A PHASE III, OPEN-LABEL, MULTICENTER, RANDOMIZED STUDY EVALUATING THE EFFICACY AND SAFETY OF ATEZOLIZUMAB (MPDL3280A, ANTI-PD-L1 ANTIBODY) IN COMBINATION WITH CARBOPLATIN + PACLITAXEL OR MPDL3280A IN COMBINATION WITH CARBOPLATIN + NAB PACLITAXEL VERSUS CARBOPLATIN + NAB-PACLITAXEL IN CHEMOTHERAPY NAÏVE PATIENTS WITH STAGE IV SQUAMOUS NON-SMALL CELL LUNG CANCER

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Unless otherwise specified, efficacy objectives will be analyzed for the following two treatment comparisons:• Atezolizumab + carboplatin + nab-paclitaxel (Arm B) versus carboplatin + nab- paclitaxel (Arm C)• Atezolizumab + carboplatin + paclitaxel...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms benign (excl mesotheliomas)
Study type	Interventional

Summary

ID

NL-OMON47153

Source

ToetsingOnline

Brief title
GO29437

Condition

- Respiratory and mediastinal neoplasms benign (excl mesotheliomas)

Synonym
Stage IV squamous non-small cell lung cancer - Lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: F Hoffmann-La Roche Ltd

Intervention

Keyword: Chemotherapy-naive patients, Open-Label, Randomized, Squamous non-small cell lung cancer

Outcome measures

Primary outcome

The co-primary efficacy outcome measures for this study are the following:

• PFS, defined as the time from randomization to the first occurrence of the

disease progression as determined by the investigator using RECIST v1.1 or

death from any cause, whichever occurs first in the tGE population and ITT

population

• OS, defined as the time from randomization to death from any cause in the ITT

population

Secondary outcome

The secondary efficacy outcome measures for this study are the following:

• OS in the tGE population

• PFS, as determined by the investigator according to RECIST v1.1, and OS in the TC2/3 or IC2/3 population and the TC1/2/3 or IC1/2/3 population

• Objective response, defined as partial response (PR) or complete response (CR) as determined by the investigator according to RECIST v1.1 in the tGE population and ITT population

• DOR, defined as the time interval from the first occurrence of a documented objective response to the time of disease progression as determined by the investigator using RECIST v1.1, or death from any cause, whichever occurs first in the tGE population and ITT population

• OS rates at 1 and 2 years for the tGE population and ITT population

• TTD in patient reported lung cancer symptoms, defined as time from randomization to deterioration (10 point change) on each of the EORTC QLQ-C30 and EORTC QLQ-LC13 symptom subscales (cough, dyspnea [single item], dyspnea [multi-item subscale], chest pain, and arm/shoulder pain) in the tGE population and ITT population

• Change from baseline in patient reported lung cancer symptoms (cough, dyspnea, and chest pain) on the symptom severity score of the SILC scale in the tGE population and ITT population

• PFS, as determined by the investigator according to RECIST v1.1, and OS in the two atezolizumab-containing arms in the tGE population and the ITT population

Study description

Background summary

Lung cancer remains the leading cause of cancer deaths worldwide; it is the most common cancer in both men and women and accounted for approximately 13% of all new cancers in 2008. Encouraging clinical data emerging in the field of tumor immunotherapy have demonstrated that therapies focused on enhancing T-cell responses against cancer can result in a significant survival benefit in patients with Stage IV cancer

Study objective

Unless otherwise specified, efficacy objectives will be analyzed for the following two treatment comparisons:
• Atezolizumab + carboplatin + nab-paclitaxel (Arm B) versus carboplatin + nab-paclitaxel (Arm C)
• Atezolizumab + carboplatin + paclitaxel (Arm A) versus carboplatin + nab-paclitaxel (Arm C)

The term *tumor gene expression* (tGE) refers to randomized patients with a defined level of expression of a PD-L1 and T-effector gene signature in tumor tissue, as analyzed through use of a centrally performed RNA-based assay. Some efficacy endpoints will be analyzed in a population of randomized patients with a defined level of PD-L1 expression on tumor cells (TCs) and tumor-infiltrating immune cells (ICs), as analyzed through use of a centrally performed immunohistochemistry (IHC) test.
Efficacy Objectives

