Phase I/II Study of PDR001 in Patients With Advanced Malignancies

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Main Information

Primary registry identifying number
LBCTR2019060201

Protocol number
CPDR001X2101

MOH registration number
7805/ص

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Retrospective

Type of registration: Justify
LCTR was recently initiated, original file was previously submitted by Paper

Date of registration in national regulatory agency
26/08/2016

Primary sponsor
Novartis Pharma Services Inc.

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
15/10/2019

Date of registration in national regulatory agency
26/08/2016

Public title
Phase I/II Study of PDR001 in Patients With Advanced Malignancies

Acronym

Scientific title
Open Label Multicenter Phase I/II Study of the Safety and Efficacy of PDR001 Administered to Patients With Advanced Malignancies

Acronym

Brief summary of the study: English
The purpose of this "first-in-human" study of PDR001 is to characterize the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and antitumor activity of PDR001 administered i.v. as a single agent to adult patients with solid tumors.
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.
This study has been designed as a phase I/II, multi-center, open-label study starting with a phase I dose escalation part followed by a phase II part.
PDR001 will be administered every 2 weeks until patient experiences unacceptable toxicity, progressive disease per immune related Response Criteria (irRC) and/or treatment is discontinued at the discretion of the investigator or the patient.

Brief summary of the study: Arabic
دراسة مفتوحة اللصاقة متعددة المراكز في المرحلتين الأولى والثانية حول سلامة وفعاليّة PDR001 المعطى للمرضى الذين يعانون من أورام خبيثة متقدّمة

Health conditions/problem studied: Specify
Patients with advanced malignancies : melanoma, NSCLC, TNBC and anaplastic thyroid cancer

Interventions: Specify

Biological: PDR001
anti-PD1 antibody

Key inclusion and exclusion criteria: Inclusion criteria

•Written informed consent must be obtained prior to any screening procedures
•Phase I part: Patients with advanced/metastatic solid tumors, with measurable or non-measurable disease as determined by RECIST version 1.1 (refer to Appendix 1), who have progressed despite standard therapy or are intolerant of standard therapy, or for whom no standard therapy exists.

•Phase II part: Patients with advanced/metastatic solid tumors, with at least one measurable lesion as determined by RECIST version 1.1, who have progressed following their last prior therapy, and fit into one of the following groups:
◦Group 1a and 1b: NSCLC:

Patients with NSCLC must have had disease recurrence or progression during or after no more than one prior systemic chemotherapy regimen (platinum doublet-based) for advanced or metastatic disease. Prior maintenance therapy is allowed (e.g. pemetrexed, erlotinib, bevacizumab).

Only patients with EGFR mutation-negative tumor are eligible (defined as negative for exon 19 deletions and for the L858R mutation in EGFR at a minimum; however, if more extensive EGFR mutation testing has been performed, the tumor must not harbor any known activating EGFR mutations in Exons 18-21 in order to be considered EGFR mutation-negative). All patients must be tested for EGFR mutational status and, for ALK translocation status if no mutation is detected in EGFR. Patients with ALK translocation-positive NSCLC must have had disease progression following treatment with a corresponding inhibitor and no more than one systemic chemotherapy regimen (platinum doublet-based), in any sequence.
•Group 2: Melanoma:

All patients must have been tested for BRAF mutations. Patients with V600 mutation positive melanoma must have clinical or radiological evidence of disease progression during or after treatment with a BRAF inhibitor alone or in combination with other agents.
•Group 3: Triple negatice breast cancer.
•Group 4: Anaplastic thyroid cancer
•Patients are not required to have received or progressed on a prior therapy.
•Patients 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.
◦ECOG Performance Status ≤ 1.
◦Patients must have a site of disease amenable to biopsy, and be a candidate for tumor biopsy. Patient must be willing to undergo a new tumor biopsy at baseline or at molecular pre-screening if applicable, and during therapy on this study. For patients in the phase II part of the study, exceptions may be granted after documented discussion with Novartis. After a sufficient number of paired biopsies are collected, the decision may be taken to stop the collection of biopsies.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

