

A Phase 3, Randomized, Open-Label Study to Compare Ociperlimab (BGBA1217) Plus Tislelizumab (BGB-A317) Versus Durvalumab in Patients With Locally Advanced, Unresectable, PD L1 Selected Non- Small Cell Lung Cancer Whose Disease Has Not Progressed After Concurrent Chemoradiotherapy

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Primary: • Compare progression-free survival (PFS) as assessed by the Independent Review Committee (IRC) per Response Evaluation Criteria in Solid Tumors (RECIST) Version (v) 1.1 in ociperlimab plus tislelizumab (Arm A) versus Durvalumab (Arm C) among...

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

Summary

ID

NL-OMON52181

Source

ToetsingOnline

Brief title

BGB-A317-A1217-301 (AdvanTIG-301)

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym

Non-Small Cell Lung Cancer (NSCLC)

Research involving

Human

Sponsors and support

Primary sponsor: BeiGene, Ltd.

Source(s) of monetary or material Support: BeiGene;Ltd.

Intervention

Keyword: BGB-A1217, BGB-A317, Non-Small Cell Lung Cancer (NSCLC), Phase 3

Outcome measures

Primary outcome

- PFS by the IRC, defined as the time from the date of randomization to the date of first documentation of disease progression as assessed by the IRC per RECIST v1.1 or death, whichever occurs first

Secondary outcome

- OS defined as the time from the date of randomization until the date of death due to any cause
- RR, defined as the proportion of patients who achieve a complete response (CR) or partial response (PR) assessed by both the IRC and investigators per RECIST v1.1
- DOR, defined as the time from the first determination of a confirmed objective response as assessed by both the IRC and investigators per RECIST v1.1 until the first documentation of disease progression or death,

whichever occurs first

- TTDM, defined as the time from the date of randomization until the first date of distant metastasis as assessed by both the IRC and investigators, or death. Distant metastasis is defined as any new lesion that is outside of the radiation field per RECIST v1.1 or proven by biopsy
- PFS2, defined as the time from randomization to the disease progression after next line of treatment, or death from any cause, whichever occurs first
- Safety and tolerability, defined as adverse events (AEs) (using NCI-CTCAE v5.0), laboratory tests, vital signs, Eastern Cooperative Oncology Group (ECOG) Performance Status, physical examinations, concomitant medications, and dose modifications
- HRQoL, measured via patient-reported outcomes (PROs) using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 (EORTC QLQ-LC13), and the 5-Level EuroQol 5-Dimension (EQ-5D-5L)
- Serum concentrations of ociperlimab and tislelizumab at specified timepoints
- Immunogenic responses to ociperlimab and tislelizumab evaluated through detection of antidrug antibodies
- PD-L1 and TIGIT expression in archival and/or fresh tumor tissues before study treatment or at disease progression/reoccurrence, and their

Study description

Background summary

Tislelizumab and ociperlimab are study drugs. This means that they have not been approved for use by the regulatory agencies in Netherlands and other regulatory agencies outside Netherlands.

Tislelizumab has been approved by National Medical Products Administration (NMPA) in China for three indications, which are Hodgkin's lymphoma, Urothelial carcinoma and Squamous non-small cell lung cancer. As of 20 May 2020, tislelizumab has been given to 1917 participants who are taking part in other research studies with tislelizumab as a single drug or in combination with another anticancer drug. As of 16 June 2020, ociperlimab has been given to 11 participants in combination with another anticancer drug.

Tislelizumab and ociperlimab are both monoclonal antibodies. An antibody is a common type of protein found in your body that finds and destroys bacteria, viruses, and other foreign molecules. Antibodies can also be produced in the laboratory and used for the treatment of patients. At present, several antibodies have been approved for the treatment of cancer and other diseases. Durvalumab is approved by European Medicines Agency (EMA) for the treatment of patients with locally advanced, unresectable stage III non-small-cell lung cancer (NSCLC) who have not progressed following chemoradiotherapy whose tumours express programmed death-ligand 1 (PD-L1) on $\geq 1\%$ of tumour cells. Concurrent Chemoradiotherapy

The concurrent chemoradiotherapy treatment regimen contains the current clinical standard chemotherapy of 4 combinations of chemotherapy regimens including cisplatin+etoposide, carboplatin+paclitaxel, cisplatin+pemetrexed, carboplatin+pemetrexed. It is at your investigator's discretion which combination will be used. These treatment regimens are approved by the EMA.

