# A PHASE III, OPEN-LABEL, RANDOMIZED STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF ATEZOLIZUMAB (ANTI-PD L1 ANTIBODY) COMPARED WITH BEST SUPPORTIVE CARE FOLLOWING ADJUVANT CISPLATIN BASED CHEMOTHERAPY IN PATIENTS WITH COMPLETELY RESECTED STAGE IB-IIIA NON-SMALL CELL LUNG CANCER.

Published: 28-10-2015
Last updated: 21-09-2024

This study has been transitioned to CTIS with ID 2023-505981-26-00 check the CTIS register for the current data. Primary Efficacy ObjectiveThe primary efficacy objective of the study is as follows:• To evaluate the efficacy of 16 cycles of...

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

## Summary

### ID

NL-OMON54656

**Source**
ToetsingOnline

**Brief title**
GO29527

## Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

**Synonym**
NSCLC, Previously fully resected Non-small cell lung cancer by surgery

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Hoffmann-La Roche
**Source(s) of monetary or material Support:** Farmaceutische industrie

## Intervention

**Keyword:** ANTI□PD-L1 ANTIBODY, Atezolizumab, Non-small cell lung cancer

## Outcome measures

**Primary outcome**

The primary efficacy outcome measure

DFS, defined as the time from randomization to the date of occurrence of any of the following, whichever occurs first:

- First recurrence of NSCLC, as determined by the investigator after an integrated assessment of radiographic data, biopsy sample results (if available), and clinical status

- Occurrence of new primary NSCLC, as assessed by the investigator

- Death from any cause

This efficacy outcome measure will be assessed in PD-L1-selected subpopulations (defined by the SP142 IHC assay) within the Stage II-IIIA subpopulation, in all

randomized patients with Stage II-IIIA NSCLC, and in the ITT population.

**Secondary outcome**

Secundary study parameters/outcome of the study

The secondary efficacy outcome measures for this study are as follows:

• Overal Survival, defined as the time from randomization to death from any cause, in the ITT population

• Disease Free Survival rates at 3 years and 5 years in the PD-L1 subpopulation and in the stage II-IIIA population and in the ITT population

• Disease Free Survival within the subpopulations within patient with Stage II-IIIA NSCLC.

The safety outcome measures for this study are as follows:

• Incidence, nature, and severity of adverse events, serious adverse events, and adverse events of special interest graded according to the NCI CTCAE v4.0

• Changes from baseline in vital signs, physical findings, and targeted clinical laboratory results

• Incidence of ATA response to atezolizumab and potential correlation with PK, pharmacodynamic, safety, and efficacy parameters

Pharmacokinetic Outcome Measures

The PK outcome measures for this study are as follows:

• Atezolizumab maximum serum concentration (Cmax) observed after infusion on Day 1 of Cycle 1

• Atezolizumab minimum serum concentration under steady-state conditions within a dosing interval (Cmin) prior to the infusion on Day 1 of Cycles 2, 3, 4, 8, and 16 and at studytermination

Exploratory Outcome Measures

The exploratory outcome measures for this study are as follows:

• Status of PD-L1, immune- and NSCLC-related and other exploratory biomarkers in tumor tissues, and blood collected before, during, or after treatment with atezolizumab or at first evidence of radiographic disease recurrence or confirmation of new primary NSCLC

• Status of ICs and exploratory biomarkers in biopsy specimens and blood collected at the first evidence of radiographic disease recurrence or confirmation of new primary NSCLC

# Study description

**Background summary**

Adjuvant chemotherapy is the standard of care for fully resected (Stage IB*IIIA) NSCLC. Additional studies are looking at the role of molecularly targeted adjuvant studies in relatively uncommon molecular subsets (epidermal growth factor receptor [EGFR], anaplastic lymphoma kinase) that account for < 15% of NSCLC. There is currently no active adjuvant study for the general NSCLC patient population. Atezolizumab targets human programmed death*ligand 1 (PD-L1) and inhibits its interaction with its receptors, programmed death*1 (PD-1) and B7.1 (CD80, B7-1). Both of these interactions are reported to

provide inhibitory signals to T cells. Given the evidence of the clinical activity of atezolizumab in previously treated NSCLC, and the need to continue to improve upon the survival for patients with resected NSCLC treated with adjuvant cisplatin-based chemotherapy, the Sponsor proposes Study GO29527.

