A Phase 2, multi-center, open label study of NIR178 in combination with PDR001 in patients with selected advanced solid tumors and non-Hodgkin lymphoma (CNIR178X2201)

Published: 02-08-2017
Last updated: 12-04-2024

Primary: • Part 1:To evaluate the efficacy of NIR178 and PDR001 combination in patients with selected advanced solid tumors and diffuse large B cell lymphoma (DLBCL). • Part 2: To assess the efficacy of several intermittent dosing schedules of...

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

Summary

ID

NL-OMON55643

Source
ToetsingOnline

Brief title
CNIR178X2201

Condition

- Other condition
- Lymphomas non-Hodgkin's B-cell
- Respiratory tract neoplasms

Synonym
breast cancer, cancer of head- and neck, Lungcancer, Lymphnode cancer, melanoma, pancreatic cancer, Prostate cancer, Renal Cell Cancer, Solid tumor

Health condition

Neoplasmata, maligne, solide tumoren

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: A2a Receptor, Immunotherapy, NIR178, PDR001

Outcome measures

Primary outcome

• Part 1: Overall Response Rate (ORR)

• Part 2: ORR

• Part 3: ORR.

Secondary outcome

Disease control rate, Duration of response, Progression free survival, 2y

Overall survival rate. Adverse events. Change from baseline in tumor

infiltrating lymphocytes. PK parameters, Antidrug-antibodies.

Study description

Background summary

Combination therapies using multiple inhibitors of immune function can significantly improve response rates. For example, a nivolumab/ipilimumab combination providing blockade of the PD-1 and CTLA-4 immune checkpoints significantly improved responses for patients with advanced melanoma. Expanding the depth, breadth and durability of responses to treatment is now an important focus of clinical oncology research.

NIR178 activates the immune system by blocking the adenosine A2a receptor (A2aR). Two healthy volunteer studies were conducted with NIR178 and there is one ongoing Phase I/Ib trial of NIR178 as single agent and in combination with PDR001 in patients with advanced non-small cell lung cancer. See protocol page 27-28 for details.
PDR001 is an anti-PD-1 antibody that blocks the binding of PD-L1 and PD-L2 to PD-1. In the mean time 11 early phase studies with PDR001 as a monotherapy or in combination are ongoing. As observed with other PD-1 inhibitors, immune-mediated toxicities observed with PDR001 are reversible in many cases. In some cases, they may require treatment with corticosteroids. Certain toxicities are expected to be lifelong and may require replacement therapy with hormones. Based on the preliminary data, PDR001 was well tolerated with a safety profile similar to those of other marketed anti-PD-1 antibodies.
The purpose of this phase 2 study is to evaluate the efficacy and safety of NIR178 in combination with PDR001 in multiple solid tumors and diffuse large B-cell lymphoma (DLBCL) and further explore schedule variations of NIR178 to optimize immune activation through inhibition of A2aR.
The study has three parts:
• Part 1: Multi-arm Bayesian adaptive signal finding design in 7 types of solid tumors and non-Hodgkin lymphoma.
• Part 2: NIR178 schedule exploration in NSCLC.
• Part 3: Further evaluation of intermittent dosing schedules of NIR178 in combination with PDR001 in TNBC and one additional tumor types, if part 2 identifies an intermittent dosing schedule of NIR178 as warranting further exploration.

Study objective

Primary:
• Part 1:To evaluate the efficacy of NIR178 and PDR001 combination in patients with selected advanced solid tumors and diffuse large B cell lymphoma (DLBCL).
• Part 2: To assess the efficacy of several intermittent dosing schedules of NIR178 in combination with PDR001 in NSCLC.
• Part 3: To evaluate efficacy of intermittent dosing schedule of NIR178 in TNBC and another tumor type. This additional tumor type will be selected based on the emerging data from part 1 and may only begin enrollment following implementation via formal protocol amendment.
Secondary:
Efficacy of NIR178 plus PDR001 in selected advanced solid tumors and lymphoma, safety and tolerability of the combination, changes in the immune infiltrate in tumors, pharmacokinetics (PK), immunogenicity of PDR001.

Study design

Multi-center, open label, phase 2 study to evaluate efficacy of the NIR178 and PDR001 combination in solid tumors and non-Hodgkin lymphoma.