Study objective

Primary:

- Compare progression-free survival (PFS) as assessed by the Independent Review Committee (IRC) per Response Evaluation Criteria in Solid Tumors (RECIST) Version (v) 1.1 in ociperlimab plus tislelizumab (Arm A) versus Durvalumab (Arm C) among patients with locally advanced non-small cell lung cancer (LA NSCLC) whose disease has not progressed after concurrent chemoradiotherapy (cCRT) and with PD-L1 $\geq 50\%$
- Compare PFS as assessed by the IRC per RECIST v1.1 in ociperlimab plus tislelizumab (Arm A) versus Durvalumab (Arm C) among patients

with LA NSCLC whose disease has not progressed after cCRT and with PD-L1 $\geq 1\%$

Secondary:

- Compare overall survival (OS) in Arm A versus Arm C among patients with PD-L1 $\geq 50\%$
- Compare OS in Arm A versus Arm C among patients with PD-L1 $\geq 1\%$
- Evaluate overall response rate (ORR) and duration of response (DOR) as assessed by both the IRC and investigators in Arm A versus Arm C among patients with PD-L1 $\geq 50\%$ and $\geq 1\%$
- Evaluate time to death or distant metastasis (TTDM) in Arm A versus Arm C among patients with PD-L1 $\geq 50\%$ and $\geq 1\%$
- Evaluate PFS2 in Arm A versus Arm C among patients with PD-L1 $\geq 50\%$ and $\geq 1\%$
- Evaluate safety and tolerability in 3 treatment arms among patients with PD-L1 $\geq 50\%$ and $\geq 1\%$
- Compare impact of treatments on patient health related quality of life (HRQoL) in Arm A versus Arm C among pts with PD-L1 $\geq 50\%$ and $\geq 1\%$
- Characterize the pharmacokinetics (PK) of ociperlimab and tislelizumab
- Assess host immunogenicity to ociperlimab and tislelizumab
- Evaluate the association of PD-L1 and T-cell immunoglobulin and ITIM domain (TIGIT) expression with clinical efficacy to ociperlimab plus tislelizumab or tislelizumab or durvalumab only

Study design

This is an open-label, randomized, multicenter, Phase 3 study to compare the efficacy and safety of anti-T-cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains

(anti-TIGIT) monoclonal antibody ociperlimab plus tislelizumab versus durvalumab in patients with

unresectable LA NSCLC whose disease has not progressed after definitive, platinum-based cCRT and

with PD-L1 expression on $\geq 1\%$ of tumor cells (TC) as assessed by the central lab using the VENTANA

PD-L1 (SP263) assay.

The primary endpoints are PFS by the IRC per RECIST v1.1 in the PD-L1 $\geq 50\%$ Analysis Set in Arm A

and Arm C, and PFS by the IRC per RECIST v1.1 in the PD-L1 $\geq 1\%$ Analysis Set in Arm A and

Arm C. Patients with histologically or cytologically confirmed, unresectable LA NSCLC whose disease

has not progressed after cCRT and with PD-L1 $\geq 1\%$ are eligible.

Approximately 700 patients will be randomized in a 3:1:3 ratio to receive the study treatment in the

following 3 arms:

- Arm A: ociperlimab (900 mg intravenously [IV]) combined with tislelizumab (200 mg IV) every

3 weeks (Q3W)

- Arm B: tislelizumab 200 mg IV Q3W
- Arm C: durvalumab 10 mg/kg IV once every 2 weeks (Q2W) (or 1500 mg every 4 weeks [Q4W])

where the dosage has been approved by the local health authority)

Intervention

Ociperlimab, 300 mg/15 mL, 900 mg Q3W administered by intravenous infusion.

Tislelizumab, 100 mg/10 mL, 200 mg Q3W administered by intravenous infusion.

Durvalumab, 120 mg/2.4 mL (50 mg/mL) and 500 mg/10 mL (50 mg/mL), 10 mg/kg Q2W (or 1500 mg

Q4W where the dosage has been approved by the local health authority)

administered by intravenous infusion.