**Study objective**

This study has been transitioned to CTIS with ID 2023-505981-26-00 check the CTIS register for the current data.

Primary Efficacy Objective
The primary efficacy objective of the study is as follows:
• To evaluate the efficacy of 16 cycles of atezolizumab treatment compared with best supportive care as measured by disease-free survival (DFS) as assessed by the investigator in PD-L1-subpopulation within the Stage II-IIIA population, in all randomized patients Stage II-IIIA NSCLC, and in the ITT population

Secondary Efficacy Objective
The secondary efficacy objective of the study are to evaluate the efficacy of atezolizumab monotherapy treatment compared with BSC on the basis of the following outcome measures
- OS in the ITT population
- 3-year and 5-year DFS rates in the PD-L1 subpopulation within the Stage II-IIIA population, in all-randomized patients with Stage II-IIIA NSCLC, and in the ITT population (i.e., all randomized patients in this study)
- DFS within the PD-L1-selected populations (defined by the SP263 IHC assay) in the evaluable Stage II-IIIA subpopulation and within the evaluable ITT population

Safety objectives
The safety objectives of the study are as follows:
• To evaluate the safety and tolerability of atezolizumab treatment after up to four cycles of cisplatin-based chemotherapy in the adjuvant setting
• To evaluate the incidence and titers of ATAs against atezolizumab in the adjuvant setting and to explore the potential relationship of the immunogenicity response with pharmacokinetics, safety, and efficacy

pharmacokinetic objective
The PK objective of the study is as follows:
• To characterize the PK of atezolizumab treatment in the adjuvant setting

Exploratory Objectives
• To evaluate the relationship between tumor and blood based biomarkers (including but not limited to PD-L1, PD-1, and others), as defined by IHC, quantitative reverse transcriptase polymerase chain reaction (qRT-PCR), and/or other methods

• To assess predictive, prognostic, and pharmacodynamic exploratory biomarkers in archival and/or fresh tumor tissue and blood and their association with disease status, mechanisms of resistance, and/or response to atezolizumab in the adjuvant treatment setting
• To evaluate biomarkers at the time of apparent recurrence of primary disease (i.e., NSCLC primary disease recurrence, occurrence of new primary NSCLCs) and to distinguish any immunomodulatory activity of atezolizumab (i.e., pseudoprogression/tumor-immune infiltration) in patients with confirmed recurrence of disease in patients assigned to atezolizumab.

**Study design**

This study is a Phase III, global, multicenter, open-label, randomized study.

**Intervention**

Eligible patients will go on to be randomized in a 1:1 ratio to receive either atezolizumab (Arm A) or BSC (Arm B). In Arm A, atezolizumab will be administered intravenously on Day 1 of each 21-day cycle. Patients randomized to Arm B will be continually followed starting on Day 1 of each 21-day cycle. No crossover will be allowed from Arm B to Arm A.

**Study burden and risks**

Many of the tests and procedures done during the study are part of the regular medical care and would also be done if the subject was not taking part in the study. Additional blood and urine samples will be taken for study purposes. Electrocardiograms (ECG) will be done. CT or MRI scans will be performed more frequent than would normally be done.
The subjects may experience side effects of the medication or experience risks or discomforts of the study procedures (e.g. blood drawing, scans and biopsies) The most common side effects reported with atezolizumab (occurring in 10% or more of patients) are:
• Back pain
• Fatigue
• Joint pain (arthralgia)
• Lack of energy (asthenia)
• Decreased appetite
• Diarrhea
• Muscle and bone pain (myalgia, musculoskeletal pain and bone pain)
• Urinary tract infection
• Shortness of breath (dyspnea)
• Itching of the skin
• Nausea
• Fever
• Rash

