Open label multicenter Phase I/II study of the safety and efficacy of PDR001 administered to patients with advanced malignancies (CPDR001X2101)

Published: 12-06-2015
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Primary: Phase 1: To estimate the RP2D and/or the MTD for PDR001.Phase II: To estimate the anti-tumor activity of PDR001.Secondary: Both phases: Safety and tolerability, PK profile, emergence of anti-PDR001 antibodies, other parameters for...

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

Summary

ID

NL-OMON47776

Source
ToetsingOnline

Brief title
CPDR001X2101 Phase I / II study with PDR001 in advanced malignancies

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
immuno therapy; cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: Anaplatic thyroid cancer, anti PD-1, NSCLC, phase I

Outcome measures

Primary outcome

Phase I: DLTs.

Phase II: Overall response rate.

Secondary outcome

Both phases: Adverse events, dose interruptions and reductions, PK parameters,

anti-PDR001 antibodies, progression free survival, duration of response,

disease control rate.

Study description

Background summary

PDR001 is a high-affinity, ligand-blocking, humanized anti-PD-1 IgG4 antibody that blocks the binding of PD-L1 and PD-L2 to PD-1. PDR001 shows functional activity in vitro/ex vivo.
This first-in-humans study will characterize the safety, tolerability, pharmacokinetics, pharmacodynamics and antitumor activity of PDR001 administered i.v. as a single agent. By blocking the interaction between PD-1 and its ligands, PD-L1 and PD-L2, PDR001 inhibits the PD-1 immune checkpoint, resulting in activation of an antitumor immune response by activating effector T-cells and inhibiting regulatory T-cells. From ongoing studies with anti-PD-1 antibodies, such as nivolumab and pembrolizumab, it is evident that PD-1 checkpoint inhibition results in clinically important anti-tumor activity.
This study is designed both to establish a recommended dose and schedule for PDR001, and to determine PDR001 antitumor activity in non-small cell lung cancer (NSCLC) and melanoma, and in 3 exploratory indications: gastric cancer

and esophageal adenocarcinoma, colorectal cancer and anal cancer. This FIH study is also designed to provide data to support future disease-specific registration studies in cancers for which anti-PD-1 therapy has not yet been explored.

Study objective

Primary:
Phase 1: To estimate the RP2D and/or the MTD for PDR001.
Phase II: To estimate the anti-tumor activity of PDR001.
Secondary:
Both phases: Safety and tolerability, PK profile, emergence of anti-PDR001 antibodies, other parameters for preliminary anti-tumor activity.

Study design

Multicenter phase I/II open-label dose escalation and dose expansion study of PDR001 monotherapy.
During phase II prescreening for PD-L1 status for patients with gastric cancer and esophageal adenocarcinoma, colorectal cancer and anal cancer.
The study treatment will be administered during 28-days cycles. PDR001 administration on days 1 and 15 or day 1 (once every 4 weeks). A once every 3 weeks schedule may be explored.
Treatment period until disease progression or unacceptable side effects.
Approx. 288 patients (58 for dose escalation and 230 for dose expansion) .
Independent DSMB.

Intervention

Treatment with PDR001.

Study burden and risks

Risk: Adverse effects of PDR001. First-in-human study.
Burden: Cycles of 4 weeks.
Screening visit, Cycle 1 and 3: 7 visits, cycle 2 2 visits, from cycle 4 onwards 2 visits (in case of a once per 4 weeks dosing schedule: 1 visit per cycle. Duration mostly 1-4 hours.

IV infusions of PDR001 once per 2 weeks and once per 4 weeks (once per 3 weeks may be explored). Duration 0,5-2 hours.
Physical examination: at screening, cycle 1: 3 times, cycle 2: 2 times, from cycle 3 onwards: once per cycle.
Blood tests (4-30 ml/occasion): at screening, cycle 1-2-3: all visits. From cycle 4 onwards: once per cycle.
ECG: At screening and cycles 1, 3 and 6 at day 1 prior and after administration

of PDR001, end of Study visit.
3 tumor biopsies: at screening and cycle 3 between Day 1 an d 15 and at progression (only in patients who had a response)
CT-/MRIscan: At screening, cycle 3 and every 8 weeks (every 2nd cycle) thereafter until cycle 11 and every 12 weeks thereafter.
Optional storage and use of the remaining blood and tissue for future research.

