A PHASE II, MULTICENTER, SINGLE-ARM STUDY OF ATEZOLIZUMAB IN PATIENTS WITH PD L1-POSITIVE LOCALLY ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER

Published: 27-02-2014
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45051

Source
ToetsingOnline

Brief title
GO28754 (BIRCH)

Condition

- Other condition

Synonym
Lungcancer, non small cell lung cancer

Health condition

NIET-KLEINCELLIG LONGCARCINOOM (NSCLC)

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: ATEZOLIZUMAB, NSCLC, PD-L1□POSITIVE, Phase 2

Outcome measures

Primary outcome

The primary efficacy objective analysis will be performed in patients who are PD-L1 positive (defined as IHC 2 and IHC 3 on the basis of tumor PD-L1 expression) and when appropriate may be performed in different patient subpopulations according to the two IHC categories.

PRIMARY OBJECTIVE

The primary objective for this study is to evaluate the efficacy of MPDL3280A in patients with PD-L1* positive locally advanced or metastatic NSCLC, as measured by:

* Independent review facility (IRF)-assessed ORR according to RECIST v1.1

The efficacy analysis will follow a hierarchical fixed-sequence procedure.

Secondary outcome

SECONDARY OBJECTIVES

The secondary objectives for this study are as follows:

* To evaluate PFS and DOR, and time in response (TIR) according to RECIST v1.1 as assessed by IRF and according to modified RECIST as assessed by the

investigators

* To evaluate ORR, DOR, TIR, and PFS according to RECIST v1.1 as assessed by the investigators

* To evaluate the investigator-assessed ORR according to modified RECIST

* To evaluate OS and 1-year OS

* To evaluate 1-year PFS as determined by the IRF per RECIST v1.1 and 1-year PFS as determined by the investigator per RECIST v1.1 and per modified RECIST

* To evaluate the safety and tolerability of MPDL3280A

* To characterize the pharmacokinetics of MPDL3280A

* To evaluate the incidence and titers of ATAs against MPDL3280A and to explore the potential relationship of the immunogenicity response with pharmacokinetics, safety, and efficacy

EXPLORATORY OBJECTIVES

The exploratory objectives for this study are as follows:

* To evaluate IRF-assessed ORR according to modified RECIST

* To evaluate disease control rate (DCR)

* To evaluate tumor burden using change in sum of longest diameters (SLD)

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

* To assess predictive, prognostic, and pharmacodynamic exploratory biomarkers in archival and/or fresh tumor tissue and blood and their association with

disease status 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 MPDL3280A (i.e., pseudoprogression/tumor immune

infiltration) from true disease progression

* To evaluate patient-reported outcomes (PROs) of lung cancer symptoms, patient

functioning, and health-related quality of life (HRQoL) as measured by the

European Organisation for the Research and Treatment of Cancer Quality-of-Life

Questionnaire Core 30 (EORTC QLQ-C30) and the lung cancer module (QLQ-LC13)

Study description

Background summary

MPDL3280A is a human Ig G1 monoclonal antibody consisting of two heavy chains (448 amino acids) and two light chains (214 amino acids) and is produced in Chinese hamster ovary cells. MPDL3280A was engineered to eliminate Fc-effector function via a single amino acid substitution at position 298 on the heavy chain, which results in a non-glycosylated antibody that has minimal binding to Fc receptors and prevents Fc-effector function at expected concentrations in humans. MPDL3280A targets human PD-L1 and inhibits its interaction with its receptors,PD-1 and B7.1 (CD80, B7-1). Both of these interactions are reported to provide inhibitory signals to T cells.
MPDL3280A is being investigated as a potential therapy against solid tumors and hematologic malignancies in humans.

For more information, please see also study protocol pages 53 - 64

Study objective

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The efficacy analysis will follow a hierarchical fixed-sequence procedure.

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* To evaluate PFS and DOR, and time in response (TIR) according to RECIST v1.1 as assessed by IRF and according to modified RECIST as assessed by the investigators
* To evaluate ORR, DOR, TIR, and PFS according to RECIST v1.1 as assessed by the investigators
* To evaluate the investigator-assessed ORR according to modified RECIST
* To evaluate OS and 1-year OS
* To evaluate 1-year PFS as determined by the IRF per RECIST v1.1 and 1-year PFS as determined by the investigator per RECIST v1.1 and per modified RECIST
* To evaluate the safety and tolerability of MPDL3280A
* To characterize the pharmacokinetics of MPDL3280A
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* To evaluate IRF-assessed ORR according to modified RECIST
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* To evaluate tumor burden using change in sum of longest diameters (SLD)
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* To assess predictive, prognostic, and pharmacodynamic exploratory biomarkers in archival and/or fresh tumor tissue and blood and their association with disease status 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 MPDL3280A (i.e., pseudoprogression/tumor immune infiltration) from true disease progression
* To evaluate patient-reported outcomes (PROs) of lung cancer symptoms, patient functioning, and health-related quality of life (HRQoL) as measured by the European Organisation for the Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 (EORTC QLQ-C30) and the lung cancer module (QLQ-LC13)

Study design

This is a phase II, multicenter, single-arm study to evaluate the efficacy of

MPDL3280A in patients with PD-L1*positive locally advanced or metastatic non-small cell lung cancer.

For more detailed information, please see pages 39-49 of the study protocol.

Intervention

Eligible patients will be placed in Cohort I, 2 or 3, depending on their medical history.

MPDL3280A IV (fixed dose of 1200 mg) will be administered on Day 1 of 21-day cycles. During the initial treatment stage, MPDL3280A treatment may be continued as long as patients are experiencing clinical benefit as assessed by the investigator, i.e., in the absence of unacceptable toxicity or symptomatic deterioration attributed to disease progression after an integrated assessment of radiographic
data, biopsy results (if available), and clinical status.
For more information, see also pages 66-68 of the study protocol.

Study burden and risks

For more information, please see the answer on question number E9.

Contacts

Public
Roche Nederland B.V.

Beneluxlaan 2A
Woerden 3446 GR
NL
Scientific
Roche Nederland B.V.

Beneluxlaan 2A
Woerden 3446 GR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Histologically or cytologically documented Stage IIIB (not eligible for definitive chemoradiotherapy), Stage IV, or recurrent NSCLC ;* PD-L1-positive status as determined by an IHC assay based on PD-L1 expression on tumor infiltrating immune cells and/or tumor cells performed by a central laboratory;* ECOG performance status of 0 or 1;* Life expectancy * 12 weeks;* Measurable disease, as defined by RECIST v1.1 ;* 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

Exclusion criteria

* Treatment with any other investigational agent or participation in another clinical trial with therapeutic intent within 28 days prior to enrollment;* Known CNS disease, including treated brain metastases;* Leptomeningeal disease;* History of auto-immune disease

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-07-2014
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab

Ethics review

Approved WMO Date:	27-02-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-04-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-07-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-08-2014

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2017
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-10-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2013-003330-32-NL
ClinicalTrials.gov	NCT02031458
CCMO	NL46632.056.14