99

Key inclusion and exclusion criteria: Exclusion criteria

•History of severe hypersensitivity reactions to other mAbs
•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.
•Active infection requiring systemic antibiotic therapy.
•HIV infection.
•Active HBV or HCV infection.
•Patients with ocular melanoma.
•Systemic anti-cancer therapy within 2 weeks of the first dose of study treatment. For cytotoxic agents that have major delayed toxicity, e.g. mitomycin C and nitrosoureas, 4 weeks washout period. For patients receiving anticancer immunotherapies such as CTLA-4 antagonists, 6 weeks is indicated as the washout period.
•Prior PD-1- or PD-L1-directed therapy.
•Patients requiring chronic treatment with systemic steroid therapy, other than replacement-dose steroids in the setting of adrenal insufficiency. Topical, inhaled, nasal and ophthalmic steroids are not prohibited.
•Patients receiving systemic treatment with any immunosuppressive medication (other than steroids as described above).
•Use of any vaccines against infectious diseases (e.g. influenza, varicella, pneumococcus) within 4 weeks of initiation of study treatment.
•Presence of ≥ CTCAE grade 2 toxicity (except alopecia, peripheral neuropathy and ototoxicity, which are excluded if ≥ CTCAE grade 3) due to prior cancer therapy

Other protocol defined Inclusion/Exclusion may apply.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Non-randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

Dose comparison

Study phase

1 to 2

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Single

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

PDR001

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

PDR001 is a humanized monoclonal antibody and is a high-affinity, ligand-blocking, humanized immunoglobulin G4 (IgG4) directed against PD-1 and blocks the binding of PD-L1 and PD-L2.

Therapeutic indication

PD-1 is a critical immune checkpoint receptor that is expressed on CD4 and CD8 T cells upon activation (Freeman 2008). Engagement of PD-1 by its ligands, PD-L1 and PD-L2, transduces a signal that inhibits T-cell proliferation, cytokine production, and cytolytic function (Riley 2009). During tumorigenesis, cancer cells from a wide range of tumor types exploit immune checkpoint pathways, such as PD-1/PD-L1, to avoid detection by the adaptive immune system (Murphy 2011). mAb inhibitors of immunological checkpoints, including PD-1 and PD-L1, have demonstrated significant antitumor activity in patients with various solid tumors with less toxicity than broad immune activators, such as interleukin-2 (IL-2) and Interferon-alpha (IFN-α) (Topalian et al 2012, Hamid et al 2013, Topalian et al 2014, Seiwert et al 2014).

Therapeutic benefit

Progression free survival

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

Time perspective: Specify perspective

N/A

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

Samples for circulating tumor DNA will be shipped to central laboratory designated by Novartis.

Target sample size

3

Actual enrollment target size

3

Date of first enrollment: Type

Actual

Date of first enrollment: Date

10/01/2017

Date of study closure: Type

Actual

Date of study closure: Date

18/11/2020

Recruitment status

Complete

Recruitment status: Specify

Date of completion

12/06/2017

IPD sharing statement plan

No

IPD sharing statement description

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on www.clinicalstudydatarequest.com

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT02404441?term=PDR001&recrs=de&rank=4

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinicaltrials.gov	NCT02404441

Sources of Monetary or Material Support

Name
Novartis Pharma Services Inc.

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Joseph Kattan	Beirut	Lebanon	03635913	jkattan62@hotmail.com	Hotel Dieu De France
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Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Joseph Kattan	Hematology Oncology	Approved
Bellevue Medical Center	Fadi El Karak	Hematology Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	06/04/2017	Nancy Alam	nancy.alam@usj.edu.lb	+961 (0) 1 421000 ext 2335
Bellevue Medical Center	02/10/2017	Ghassan Maalouf	gmaalouf@bmc.com.lb	+961 (0) 1 682666 ext 7600

Countries of Recruitment

Name
Lebanon
Canada
France
Germany
Hungary
Italy
Netherlands
Norway
Poland
Spain
Taiwan
United States of America
Turkey

Health Conditions or Problems Studied

Condition	Code	Keyword
NSCLC	Bronchus or lung, unspecified (C34.9)	NSCLC

Interventions

Intervention	Description	Keyword
ICF, medical history, demography, radiology, vital signs, IMP administration	ICF, medical history, demography, radiology, vital signs, IMP administration	ICF, medical history, demography, radiology, vital signs, IMP administration

Primary Outcomes

Name	Time Points	Measure
Overall response Rate (ORR)	6 cycles	all patients have completed at least 6 cycles of treatment

Key Secondary Outcomes

Name	Time Points	Measure
•Safety and Tolerability as assessed by incidence and severity of adverse events, dose interruptions, reductions and dose intensity	Continuously	Continuously
•Overall Response Rate (ORR)	every 8 weeks until cycle 11 and then every 12 weeks from the start of study until end of disease progression	every 8 weeks until cycle 11 and then every 12 weeks from the start of study until end of disease progression
•Progression Free Survival (PFS)	every 8 weeks until cycle 11 and then every 12 weeks from the start of study until end of disease progression	every 8 weeks until cycle 11 and then every 12 weeks from the start of study until end of disease progression

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files