The co-primary objectives of this study are the following:
• To evaluate the efficacy of atezolizumab as measured by investigator assessed progression-free survival (PFS) according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1) in the tGE population and the intent-to-treat (ITT) population
• To evaluate the efficacy of atezolizumab as measured by overall survival (OS) in the ITT population

The secondary efficacy objectives for this study are the following:
• To evaluate the efficacy of atezolizumab as measured by OS in the tGE population
• To evaluate the efficacy of atezolizumab as measured by investigator-assessed PFS according to RECIST v1.1 and OS in the TC2/3 or IC2/3 population and the TC1/2/3 or IC1/2/3 population
• To evaluate the efficacy of atezolizumab as measured by investigator assessed objective response rate (ORR) according to RECIST v1.1 in the tGE population

and the ITT population
• To evaluate the efficacy of atezolizumab as measured by investigator assessed duration of response (DOR) according to RECIST v1.1 in the tGE population and the ITT population
• To evaluate the OS rate at 1 and 2 years in each treatment arm for the tGE population and the ITT population n
• To determine the impact of atezolizumab as measured by time to deterioration (TTD) in patient reported lung cancer symptoms of cough, dyspnea (single item and multi item subscales), chest pain, or arm/shoulder pain, using the European Organisation for the Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core (QLQ C30) and the supplemental lung cancer module (QLQ LC13) in the tGE population and the ITT population
• To determine the impact of atezolizumab as measured by change from baseline (i.e., improvement or deterioration based upon presenting symptomatology) in patient reported lung cancer symptom (chest pain, dyspnea, and cough) score using the Symptoms in Lung Cancer (SILC) scale symptom severity score in the tGE population and the ITT population
• To evaluate the efficacy of the treatment regimen of atezolizumab + carboplatin + paclitaxel versus atezolizumab + carboplatin + nab paclitaxel as measured by investigator assessed PFS according to RECIST v1.1 and OS in the tGE population and the ITT population

The safety objectives for this study are the following:
• To evaluate the safety and tolerability of atezolizumab in each of the two treatment comparisons
• To evaluate the incidence and titers of anti-therapeutic antibodies (ATAs) against atezolizumab and to explore the potential relationship of the immunogenicity response with pharmacokinetics, safety, and efficacy

The pharmacokinetic (PK) objectives for this study are the following:
• To characterize the pharmacokinetics of atezolizumab when given in combination with carboplatin + paclitaxel (Arm A) or with carboplatin + nab-paclitaxel (Arm B)
• To characterize the pharmacokinetics of carboplatin when given in combination with paclitaxel and atezolizumab (Arm A) or with nab-paclitaxel with and without atezolizumab (Arms B and C)
• To characterize the pharmacokinetics of paclitaxel when given in combination with atezolizumab and carboplatin (Arm A)
• To characterize the pharmacokinetics of nab-paclitaxel (reported as total paclitaxel) when given in combination with carboplatin with and without atezolizumab (Arms B and C)

The exploratory objectives for this study are the following:
• To evaluate PFS at 6 months and at 1 year in each treatment arm
• To evaluate the OS rate at 3 years in each treatment arm
• 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 study treatment
• To evaluate the utility of biopsy at the time of apparent disease progression to distinguish apparent increases in tumor volume related to the immunomodulatory activity of atezolizumab (i.e., pseudoprogression/tumor immune infiltration) from true disease progression
• To evaluate and compare patient*s health status as assessed by the EuroQoL 5 Dimensions 3-Level (EQ-5D 3L) questionnaire to generate utility scores for use in economic models for reimbursement
• To determine the impact of atezolizumab as measured by change from baseline in patient-reported outcomes of health-related quality of life, lung cancer-related symptoms, and functioning as assessed by the EORTC QLQ C30 and LC13

Study design

This is a randomized, Phase III, multicenter, open-label study (IMpower131) designed to evaluate the safety and efficacy van atezolizumab (ANTI-PD-L1 ANTIBODY) in combination with CARBOPLATIN + PACLITAXEL or atezolizumab IN COMBINATION with CARBOPLATIN + NAB PACLITAXEL VERSUS CARBOPLATIN + NAB-PACLITAXEL in chemotherapy naive patients with stage IV Squamous Non-small Cell Lung cancer.

