A phase II multicenter, single-arm study of MPDL3280A in patients with PD-L1 positive locally advanced or metastatic non small cell lunch cancer

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The primary efficacy objective for this study is to evaluate the efficacy of MPDL3280Ain patients with PD-L1*positive locally advanced or metastatic NSCLC, as measuredby investigator-assessed ORR according to modified RECIST.SECONDARY OBJECTIVESThe...

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

Summary

ID

NL-OMON44922

Source
ToetsingOnline

Brief title
NSCL cancer

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
Lung cancer, Non□small Cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Genentech, Inc
Source(s) of monetary or material Support: Pharmaceutical Industry; Genentech;Inc.

Intervention

Keyword: MPDL3280A, Non-small cell lung cancer, PD-L1 positive, Phase 2

Outcome measures

Primary outcome

The primary efficacy outcome measure is investigator-assessed objective response (confirmed PR or confirmed CR) according to modified RECIST.

Secondary outcome

Objective response (confirmed PR or confirmed CR) per RECIST v1.1 as determined by the investigator

• DOR, defined as the time from the first occurrence of a documented objective response to the time of radiographic progression per RECIST v1.1 as determined by the investigator, or death from any cause on study

• PFS, defined as the time from first dose of MPDL3280A to the time of radiographic progression per RECIST v1.1 as determined by the investigator, or death from any cause on study

• PFS per modified RECIST, defined as follows:

For patients who discontinue at first documented radiographic progression or who die on study: the time from first dose of MPDL3280A to the time of progression or death

For patients who continue beyond first documented radiographic progression and have confirmed progression at the follow-up tumor assessment or who die on study: the time from first dose of MPDL3280A to the time of first documented progression or death

For patients who continue beyond first documented progression and do not have confirmed progression at the follow-up tumor assessment: the time from first dose of MPDL3280A to the time of subsequent radiographic progression (i.e., after the first instance) or death

• DOR, defined as the time from the first occurrence of a documented objective response to the time of radiographic progression per modified RECIST as determined by the investigator, or death from any cause on study

• OS, defined as the time from the first dose of MPDL3280A to the time of death from any cause on study

Safety Outcome Measures

The safety outcome measures for this study are as follows:

• Incidence, nature, and severity of AEs, graded according to the NCI CTCAE v4.0

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

• Incidence of ATA response to MPDL3280A and potential correlation with pharmacokinetic

(PK), pharmacodynamic, safety, and efficacy parameters

Biomarker Outcome Measure

The biomarker outcome measure for this study is as follows:

• PD-L1 expression status defined according to IHC and qPCR criteria

Pharmacokinetic Outcome Measures

The PK outcome measures for this study are as follows:

• MPDL3280A maximum serum concentration (Cmax) after infusion on Day 1 of Cycle 1

• MPDL3280A minimum serum concentration (Cmin) prior to the infusion on Day 1 of Cycles 2, 4, and 8 and at study termination

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 archival and/or freshly obtained tumor tissues and blood collected before, during, or after treatment with MPDL3280A or at progression

• Status of exploratory biomarkers in blood, plasma, or serum (including but not limited to cytokines such as IFN-γ)

• Status of tumor-infiltrating immune cells and biomarkers in biopsy specimens and blood collected at the first evidence of radiographic disease progression

• Status of FDG-PET scans performed at the first evidence of radiographic disease progression compared with baseline and early on-treatment scans

• Global health status/quality of life as measured by the EORTC QLQ-C30 and

QLQ-LC13

Study description

Background summary

Despite recent improvements in treatment, the prognosis for patients with advanced
NSCLC remains dismal, with median OS of approximately 12.5 months (Sandler et al. 2006). Patients who receive second-line treatment for their disease have
an even more limited prognosis, with a median survival duration of approximately 8*9 months (Stinchcombe et al. 2008). Approved therapies are associated with significant toxicities (e.g., neuropathy, febrile neutropenia, myelosuppression, and
alopecia) that negatively impact quality of life. Therefore, there is a continuing need
for more efficacious, better-tolerated treatments.
Inhibition of PD-L1/PD-1 signaling has been shown to produce durable responses in
some patients, and expression of PD-L1 by tumor cells in several tumor types (including NSCLC) correlates with response to therapy (Topalian et al. 2012).
Early unpublished data from the Phase Ia Study PCD4989g suggest that tumor PD-L1 status as determined by IHC in patients with NSCLC correlates with response to MPDL3280A. Four of 4 patients with PD-L1*positive NSCLC achieved a partial response (PR; clinical partial response or unconfirmed partial response). Only 4 of
26 (15%) patients with PD-L1*negative NSCLC achieved an objective response.
A potential benefit in terms of OS or durable disease control remains to be tested in
controlled studies.
No targeted therapy currently exists for NSCLC patients with PD-L1*positive tumors.
These data provide a rationale for evaluating the efficacy of MPDL3280A in patients
with NSCLC selected on the basis of tumor PD-L1 expression.

