive 2 infusions on Day 1 of each cycle. Study treatments will be prepared by unblinded pharmacists, who will mask treatments to ensure that patients and study staff remain blinded. As of the approval date of protocol amendmnet version 2.0, eligible participants will be randomized in a 5:5:2 ratio to receive ociperlimab + tislelizumab (Arm A), pembrolizumab + placebo (Arm B), or tislelizumab + placebo (Arm C) instead of 5:5:1 as specified in protocol amendment version 1.0.

Study treatments will be given as follows:
• Arm A: Tislelizumab 200 mg intravenously followed by ociperlimab 900 mg intravenously once every 3 weeks
Note: As of Protocol Amendment Version 3.0, the ociperlimab dose that will be administered to Japanese patients allocated in Arm A was determined to be 900 mg based on the results from the safety run-in substudy
• Arm B: Pembrolizumab 200 mg intravenously followed by placebo intravenously once every 3 weeks
• Arm C: Tislelizumab 200 mg intravenously followed by placebo intravenously once every 3 weeks.

All study treatments will be administered until intolerable toxicity, withdrawal of informed consent, or the timepoint at which, in the opinion of the investigator, the patient is no longer benefiting from study therapy. Crossover is not permitted. Treatment beyond the initial investigator-assessed, RECIST v1.1 defined disease progression is permitted in all arms if the criteria below are met:
• Absence of clinical symptoms and signs of progressive disease (including

clinically significant worsening of laboratory values)
• Eastern Cooperative Oncology Group (ECOG) Performance Status <= 1
• Absence of rapid progression of disease or of progressive tumor at critical anatomical sites (eg, spinal cord compression) that requires urgent alternative medical intervention
• Investigators must obtain written informed consent for treatment beyond radiologic disease progression and inform patients that this practice is not considered standard in the treatment of cancer. Patients must be informed that they may be forgoing treatment that has shown benefit by continuing treatment beyond progression
• The decision to continue study drug(s) beyond initial investigator-assessed progression must be agreed with the sponsor medical monitor
Patients who receive study treatment beyond progression will have tumor assessments performed according to the original schedule until study treatment discontinuation. Patients will be permanently discontinued from study treatment if the patient is deemed to meet criteria for RECIST v1.1 defined disease progression as determined by both the investigator and the BIRC. Tumor assessments are required to be performed on schedule regardless of whether study treatment has been administered or held (i.e. their schedule should not be adjusted for delays in cycles).

Intervention

Study treatments will be given as follows:
• Arm A: Tislelizumab 200 mg intravenously followed by ociperlimab 900 mg intravenously once every 3 weeks
• Arm B: Pembrolizumab 200 mg intravenously followed by placebo intravenously once every 3 weeks
• Arm C: Tislelizumab 200 mg intravenously followed by placebo intravenously once every 3 weeks.

Study burden and risks

There are risks that are not known or do not happen often when patients take the study treatment. The investigator will inform the patient in a timely manner of any new information, findings, or changes to the way the research will be done that might influence your willingness to continue to take part in this study.

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.Able to provide written informed consent and can understand and agree to comply with the requirements of the study and the schedule of assessments. 2.Age >= 18 years on the day of signing the informed consent form (or the legal age of consent in the jurisdiction in which the study is taking place). 3.Histologically or cytologically documented locally advanced or recurrent NSCLC that is not eligible for curative surgery and/or definitive radiotherapy with or without chemoradiotherapy, or metastatic nonsquamous or squamous NSCLC. 4.No prior systemic treatment for metastatic NSCLC. 5.Agreement to provide archival tissue (formalin-fixed paraffin-embedded block containing tumor [preferred] or approximately 6 to 15 freshly cut unstained slides) or fresh biopsy (if archival tissue is not available) for central evaluation of PD-L1 levels and retrospective analysis of other biomarkers. 6.Tumors with PD-L1 expressed in >= 50% tumor cells as determined centrally (or locally in the US sites). 7.At least 1 measurable lesion as defined per RECIST v1.1. 8.ECOG Performance Status <= 1. 9.Adequate organ function as indicated by the following laboratory values during screening: a.Patients must not have required blood transfusion or growth factor support <= 14 days before sample collection at Screening for the following: *Absolute neutrophil count (ANC) >= 1.5 x 10^9/L

*Platelets >= 75 x 10^9/L *Hemoglobin >= 90 g/L b.Serum creatinine <= 1.5 x upper limit of normal (ULN) or estimated Glomerular Filtration Rate >= 60 mL/min/1.73 m2 by Chronic Kidney Disease Epidemiology Collaboration equation (Appendix 8). Note: for France only: Serum creatinine <= 1.5 x ULN and estimated glomerular filtration rate or estimated creatinine clearance >= 60 mL/min/1.73 m2 by CKD-EPI and Cockcroft and Gault equations, respectively (Appendix 8). c.Serum total bilirubin <= 1.5 x ULN (total bilirubin must be < 3 x ULN for patients with Gilberts syndrome). d.AST and ALT <= 2.5 x ULN or < 5 x ULN if hepatic metastases present. 10.Females of childbearing potential must be willing to use a highly effective method of birth control for the duration of the study, and for >= 120 days after the last dose of study drug, and must have a negative urine or serum pregnancy test <= 7 days before randomization. 11.Nonsterile males must be willing to use a highly effective method of birth control for the duration of the study and for >= 120 days after the last dose of study drug. •A sterile male is defined as one for whom azoospermia has been previously demonstrated in a semen sample examination as definitive evidence of infertility. •Males with known "low sperm counts" (consistent with "subfertility") are not to be considered sterile for purposes of this study.