Intervention

Investigational Medicinal Products Test Product (Investigational Drug)
MPDL3280A (1200 mg IV) will be administered on Day 1 of each 21-day cycle.

Non-Investigational Medicinal Products Comparator
- Carboplatin will be administered by IV infusion to achieve an initial target area under the curve (AUC) of 6 mg/mL/min on Day 1 of each 21-day cycle for 4 or 6 cycles during the induction phase
- Nab-paclitaxel (100 mg/m2 IV) will be administered on Days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles during the induction phase.
- Paclitaxel (200 mg/m2 IV) will be administered on Day 1 of each 21-day cycle for 4 or 6 cycles during the induction phase. Carboplatin and paclitaxel will be administered to patients randomized to Arm A.

Carboplatin and nab-paclitaxel will be administered to patients in Arms B and C. Nab-paclitaxel will be considered an IMP for study purposes in countries where nab-paclitaxel is considered an IMP by local regulations.

Study burden and risks

- Risks (adverse events) related to atezolizumab described in the study protocol under chapter 5.1.1 Risks Associated with atezolizumab.
- Risks(adverse events) associated with carboplatine described in the study

protocol under chapter 5.1.2 Risks Associated with carboplatine.
- Risks (adverse events) associated with paclitaxel are described in the study protocol under Section 5.1.3 Risks Associated with paclitaxel
- Risks (adverse events) related to nab-paclitaxel are described in the study protocol under chapter 5.1.4 Risks Associated with nab-paclitaxel

Besides the possible adverse reactions as described in the study protocol, the collection of blood samples can cause mild pain, redness, bruising and or irritation at the injection site. CT examinations may be uncomfortable for a patient and CT examinations that require a contrast injection may cause slight, temporary discomfort while the intravenous needle is placed.

Lungcancer remains the most important cause of death by cancer in the world; it is the most prevalent form of cancer in both men and women. In 2008 lungcancer was 13% of all new cancer patients. Promising clinical research data op the area of immunotherapy have shown that therapies aimed at improving the T-cell response to cancer can result in a significant chance of longer survival in patients with phase IV cancer. The treatment with atezolizumab, next to platinumchemotherapy, offers the opportunity for clinical advantage in NSCLC patients.

In chapter 1.4: Study Rationale and Benefit-Risk Assessment, of the study protocol the rationale of the research is described.

Contacts

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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

• ECOG performance status of 0 or 1
• Histologically or cytologically confirmed, Stage IV squamous NSCLC
• No prior treatment for Stage IV squamous NSCLC
Patients with a sensitizing mutation in the EGFR gene must have experienced disease progression (during or after treatment) or intolerance to treatment with erlotinib, gefitinib, or another EGFR tyrosine kinase inhibitor (TKI) appropriate for the treatment of EGFRmutant NSCLC.
Patients with an ALK fusion oncogene must have experienced disease progression (during or after treatment) or intolerance to treatment with one or more ALK inhibitors (i.e. crizotinib) appropriate for the treatment of NSCLC in patients having an ALK fusion oncogene.
• Patients who have received prior neo-adjuvant, adjuvant radiotherapy, chemotherapy, or chemoradiotherapy with curative intent for nonmetastatic disease must have experienced a treatment-free interval of at least 6 months from randomization since the last chemotherapy, radiotherapy or completion of chemoradiotherapy.
• Measurable disease, as defined by RECIST v1.1

Exclusion criteria

• Active or untreated CNS metastases as determined by CT or MRI evaluation during screening and prior radiographic assessments
• Spinal cord compression not definitively treated with surgery and/or radiation or previously diagnosed and treated spinal cord compression without evidence that disease has been clinically stable for > 2 weeks prior to randomization
• Leptomeningeal disease
• Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently)
• History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins

• Positive test for HIV

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:	Recruitment stopped
Start date (anticipated):	19-01-2016
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Abraxane
Generic name:	nab-paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	N.A.
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	N.A.
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Tarceva
Generic name:	Erlotinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-04-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-10-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-10-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	28-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-08-2017
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	12-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-08-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-05-2020
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
EudraCT	EUCTR2014-003208-59-NL
ClinicalTrials.gov	NCT02367794
CCMO	NL52156.100.15

Study results

Results posted: 03-03-2022

First publication
30-11-2021