Study objective

The primary efficacy 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 investigator-assessed ORR according to modified RECIST.

SECONDARY OBJECTIVES
The secondary objectives for this study are as follows:
• To evaluate PFS and DOR according to modified RECIST
• To evaluate the efficacy of MPDL3280A, as measured by investigator-assessed ORR, DOR, and PFS, where all response endpoints are determined according to RECIST v1.1
• To evaluate OS
• To evaluate PFS in patients who experience a confirmed PR or confirmed CR per modified RECIST at any time on study treatment
• 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

Study design

This is a Phase II, global, multicenter, single-arm trial designed to evaluate the efficacy
and safety of MPDL3280A in patients with PD-L1*positive locally advanced or metastatic NSCLC.
Approximately 130 patients in total will be enrolled; approximately 45 study participants will be patients who have not received prior chemotherapy for advanced
disease (Cohort 1) and approximately 75 will be patients who have progressed during or
following a prior platinum-based chemotherapy regimen for advanced disease (Cohort 2;
the maximum number of prior therapies for patients in Cohort 2 is unrestricted). A
separate cohort (Cohort 3) will enroll approximately 10 selected second-line (or greater)
patients with previously treated brain metastases

Intervention

MPDL3280A IV (fixed dose of 1200 mg) will be administered on Day 1 of 21-day cycles.

Study burden and risks

treatment with MPDL3280A offers the potential for clinical benefit in NSCLC patients selected on the basis of tumor PD-L1 expression. Because most MPDL3280A-related toxicities observed to date have been mild and transient in nature
and do not overlap with the adverse effects of chemotherapy, patients who do not

respond to study treatment are considered likely to be able to subsequently receive
standard therapies for which they would otherwise have been eligible. Patients will be
fully informed of the risk of continuing study treatment in spite of apparent radiographic
progression (applies only to patients in Cohorts 2 and 3; does not apply to first-line
patients enrolled in Cohort 1), and investigators should make a careful assessment of
the potential benefit of doing so, considering radiographic data, biopsy results, and the
clinical status of the patient.

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

• Age >= 18 years
• 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 performed by a central laboratory
• ECOG performance status of 0 or 1
• Measurable disease as defined by RECIST v1.1
• For female patients of childbearing potential, agreement (by patient) to remain abstinent (refrain from heterosexual intercourse) or to use highly effective form(s) of contraception (i.e., one that results in a low failure rate [< 1% per year] when used consistently and correctly) during the treatment period and to continue its use for 5 months after the last dose of atezolizumab;Inclusion Criteria Unique to Cohort 1
• No prior chemotherapy for locally advanced or metastatic (i.e., Stage IIIB not eligible for definitive chemoradiotherapy, Stage IV, or recurrent) NSCLC;Inclusion Criteria Unique to Cohorts 2 and 3
• Disease progression during or following prior platinum-based chemotherapy for locally advanced or metastatic (i.e., Stage IIIB not eligible for definitive chemoradiotherapy, Stage IV, or recurrent) NSCLC;Inclusion Criteria Unique to Cohort 3
• Diagnosis of brain metastases by brain MRI or contrast-enhanced CT;For more detailed information please refer to protocol section 4.1

Exclusion criteria

Cancer-Specific Exclusions
• Any approved anti-cancer therapy, including chemotherapy, or hormonal therapy within 3 weeks prior to initiation of study treatment
• 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: Cohorts 1 and 2
• Leptomeningeal disease;For more detailed information please refer to protocol section 4.1

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-12-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	26-09-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-12-2013
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-08-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-12-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-11-2016

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-12-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2013-000177-69-NL
ClinicalTrials.gov	NCT01846416
CCMO	NL45044.031.13