Exclusion criteria

1.Known mutation in a. EGFR gene b. ALK fusion oncogene c. BRAF V600E d. ROS1 2.Prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-TIGIT, or any other antibody or drug specifically targeting T-cell costimulation or checkpoint pathways. 3.Active leptomeningeal disease or uncontrolled, untreated brain metastasis. Note: Patients with a history of treated and, at the time of screening, stable central nervous system (CNS) metastases are eligible, provided they meet all the following: *Brain imaging at Screening shows no evidence of interim progression, patient is clinically stable for at least 2 weeks and without evidence of new brain metastases. *Measurable and/or evaluable disease outside the CNS. *No ongoing requirement for corticosteroids as therapy for CNS disease; off steroids 3 days before randomization; anticonvulsants at a stable dose are allowed. *No stereotactic radiation or whole-brain radiation within 14 days before randomization. 4.Active autoimmune diseases or history of autoimmune diseases that may relapse. 5.Any active malignancy <= 5 years before randomization except for the specific cancer under investigation in this study, those with a negligible risk of metastasis or death, and any locally recurring cancer that has been treated curatively (eg, resected basal or squamous cell skin cancer, superficial bladder cancer, localized prostate cancer, or carcinoma in situ of the cervix or breast). 6.Any condition that required systemic treatment with either corticosteroids (> 10 mg daily of prednisone [in Japan, prednisolone] or equivalent) or other immunosuppressive medication <= 14 days before randomization. 7.Uncontrolled diabetes or > Grade 1 laboratory test abnormalities in potassium, sodium, or corrected calcium despite standard medical management or >= Grade 3

hypoalbuminemia <= 14 days before randomization. 8.Uncontrollable pleural effusion, pericardial effusion, or ascites requiring frequent drainage (recurrence within 2 weeks of intervention). Patients with symptomatic pleural effusion are excluded unless the patient undergoes a therapeutic thoracentesis or has had pleurodesis (more than 2 weeks prior) and has subsequently stable effusions. 9.History of interstitial lung disease, noninfectious pneumonitis or uncontrolled lung diseases including pulmonary fibrosis, acute lung diseases, etc. All patients must undergo an assessment of pulmonary function at Screening 10.Infection (including tuberculosis infection, etc) requiring systemic antibacterial, antifungal, or antiviral therapy within 14 days before randomization, or patients who tested positive for COVID-19 antigen by a licensed test during screening. 11.Untreated chronic hepatitis B or chronic HBV carriers with HBV DNA > 500 IU/mL (or>2500 copies/mL) at Screening. 12.Patients with active hepatitis C. 13.Known history of human immunodeficiency virus (HIV) infection, or if HIV status is unknown, positive HIV test at Screening. 14.Any major surgical procedure <= 28 days before randomization. Patients must have recovered adequately from the toxicity and/or complications from the intervention before randomization. 15.Prior allogeneic stem cell transplantation or organ transplantation. 16.Any of the following cardiovascular risk factors: a.Cardiac chest pain, defined as moderate pain that limits instrumental activities of daily living, <= 28 days before randomization.b. Symptomatic pulmonary embolism diagnosed <= 28 days before randomization.c.Any history of acute myocardial infarction <= 6 months before randomization.d.Any history of heart failure meeting New York Heart Association (NYHA) Classification III or IV (Appendix 6) <= 6 months before randomization.e.Any event of ventricular arrhythmia >= Grade 2 in severity <= 6 months before randomization.f.Any history of cerebrovascular accident <= 6 months before randomization.g.Uncontrolled hypertension that cannot be managed by standard antihypertension medications <= 28 days before randomization.h.Any episode of syncope or seizure <= 28 days before randomization. 17.A history of severe hypersensitivity reactions to other monoclonal antibodies or a history of hypersensitivity to the ingredients of tislelizumab or ociperlimab. 18.Was administered a live vaccine <= 28 days before randomization. 19.Underlying medical conditions (including laboratory abnormalities) or alcohol or drug abuse or dependence that will be unfavorable for the administration of study drug, or affect the explanation of drug toxicity or AEs, or result in insufficient or impaired compliance with study conduct. 20.Women who are pregnant or are breastfeeding. 21. Concurrent participation in another therapeutic clinical study.

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:	Recruiting
Start date (anticipated):	10-05-2022
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	not available
Generic name:	Ociperlimab
Product type:	Medicine
Brand name:	not available
Generic name:	Tislelizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	10-05-2021
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	28-10-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	04-10-2022
Application type:	Amendment
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Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	METC NedMec
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Application type:	Amendment
Review commission:	METC NedMec
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Application type:	Amendment
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Application type:	Amendment
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Approved WMO Date:	02-03-2023
Application type:	Amendment
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Approved WMO Date:	01-07-2023
Application type:	Amendment
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Approved WMO Date:	02-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-08-2023
Application type:	Amendment

Review commission:	METC NedMec
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Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-10-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-10-2023
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2023-507317-10-00
EudraCT	EUCTR2020-004985-21-NL
CCMO	NL76777.031.21