# 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 Criteriain Solid Tumors (RECIST) Version (v) 1.1 in ociperlimab plus tislelizumab (Arm A) versus Durvalumab (Arm C) among...

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| **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

association with clinical efficacy

# 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 >=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
>= 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 >= 1%
Secondary:
• Compare overall survival (OS) in Arm A versus Arm C among patients with PD-L1 >= 50%
• Compare OS in Arm A versus Arm C among patients with PD-L1 >= 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 >= 50% and >= 1%
• Evaluate time to death or distant metastasis(TTDM) in Arm A versus Arm C among patients with PD-L1 >= 50% and >= 1%
• Evaluate PFS2 in Arm A versus Arm C among patients with PD-L1 >= 50% and >= 1%
• Evaluate safety and tolerability in 3 treatment arms among patients with PD-L1 >= 50% and >= 1%
• Compare impact of treatments on patient health related quality of life (HRQoL) in Arm A versus Arm C among pts with PD-L1 >= 50% and >= 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 >= 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 >= 50% Analysis Set in Arm A
and Arm C, and PFS by the IRC per RECIST v1.1 in the PD-L1 >= 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 >= 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

**Public**
BeiGene, Ltd.

2955 Campus Drive, San Mateo Suite 200
CA 94403
US
**Scientific**
BeiGene, Ltd.

2955 Campus Drive, San Mateo Suite 200
CA 94403
US

# 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 >= 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 treatedcuratively.
• Any conditions that required systemic treatment with either corticosteroids (> 10 mg daily ofprednisone [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

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|---|---|
| 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

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| 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 |