The study has three parts:
• Part 1: Multi-arm Bayesian adaptive signal finding design in 7 types of solid tumors and non-Hodgkin lymphoma.
• Part 2: NIR178 schedule exploration in NSCLC.
• Part 3: Further evaluation of intermittent dosing schedules of NIR178 in combination with PDR001 in TNBC and one additional tumor types, if part 2 identifies an intermittent dosing schedule of NIR178 as warranting further exploration.
Patients will receive NIR178 160 mg either BID continuously or based on the assigned intermittent schedule within 60 minutes prior to PDR001 infusion.
PDR001 will be administered via IV infusion over 30 minutes once every 4 weeks.
Treatment cycles of 4 weeks.
Treatment until disease progression or unacceptable toxicity.
Patient numbers: Part 1: n=80-240 (depending on treatment effects in the various disease groups. Part 2: n=60. Part 3: n=40.

Intervention

Treatment with NIR178 in combination with PDR001.

Study burden and risks

Risk: Adverse effects of the combination of NIR178 plus PDR00 and risks associates with the assessments.
Burden: Cycles of 4 weeks. 6 visits during cycle 1, 2 during cycles 2-3 and 1 during every cycle thereafter. Visit duration mostly 1-4 hours.
IV infusions of PDR001 on day 1 of every cycle. Infusions of 250 mL. Duration of PDR001 infusion standard 0,5 hour (up to 2 hours is accepted).
Physical examination: day 1 (and 15 during cycle 1) of every cycle, screening, end of treatment.
Blood tests (10-30 mL/occasion):
• Safety tests: 2 times during cycle 1-3, once during every cycle thereafter, screening, once during follow-up.
• PK: 6 visits during cycle 1, 2 visits during cycle 3, once during cycles 4, 5, 6. 2 visits with 9 serial blood draws. Approx. 190 mL in total).
• Biomarkers: 4 times. Approx. 80 mL in total.
ECG: once (twice during cycle 1) during every cycle, screening, end of treatment.
CT-/MRI scan: every 8-12 weeks.
Bone marrow aspiration/biopsy (lymphoma patients only): once.
3 tumor biopsies (1st might be replaced by recent archival material).
Optional: tumor biopsy at disease progression.
Optional use of the remaining blood and tissue for future research.

Contacts

Public
Novartis

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Males and females >=18 years of age.
• Histologically documented advanced or metastatic solid tumors or lymphoma.
- Part 1: histologically confirmed advanced or metastatic renal cell carcinoma, pancreatic cancer, urothelial cancer, head and neck cancer, non-Hodgkin lymphoma, microsatellite stable or mismatch repair colorectal cancer, triple negative breast cancer or cutaneous melanoma (confirmed BRAF V660E status) or mCRPC
- Part 2: histologically confirmed advanced or metastatic NSCLC (EGFR and ALK genotype).
- Part 3: histologically confirmed advanced or metastatic TNBC
• Tumor amenable to biopsy. See protocol page 52 for details.
• Part 1 - 3 only: Patients (other than those with DLBCL) must previously have

received at
least 1 and no more than 3 prior lines of therapy for their disease.

• No prior immunotherapy, except for cutaneous melanoma, I/O pre-treated head/neck ca, and TNBC patients enrolled in part 3. An additional tumor type might be added based on data.
• Measurable disease.
• ECOG performance status 0, 1, 2.
Refer to section Protocol section 5.2 for more detailed information regarding prior therapy per tumor type

Exclusion criteria

• History of another primary malignancy. .
• Active or prior documented autoimmune disease within the past 2 years.
• History of interstitial lung disease or non-infectious pneumonitis.
• Ongoing or prior treatment with A2aR inhibitors. Patients previously treated with A2aR inhibitors for non-oncologic indications may be considered for enrollment on a case by case basis.
• More than 2 or 3 prior lines of therapy (depending on the tumor type)
• Clinical laboratory abnormalities (within 21 days before 1st dose): Absolute neutrophil count <1.0 x 109/L - Platelet count <100 x 109/L (for lymphoma <75 x 109/L , Hemoglobin (Hgb) <9 g/dL (5,59 mmol/l), Creatinine > 1. x upper limit of normal (ULN) - Total bilirubin >1.5 x ULN - ALT and AST (liver) >3 x ULN
• History or current cardiac disease indicating significant risk of safety such as uncontrolled cardiac disease (see criterion 29 protocol section 5.3)
• Mean QTcF >470 ms.
• Current or prior use of immunosuppressive medication within 28 days before the first dose of PDR001.
•Smoking must be discontinued at least 7 days prior to initiating study drug administration; smoking cessation products may be used.
For more details see protocol section 5.3

Study design

Design

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

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2017
Enrollment:	18
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	02-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	23-10-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	12-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	19-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-01-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-05-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	09-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-08-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-07-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2022
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	EUCTR2017-000241-49-NL
ClinicalTrials.gov	NCT03207867
CCMO	NL62490.056.17