A PHASE III, OPEN-LABEL, RANDOMIZED STUDY OF ATEZOLIZUNAB (MPDL3280A, ANTI*PD-L1 ANTIBODY) IN COMBINATION WITH CARBOPLATIN + PACLITAXEL WITH OR WITHOUT BEVACIZUMAB COMPARED WITH CARBOPLATIN + PACLITAXEL + BEVACIZUMAB IN CHEMOTHERAPY-NAiVE PATIENTS WITH STAGE IV NON-SQUAMOUS NON*SMALL CELL LUNG CANCER.

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Primary Efficacy ObjectivesUnless otherwise specified, efficacy objectives will be analyzed for the following two treatment comparisons:• Atezolizumab + carboplatin + paclitaxel + bevacizumab (Arm B) versus carboplatin + paclitaxel + bevacizumab (...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47780

Source
ToetsingOnline

Brief title
GO29436

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Stage IV non-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, Non-squamous non-small cell lung cancer, Open-Label, Randomized

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

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

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

ITT-WT population

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

ITT-WT population

Secondary outcome

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

• OS in the tGE WT population

• PFS, as determined by the investigator according to RECIST v1.1, and OS in

the TC2/3 or IC2/3 WT population and the TC1/2/3 or IC1/2/3 WT population

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

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

• DOR, defined as the time interval from 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 1 in the tGE-WT population and the ITT-WT population

• PFS, defined as the time from randomization to the first occurrence of disease progression as determined by the IRF using RECIST v1.1 or death from any cause, whichever occurs first 1 in the tGE-WT population and the ITT-WT population

• OS rates at 1 and 2 years 1 in the tGE-WT population and the ITT-WT population

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

• Change from baseline in patient reported lung cancer symptoms (chest pain, dyspnea, and cough) on the symptom severity score of the Symptoms in Lung

Cancer scale in the tGE-WT population and the ITT-WT 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

Treatment with MPDL3280A offers the potential for clinical benefit in NSCLC patients, in addition to platinum-based chemotherapy with or without bevacizumab.

Study objective

Primary Efficacy Objectives
Unless otherwise specified, efficacy objectives will be analyzed for the following two treatment comparisons:
• Atezolizumab + carboplatin + paclitaxel + bevacizumab (Arm B) versus carboplatin + paclitaxel + bevacizumab (Arm C)
• Atezolizumab + carboplatin + paclitaxel (Arm A) versus carboplatin + paclitaxel + bevacizumab (Arm C)
The term *wild type* (WT) refers to randomized patients who do not have a sensitizing EGFR mutation or ALK translocation.
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 immune cells (ICs), as analyzed through use of a centrally performed IHC test.

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 RECIST v1.1 in the tGE-WT population and the ITT-WT population
• To evaluate the efficacy of atezolizumab as measured by overall survival (OS) in the ITT-WT population

Secondary Efficacy Objectives
The secondary efficacy objectives for this study are the following:
• To evaluate the efficacy of atezolizumab as measured by OS in the tGE WT 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 WT population and the TC1/2/3 or IC1/2/3 WT population
• To evaluate the efficacy of atezolizumab as measured by investigator-assessed PFS according to RECIST v1.1 and OS in the tGE population and the ITT population
• To evaluate the efficacy of atezolizumab as measured by investigator assessed objective response rate (ORR) according to RECIST v1.1 in the tGE-WT population and the ITT-WT population
• To evaluate the efficacy of atezolizumab as measured by investigator assessed duration of response (DOR) according to RECIST v1.1 in the tGE-WT population and the ITT-WT population
• To evaluate the efficacy of atezolizumab as measured by an Independent Review Facility (IRF)-assessed PFS according to RECIST v1.1 in the tGE-WT population and the ITT-WT population
• To evaluate the OS rate at 1 and 2 years in each treatment arm for the tGE-WT population and the ITT-WT population
• To compare the efficacy of the two atezolizumab-containing arms, Arm A versus Arm B, as measured by investigator assessed PFS according to RECIST v1.1 and by OS in the tGE-WT population and the ITT-WT population
• 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-WT population and the ITT-WT population
• To determine the impact of atezolizumab as measured by change in 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 for the tGE-WT population and the ITT-WT

