A randomized, open-label, phase II open platform study evaluating the efficacy and safety of novel spartalizumab (PDR001) combinations in previously treated unresectable or metastatic melanoma

Published: 23-05-2018
Last updated: 10-01-2025

To evaluate the efficacy of each combination arm, as measured by confirmed objective response rate (ORR)

Ethical review	Approved WMO
Status	Completed
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON55514

Source
ToetsingOnline

Brief title
PLATforM - CPDR001J2201

Condition

- Skin neoplasms malignant and unspecified
- Skin neoplasms malignant and unspecified

Synonym
melanoma, skin cancer

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: zie G2

Intervention

Keyword: melanoma, PDR001, platform

Outcome measures

Primary outcome

Confirmed ORR using RECIST v1.1, per local assessment

Secondary outcome

DoR using RECIST v1.1, per local assessment

PFS and DCR, assessed using RECIST v1.1, per local assessment

Overall survival (OS)

Incidence and severity of AE including changes in laboratory values, vital

signs and cardiac assessment.

Dose interruptions, reductions, and permanent discontinuations of study

treatments

Anti-drug antibodies (ADA) prevalence at baseline and ADA incidence on treatment

Proportion of subjects with a favorable biomarker profile (pFBP)

Study description

Background summary

Melanoma is the most aggressive form of all skin cancers. Worldwide, it is expected that over 232,000 people are diagnosed with cutaneous melanoma each year and more than 55,000 people are expected to die of this disease annually. Usually melanoma is diagnosed at an early stage in which surgical excision is curative in most cases. The management of patients with unresectable or metastatic melanoma is more difficult

Patients who do not respond to, or progress on, the approved treatments have very limited treatment options, and there is no established standard of care. Guidelines recommend enrollment in a clinical trial, treatment with ipilimumab (anti-CTLA-4), chemotherapy, or highdose interleukin-2 (IL-2) for selected patients .

Based on retrospective data from 47 patients treated in the pivotal phase III study KEYNOTE-006, single-agent checkpoint inhibitor therapy with ipilimumab has limited anti-tumor activity following failure of pembrolizumab (anti-PD-1) with a reported objective response rate (ORR) of 16% (Zimmer et al 2017). As a result, most patients are enrolled in clinical studies as there is an urgent need for new treatment options for patients who failed the available standard therapies.

Patients enrolled in this study have failed previous therapies including immune checkpoint inhibitors. The mechanisms of primary and acquired resistance to checkpoint inhibitors treatment are not well understood and are mainly due to a combination of intrinsic or extrinsic resistance mechanisms (see Section 2.1). The combinations tested in this study aim to alter the tumor and/or microenvironment in favorable way to overcome treatment resistance and restore

T cell function.

Study objective

To evaluate the efficacy of each combination arm, as measured by confirmed objective response rate (ORR)

Study design

randomized, open-label, phase II, open platform study with novel treatment combinations

Intervention

All participants will be treated with :
- PDR001 400 mg once every 4 weeks; administered via intravenous infusion over 30 minutes
- one of the treatments as specified in the protocol:

* LAG525 600 mg once every 4 weeks; administered via intravenous infusion over 30 minutes

* INC280 400 mg BID (total daily dose 800 mg), administered orally

* ACZ885 300 mg once every 4 weeks; administrated via subcutaneous injection

* LEE011 600 mg QD on days 1 to 21 of a 28-day cycle, administered orally

Study burden and risks

RISK: adverse events of treatment with PDR001 and INC280, LAG525 or ACZ885
Burden: Cycles of 4 weeks, Cycle 1: 4 visits, cycle 3: 3 visit, cycle 2, and 3,4,5 etc : 1 visit
Physical examination: once per cycle.
Blooddraws :1-2 per visit, One PK days more frequent (C1D15: 6-7 draws)
ECG:during cycle 1 and 3: two ECGs taken in triplicate (thus total 6); once in triplicate (thus 3) duiring C2 and EOT
CT-/MRI-scan: during screening, in week 12, 20, 28, 36, 44 and week 52, from week 52 every 12 weeks,

Brain MRI : once during screening, if applicable following the CT/MRI schema
Skin photographs : if applicable, following the CT/MRI schema

Contacts

Public
Novartis

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Scientific
Novartis

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Male or female must be >= 18 years
- Histologically confirmed unresectable or metastatic stage IIIB/C/D or IV melanoma
- Previously treated for unresectable or metastatic melanoma. Subjects must have at least received the following treatments.
-- V600BRAF wild type patients: must have received anti-PD-1/PD-L1 single-agent, or in combination with anti-CTLA-4 therapy
--V600BRAF mutant patients: must have received prior anti-PD-1/PD-L1 single-agent, or in combination with anti-CTLA-4 therapy. In addition, subjects must have received prior V600BRAF inhibitor therapy, either single-agent or in combination with a MEK inhibitor
-. ECOG performance status 0-2
-. At least one measurable lesion per RECIST v1.1

-. At least one lesion, suitable for sequential mandatory tumor biopsies

on non-randomized arm (1A)
- Subjects must have baseline tumor sample that is positive for LAG-3 per central assessment at the Novartis-designated laboratory

Exclusion criteria

- Presence of clinically active or unstable brain metastasis.
- Active, known or suspected autoimmune disease or a documented history of autoimmune disease.
- Active infection requiring systemic antibiotic therapy., - Known history or current interstitial lung disease or non-infectious pneumonitis
- Known history of testing positive for Human Immunodeficiency Virus (HIV) infection
- Active hepatitis B virus (HBV) infection (HBsAg positive).
- Subjects with positive test for hepatitis C virus (HCV) RNA

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	21-02-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	ILARIS
Generic name:	canakinumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	INC280
Generic name:	capmatinib
Product type:	Medicine
Brand name:	Kisqali
Generic name:	ribociclib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	LAG525
Generic name:	LAG525
Product type:	Medicine
Brand name:	PDR001
Generic name:	spartalizumab

Ethics review

Approved WMO Date:	23-05-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	27-11-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-04-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	28-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	13-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-11-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-12-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	29-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-11-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	16-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-03-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2018-000610-38-NL
ClinicalTrials.gov	NCT03484923
CCMO	NL65729.031.18

Study results

Date completed: 02-07-2021

Results posted: 08-08-2023

First publication
14-06-2023