• Vomiting
• Cough
• Headache

## Contacts

**Public**
Hoffmann-La Roche

Grenzacherstrasse 124
Basel 4070
CH
**Scientific**
Hoffmann-La Roche

Grenzacherstrasse 124
Basel 4070
CH

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

- A representative formalin-fixed paraffin-embedded (FFPE) tumor specimen in paraffin block (preferred) or 15 (or more) unstained, freshly cut, serial sections (on slides) from an FFPE resected tumor specimen is required for participation in this study. This specimen must be accompanied by the associated pathology report - ECOG performance status of 0 or 1 - Histological or cytological diagnosis of Stage IB (tumors >= 4 cm)*IIIA (T2*3 N0, T1*3 N1, T1-3 N2, T4-N0 1) non-small cell lung cancer (NSCLC) - Eligible to receive a

cisplatin-based chemotherapy regimen - For female patients of childbearing potential and male patients with partners of childbearing potential, agreement (by patient and/or partner) to use a highly effective form(s) of contraception during study treatment that results in a low failure rate of < 1% per year when used consistently and correctly. Female and male patients should continue contraceptive use for 6 months after the last dose of cisplatin-based chemotherapy (cisplatin plus vinorelbine, docetaxel, gemcitabine, or pemetrexed). Female patients treated with atezolizumab should continue contraception use for 5 months after the last dose. Women must refrain from donating eggs during this same period.

### Exclusion criteria

- Illness or condition that may interfere with a patient's capacity to understand, follow, and/or comply with study procedures
- Pregnant and lactating women
- Treatment with prior systemic chemotherapy, with the following exceptions:
•Chemotherapy for early stage of malignancy with curative intent, provided that the last dose received was more than 5 years prior to enrollment, is allowed
•Low-dose chemotherapy for non-malignant conditions is allowed
- Hormonal cancer therapy or radiation therapy as prior cancer treatment within 5 years before enrollment
- Treatment with any other investigational agent with therapeutic intent within 28 days prior to enrollment
- Known sensitivity to any component of the chemotherapy regimen the patient will be assigned to, or to mannitol
- Prior treatment with CD137 agonists or immune checkpoint blockade therapies, anti-PD-1, and anti-PD-L1 therapeutic antibodies
- Patients who have had prior anti-CTLA-4 treatment may be enrolled, provided the following requirements are met:
•Last dose of anti-CTLA-4 at least 6 weeks prior to randomization
•No history of severe immune-mediated adverse effects from anti-CTLA- 4 (NCI CTCAE Grades 3 and 4)
- Known tumor PD-L1 expression status as determined by an IHC assay from other clinical studies (e.g., patients whose PD-L1 expression status was determined during screening for entry into a study with anti-PD-1 or anti-PD-L1 antibodies but were not eligible are excluded)

## 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

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 03-04-2017 |
| Enrollment: | 35 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | MPDL3280A |
| Generic name: | Atezolizumab |

# Ethics review

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|---|---|
| Approved WMO Date: | 28-10-2015 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 08-04-2016 |
| Application type: | First submission |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 14-07-2016 |

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|---|---|
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 26-07-2016 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 26-09-2016 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 24-11-2016 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 29-11-2016 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-12-2016 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 04-01-2017 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 03-08-2017 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |

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| Approved WMO Date: | 10-08-2017 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 29-11-2017 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 12-12-2017 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 20-04-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 11-05-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 08-08-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 30-08-2018 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 03-01-2019 |
| Application type: | Amendment |

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| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 08-01-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 15-02-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 25-02-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 12-06-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 15-10-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 21-10-2019 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 07-05-2020 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |

Approved WMO

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|---|---|
| Date: | 08-05-2020 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-02-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 18-02-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 03-06-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 06-06-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 29-11-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 08-12-2021 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 07-04-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United |

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| | (Nieuwegein) |
| Approved WMO Date: | 20-04-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 12-10-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 19-10-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-11-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 25-11-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 28-12-2022 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 11-06-2023 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 16-06-2023 |

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|---|---|
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 31-08-2023 |
| Application type: | Amendment |
| Review commission: | MEC-U: Medical Research Ethics Committees United (Nieuwegein) |
| Approved WMO Date: | 04-09-2023 |
| Application type: | Amendment |
| 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 |
|---|---|
| EU-CTR | CTIS2023-505981-26-00 |
| EudraCT | EUCTR2014-003205-15-NL |
| CCMO | NL54046.100.15 |