The safety objectives for this study are:
• To evaluate the safety and tolerability of atezolizumabin each of the two treatment comparisons described in Section 2.1.1
• To evaluate the incidence and titers of ATAs against atezolizumab and to explore the potential relationship of the immunogenicity response with pharmacokinetics, safety, and efficacy

The PK objectives for this study are:
• To characterize the pharmacokinetics of atezolizumab when given in combination with carboplatin andpaclitaxel with and without bevacizumab (Arms A and B)

• To characterize the pharmacokinetics of carboplatin when given in combination with paclitaxel with and without atezolizumab and/ or bevacizumab (Arms A, B, and C)
• To characterize the pharmacokinetics of paclitaxel when given in combination with carboplatin with and without atezolizumab and/ or bevacizumab (Arms A, B, and C)
• To characterize the pharmacokinetics of bevacizumab when given in combination with carboplatin and paclitaxel with and without atezolizumab (Arms B and C)

The exploratory objectives for this study are the following:
• To evaluate the efficacy of atezolizumab as measured by investigator-assessed time to response (TTR) and time-in-response (TIR) according to RECIST v1.1
• To evaluate ORR and DOR according to RECIST v1.1 as assessed by the IRF
• To evaluate investigator-assessed ORR, PFS, and DOR according to modified RECIST for the atezolizumab-containing treatment arms
• 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 (IMpower150) designed to evaluate the safety and efficacy of atezolizumab in combination with carboplatin + paclitaxel with or without bevacizumab compared with treatment with carboplatin + paclitaxel + bevacizumab in approximately 1200 chemotherapy-naïve patients with Stage IV non-squamous NSCLC.

Intervention

Test Product (experimental drug)
- MPDL3280A (1200 mg IV) is administered on day 1 of each cycle of 21 days. MPDL3280A is administered to patients randomized to groups A and B.

Non experimental drugs (Comparator)
- Carboplatin is administered via IV infusion to an initial target area under the curve (AUC) of 6 mg / ml / min to achieve on day 1 of each cycle of 21 days, at 4 to 6 cycles during the induction phase.
- Paclitaxel (200 mg / m 2 IV) is administered on day 1 of each cycle of 21 days, with 4 or 6 cycles during the induction phase.
- Bevacizumab (15 mg / kg IV) is administered on day 1 of each cycle of 21 days, with 4 or 6 cycles during the induction phase and the treatment phase.
- Carboplatin and paclitaxel are administered to patients in all treatment groups. Bevacizumab is administered to patients randomized to groups B and C.

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

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.

Lung cancer is the most important cause of deaths by cancer in the world; it is the most prevalent form of cancer in both men and women. In 2008 lung cancer was 13% of all new cancer patients.
Promising clinical research data on the area of immunotherapy have shown that therapies aimed at improving the T-cel response to cancer can result in a significant chance for a longer survival of patients with phase IV cancer. Treatment with atezolizumab, next to platinumchemotherapy with or without bevacizumab, offers the opportunity for clinical advantage in patients with NSCLC.

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

Contacts

Public

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Scientific
Hoffmann-La Roche

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- histologically or cytologically confirmed, Stage IV non-squamous NSCLC (per the Union Internationale contre le Cancer/American Joint Committee on Cancer staging system, 7th edition; Detterbeck et al. 2009). Patients with tumors of mixed histology (i.e., squamous and nonsquamous) are eligible if the major histological component appears to be non-squamous.
- adequate hematologic and end organ function, defined by the following laboratory results obtained within 14 days prior to randomization.
- 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.
- any approved anti-cancer therapy, including chemotherapy, or hormonal therapy within 3 weeks prior to initiation of study treatment; the following exceptions

are allowed:
* hormone-replacement therapy or oral contraceptives
* TKIs approved for treatment of NSCLC discontinued > 7 days prior to randomization; the baseline scan must be obtained after discontinuation of prior TKIs.
- women who are pregnant, lactating, or intending to become pregnant during the study.
- history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.

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):	14-03-2016
Enrollment:	89
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N.A.
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Avastin

Generic name:	Bevacizumab
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:	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:	11-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-06-2016
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:	21-03-2017
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:	13-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	01-08-2017
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Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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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:	22-02-2018
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:	21-03-2019
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:	11-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-10-2019
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:	19-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-11-2019

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-05-2020
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	EUCTR2014-003207-30-NL
ClinicalTrials.gov	NCT02366143
CCMO	NL52180.100.15

Study results

Results posted: 19-01-2022

First publication
28-07-2021