Contacts

Public
Novartis

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Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* phase I part: Advanced/metastatic solid tumors, with (non)measurable disease, who have progressed despite standard therapy or are intolerant of standard therapy, or for whom no standard therapy exists.
* Phase II part: Advanced/metastatic solid tumors, with at least one measurable lesion, who

have received standard therapy or are intolerant of standard therapy, have progressed following their last prior therapy, and fit into one of the following groups: *
Group 1: NSCLC
Patients with NSCLC must have had disease recurrence or progression during or after one prior platinum doublet-based chemotherapy regimen for advanced or metastatic disease. Prior maintenance therapy is allowed (e.g. pemetrexed, erlotinib, bevacizumab).
Patients must have been tested for mutations affecting EGFR and ALK. Patients with a known mutation in one gene need not be tested for the other. Patients with ALK or EGFR-positive NSCLC must have had recurrent or progressive disease after treatment with the corresponding inhibitor and platinum doublet-based chemotherapy, in any sequence.
Group 2: Melanoma
Patients with melanoma must have clinical or radiological evidence of disease progression during or after: For patients with BRAF wild type disease, at least one cycle of systemic treatment for
advanced melanoma.
For patients with BRAF V600 mutation positive disease, treatment with a BRAF inhibitor (alone or in combination with other agents) and at least one other systemic treatment
Group 3: Triple negative breast cancer
* ECOG performance status 0-1-2.
* Disease amenable to biopsy and a candidate for tumor biopsy according to the treating institution*s guidelines. Patient must be willing to undergo a new tumor biopsy at baseline, and during therapy on this study.
Group 4: Anaplastic thyroid cancer
* Patients are not required to have received or progressed on a prior therapy.
* Patients in this indication must not be at short term risk for life threatening complications (such as airway compromise or bleeding from locoregional or metastatic disease).
* Chemoradiation and/or surgery should be considered prior to study entry for those patients with locally advanced disease if those therapies are considered to be in the best interest of the patient.

Exclusion criteria

* Symptomatic CNS metastases or CNS metastases that require local CNS-directed therapy or increasing doses of corticosteroids within the prior 2 weeks.
* Out of range laboratory values (see protocol section 5.3).
* Impaired cardiac function or clinically significant cardiac disease e.g. congestive heart failure NYHA * 2), QTcF > 470 msec
* Subjects with active, known or suspected autoimmune disease. Subjects with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
* History of drug-induced pneumonitis or current pneumonitis.
* Active infection requirings ystemic antibiotic therapy
* HIV infection, active HBV or HCV infection
* Ocular melanoma

* Systemic anti-cancer therapy within 2-4 weeks of the first dose of study treatment. Wash-out for anticancer immunotherapiessuch as CTLA-4 antagonists, 6 weeks is indicated
* Prior PD-1- or PD-L1-directed therapy.
* Treatment with systemic steroid therapy, other than in the setting of adrenal insufficiency, systemic immunosuppressive therapy.
* Vaccines against infectious diseases within 4 weeks of initiation of study treatment.
* Major surgery within 2 weeks. .
* Radiotherapy within 2 weeks, except for palliative radiotherapy to a limited field.
* CSF within 2 weeks.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-07-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet van toepassing
Generic name:	nog niet van toepassing

Ethics review

Approved WMO

Date:	12-06-2015
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	30-06-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	05-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-12-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	11-12-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-01-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-07-2016
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-07-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-12-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-02-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	19-06-2017
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-07-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	01-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	07-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-12-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	19-04-2018
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-07-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	02-08-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	31-01-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-03-2019
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2014-003929-17-NL
ClinicalTrials.gov	NCT02404441
CCMO	NL52948.058.15