A PHASE III, OPEN-LABEL, MULTICENTER, RANDOMIZED STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF MPDL3280A (ANTI-PD-L1 ANTIBODY) COMPARED WITH DOCETAXEL IN PATIENTS WITH NON-SMALL CELL LUNG CANCER AFTER PLATINUM FAILURE

Published: 04-03-2014
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Improvement in OS is generally accepted as the best measure of clinical benefit forpatients with advanced/unresectable or metastatic NSCLC. The assumption thattreatment with MPDL3280A will prolong OS compared with treatment with docetaxel isbased on...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44833

Source
ToetsingOnline

Brief title
GO28915 (OAK)

Condition

- Other condition

Synonym
Lung cancer, non small cell lung cancer

Health condition

Niet kleincellig longcarcinoom

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Anti PD-L1, MPDL3280A, NSCLC, phase 3

Outcome measures

Primary outcome

The primary efficacy objective for this study is:

* To determine if MPDL3280A treatment results in an improved overall survival

(OS)

compared with docetaxel treatment in patients with locally advanced or

metastatic

non-small cell lung cancer (NSCLC) who have progressed during or following a

platinum-containing regimen

Comparisons of OS between the treatment arms within the PD-L1 staining

categories and within the overall intent-to-treat (ITT) population will be

tested using a sequentially rejective multiple testing procedure.

Safety Objectives

The safety objectives for this study are as follows:

* To evaluate the safety and tolerability of MPDL3280A compared with docetaxel

* To evaluate the incidence of anti-therapeutic antibodies (ATAs) against

MPDL3280A and to

explore the potential

Secondary outcome

The secondary efficacy objectives for this study are:

• To evaluate efficacy of MPDL3280A compared with docetaxel with respect to

anti-tumor effects as measured by progression-free survival (PFS) per

investigator using the Response Evaluation Criteria in Solid Tumors (RECIST)

Criteria version 1.1

• To evaluate efficacy of MPDL3280A compared with docetaxel with respect to

anti-tumor effects as measured by ORR per investigator using RECIST v1.1

• To evaluate efficacy of MPDL3280A compared with docetaxel with respect to

anti-tumor effects as measured by time in response for all randomized patients

and by duration of response (DOR) per RECIST v1.1 for responding patients

Safety Objectives

The safety objectives for this study are as follows:

* To evaluate the safety and tolerability of MPDL3280A compared with docetaxel

* To evaluate the incidence of anti-therapeutic antibodies (ATAs) against

MPDL3280A and to

explore the potential

Study description

Background summary

MPDL3280A is a human immunoglobulin (Ig) G1 monoclonal antibody consisting of two heavy chains (448 amino acids) and two light chains (214 amino acids) and produced in Chinese hamster ovary cells. MPDL3280A was engineered to eliminate Fc-effector function via a single amino acid substitution (asparagine to alanine) 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 31-33

Study objective

Improvement in OS is generally accepted as the best measure of clinical benefit for
patients with advanced/unresectable or metastatic NSCLC. The assumption that treatment with MPDL3280A will prolong OS compared with treatment with docetaxel is
based on the durable response rates observed in Phase I trials with MPDL3280A, as
well as other PD-L1/PD-1 blocking agents.

The secondary efficacy endpoints of PFS and ORR will allow the evaluation of differences in response and progression patterns between the two treatment groups. Patients will be evaluated for disease progression at predefined, standard intervals to MPDL3280A*F. Hoffmann-La Roche Ltd.
Protocol GO28915, Version 4 58
minimize evaluation-time biases and will be followed off-treatment for continued safety monitoring and date of death. Safety and tolerability of study treatments will be assessed. The evaluation of efficacy data across the PD-L1 staining categories will be defined by subpopulations (TC3 or IC3, TC3 or IC2/3, TC3 or IC1/2/3, ITT) and analyzed by a hierarchal approach to define an appropriate diagnostic cutoff. MPDL3280A pharmacokinetics will be characterized and exploratory biomarker analyses performed. The MPDL3280A concentration results may be compared with available data from other MPDL3280A clinical studies and correlated with efficacy endpoints and safety events as appropriate. PRO data will allow further evaluation of the relative tolerability of treatment and the impact of therapy on disease symptoms between

the two treatment groups.

Study design

Study Design

This is a Phase III, global, multicenter, open-label, randomized, controlled study designed to evaluate the efficacy and safety of MPDL3280A compared with docetaxel in patients with locally advanced or metastatic NSCLC who have progressed during or following a platinum-containing regimen.

For more detailed information, please see pages 12-14 of the study protocol.

Intervention

Eligible patients will be stratified by PD-L1 IHC status (four categories of PD-L1 expression), by the number of prior chemotherapy regimens (1 versus 2), and by histology (nonsquamous versus squamous) and then randomized 1:1 to receive either MPDL3280A or docetaxel.

MPDL3280A at a fixed dose of 1200 mg will be administered intravenously on Day 1 of each 21-day cycle.

Docetaxel 75 mg/m2 will be administered intravenously on Day 1 of each 21-day cycle until disease progression per standard RECIST v1.1 or unacceptable toxicity

For more information, see also pages 11-13 of the study protocol

Study burden and risks

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

Contacts

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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 documented locally advanced or metastatic (i.e., Stage IIIB not eligible for definitive chemoradiotherapy, Stage IV, or recurrent) NSCLC ;•Representative formalin-fixed paraffin-embedded (FFPE) tumor specimens in paraffin blocks (preferred) or at least 15 unstained slides, with an associated pathology report, for central testing and determined to be evaluable for tumor PD-L1 expression prior to study enrollment;•Disease progression during or following treatment with a prior platinum-containing regimen for locally advanced, unresectable/inoperable or metastatic NSCLC or disease recurrence within 6 months of treatment with a platinum-based adjuvant/neoadjuvant regimen ;•Measurable disease, as defined by RECIST v1.1;•ECOG performance status of 0 or 1;•Life expectancy > 12 weeks

Exclusion criteria

•Received therapeutic oral or IV antibiotics within 2 weeks prior to randomization;•Major surgical procedure within 4 weeks prior to randomization or anticipation of need for a major surgical procedure during the course of the study other than for diagnosis;•Administration of a live, attenuated vaccine within 4 weeks prior to randomization or anticipation that such a live attenuated vaccine will be required during the study;•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):	06-10-2014
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Docetaxel
Generic name:	Docetaxel Accord
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MPDL3280A
Generic name:	MPDL3280A

Ethics review

Approved WMO

Date:	04-03-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	15-04-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2014
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:	06-01-2015
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:	12-01-2016
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:	01-04-2016
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:	02-02-2017
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	EUCTR2013-003331-30-NL
ClinicalTrials.gov	NCT02008227
CCMO	NL46629.056.14