Study burden and risks

See ICF section 7.0

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

Each patient eligible to participate in this study must meet all the following criteria:

- Histologically or cytologically confirmed, unresectable locally advanced Stage III NSCLC

(AJCC Cancer Staging Manual 2017, derived from International Association for the Study of

Lung Cancer [IASLC]) prior to cCRT.

- Have completed ≥ 2 cycles of platinum-based chemotherapy concurrent with radiotherapy.

For patients who are recovering from toxicities associated with the prior treatment, the first

dose of study drug(s) may be delayed by up to 42 days from the end of the cCRT.

It is

recommended to screen the patients within 14 days after the completion of cCRT.

- Have not experienced PD following definitive, platinum-based cCRT.

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- Agree 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 prospective central evaluation of PD-L1 levels and retrospective

analysis of other biomarkers. PD-L1 status will be assessed centrally in either a previously

obtained archival tumor tissue or fresh tissue obtained from a biopsy collected prior to the

first dose of cCRT via VENTANA PD-L1 (SP263) assay. Only patients with PD-L1 expression on $\geq 1\%$ of TC are eligible.

Exclusion criteria

Patients who meet any of the following criteria are NOT eligible to enroll:

- Prior therapy with an anti-programmed cell death-1(PD-1), anti-PD-L1, anti-PD-L2,

anti-T-cell immunoglobulin and ITIM domain (TIGIT), or any other antibody or drugs

specifically targeting T-cell co-stimulation or checkpoint pathways.

- Diagnosed with NSCLC that harbors an epidermal growth factor receptor (EGFR)sensitizing

mutation, anaplastic lymphoma kinase (ALK) gene translocation, ROS1 gene translocation, or RET

gene rearrangement.

- Distant metastasis identified by imaging assessment and/or other examinations after

definitive, platinum-based cCRT.

- Have received chemotherapy and radiotherapy with ≤ 1 cycle overlap for LA NSCLC.

- Have received systemic anticancer treatment besides the specified cCRT.

- Any unresolved toxicity CTCAE $>$ Grade 2 from the prior cCRT. Patients with irreversible

toxicity that is not reasonably expected to be exacerbated by study treatment may be

included (eg, hearing loss) after consultation with the medical monitor.

- Any grade pneumonitis from prior cCRT.

- Active autoimmune diseases or history of autoimmune diseases that may relapse.

- Any active malignancy ≤ 2 years before the first dose of study drug(s) except for the specific

cancer under investigation in this study and any locally recurring cancer that has been treated curatively.

- Any conditions that required systemic treatment with either corticosteroids (> 10 mg daily of prednisone [in Japan, prednisolone] or equivalent) or other immunosuppressive medication

≤ 14 days before the first dose of study drug(s).

- History of interstitial lung disease, non-infectious pneumonitis, or uncontrolled lung diseases

including pulmonary fibrosis, acute lung diseases, etc.

- Infections (including tuberculosis infection, etc) that required systemic antibacterial,

antifungal, or antiviral therapy within 14 days before the first dose of study drug(s).

- A history of severe hypersensitivity reactions to other monoclonal antibodies or history of

hypersensitivity to the ingredients of tislelizumab or ociperlimab.

- Receipt of any immunotherapy (eg, interleukin, interferon, thymosin [not approved in

Japan], etc) or any investigational therapies within 14 days or 5 half-lives (whichever is

longer) before the first dose of 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:	Will not start
Enrollment:	9
Type:	Anticipated

Medical products/devices used

Generic name:	IVD: VENTANA PD-L1 (SP263) Dx assay
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	durvalumab
Generic name:	durvalumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ociperlimab
Generic name:	Ociperlimab
Product type:	Medicine
Brand name:	Tislelizumab
Generic name:	Tislelizumab

Ethics review

Approved WMO

Date: 22-07-2021

Application type: First submission

Review commission: MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date: 28-01-2022

Application type: Amendment

Review commission: MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Not approved

Date: 29-12-2022

Application type: First submission

Review commission: MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2020-004656-14-NL
CCMO	NL78283.000.22