A Phase Ib, open label, multicenter study of the safety and efficacy of MIW815 (ADU-S100) administered by intratumoral injection with PDR001 to patients with advanced/metastatic solid tumors or lymphomas

Published: 02-11-2017
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Primary: To characterize safety and tolerability of MIW815 (ADU-S100) given with PDR001 and identify recommended doses and schedule for future studies.Secondary: Anti-tumor activity. Pharmacodynamics (PD). Pharmacokinetics (PK).

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

Summary

ID

NL-OMON48864

Source
ToetsingOnline

Brief title
MIW815 (ADU-S100) intratumoral injection with PDR001 (CMIW815X2102J)

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Solid tumors and lymphoma (lymph tissue cancer)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: intratumoral injection, MIW815 (ADU-S100), PDR001

Outcome measures

Primary outcome

Iincidence and severity of (serious) adverse events, including changs in

laboratory parameters, vital signs, ECGs, incidence of DLT during the 1st

cycle.

Secondary outcome

Overall response rate, progression free survival, duration of response, disease

control rate, PK parameters. Antidrug antibodies. Tumor Infiltrating

lymphocytes in (non-)injected lesions.

Study description

Background summary

The recent development of agents that enhance anti-tumor immunity is rapidly changing the treatment of cancer. Inhibitors of the PD-1/PD-L1 interaction, like PDR001, are well tolerated and active across a remarkable range of cancer types. However, they are not efficacious in all tumors or all patients and exploration of combinations are warranted. STING agonists have the potential to augment, initiate, or awaken the initial anti-cancer response.
Pre-clinical data demonstrated significant enhanced local and distal anti-tumor activity following intratumoral administration of MIW815 (ADU-S100). Local and systemic anti-tumor efficacy required activation of STING-responsive cells in the tumor microenvironment, as SC injection in sites distal from tumor masses

was not effective.
This is a Phase Ib study with the primary aim to determine if PDR001 can be safely combined with MIW815 (ADU-S100) and to identify the doses and schedule appropriate for further study.

Study objective

Primary:
To characterize safety and tolerability of MIW815 (ADU-S100) given with PDR001 and identify recommended doses and schedule for future studies.

Secondary:
Anti-tumor activity. Pharmacodynamics (PD). Pharmacokinetics (PK).

Study design

Phase Ib, multi-center, open-label dose escalation and dose expansion study of MIW815 in combination with PDR001.
Two different dosing schedules of MIW815 (cycles of 4 weeks)
1. Intratumoral injections on day 1, 8 and 15 of each cycle plus 400 mg PDR001 IV on day 1 of each cycle.
2. Intratumoral injections on day 1 of each cycle plus 400 mg PDR001 IV on day 1 of each cycle.
will be explored in groups with accessible cutaneous or subcutaneous lesions.

A dose confirmation group (fixed dose) will explore intratumoral injection of viscerally located lesions at a later stage during the study if biological activity is seen in the 2nd dosing group (once per 4 weeks). If biological activity is seen in the dose confirmation group, a dose expansion group will be opened for visceral lesions.
Approx.140 subjects (40 dose escalation part, 100 expansion part).

Intervention

MIW815 (intra tumoral) - increasing dose. 2 schedules
A) day 1-8 and 15 in a 4-week cycle
B) day 1 in a 4-week cycle

PDR001: fixed dose every 4 weeks, administered intravenously in 100ml glucose

Study burden and risks

Risk: Adverse effects of MIW815 in combination with PDR001.
Burden: Cycles of 4 weeks. 3 visits per cycle.
MIW815: 3 or 1 intratumoral injection(s) 0,5-4,0 mL per cycle.

PDR001: 1 infusion (250 mL) per cycle.
Physical examination: once per cycle.
Blood tests (20-70 mL/occasion): 1st day of every cycle (cycle 1-2: 3 times).
Urine testing: once.
Pregnancy test: every cycle and every month during safety follow-up.
ECG: 4 times.
Tumor measurements: baseline, cycle 3 and every 8 weeks thereafter up to cycle 11 and every 3rd cycle thereafter. During follow up for progression every 8-12 weeks.
Tumor biopsy: twice.
Risks related to assessments as blood draw, infusion, imaging

Contacts

Public
Novartis

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NL
Scientific
Novartis

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male and female *18 years of age.
2. Measurable disease as determined by RECIST v1.1 (for solid tumors) or Cheson 2014 criteria (for lymphoma).
3. At least two sites of disease amenable to biopsy, and willing to undergo new tumor biopsy at screening and during therapy. See protocol page 30-31 for details.
4. Dose escalation part: Advanced/metastatic solid tumors or lymphomas that have progressed despite standard therapy or where standard therapy is not tolerated, for whom no standard therapy exists or for whom standard therapy is not reasonably effective.
5. Dose expansion part: Melanoma patients with accessible cutaneous or subcutaneous lesions, who have relapsed or progressed after responding to a PD-1 inhibitor or who are refractory to PD-1 Inhibitors, HNSCC or patients with other accessible cutaneous or subcutaneous solid tumors and lymphomas, that have progressed despite standard therapy or are intolerant of standard therapy, for whom no standard therapy exists or for whom standard therapy is not reasonably effective. In addition, patients with injectable visceral lesions who have MSS CRC or other solid tumors with accessible visceral lesions, who have progressed despite standard therapy or are intolerant of standard therapy, for whom no standard therapy exists or for whom standard therapy is not reasonably effective.
6. ECOG performance status 0-1

Exclusion criteria

1. Patients who require immediate local palliative measures such as XRT or surgery.
2. Symptomatic or untreated leptomeningeal disease.
3. Symptomatic -CNS metastases, see protocol page 31 for details.
4. Laboratory abnormalities:
- Creatinine > 1.5 x upper limit of normal (ULN)
- Total bilirubin > 1.5 x ULN (except for Gilbert*s syndrome > 3.0 x ULN)
- ALT and AST (liver) > 3 x ULN (except when livermetastasis > 5 x ULN_
- Absolute neutrophil count < 1.0 x 109/L
- Platelet count < 75 x 109/L, except for patients in Group C: platelet count < 100 x 109/L
- INR > 1.5 x ULN and/or aPTT > 1.5 x ULN, except for patients in Group C: INR and aPTT must be normal
- Hemoglobin (Hgb) < 9 g/dL (5,59 mmol/l)
- Potassium, magnesium, calcium or phosphate > grade 1 using CTCAE v4.03
5. Impaired cardiac function or clinically significant cardiac disease, see protocol page 42 for details.

6. Active, known or suspected autoimmune disease or a documented history of autoimmune disease, see protocol page 43 for details.
7. Active infection requiring systemic antibiotic therapy.
8. Cytotoxic or targeted antineoplastics within 14 days prior to the first dose of study treatment, see protocol page 43 for details.
9. Systemic chronic steroid therapy (* 10mg/day prednisone or equivalent) or any immunosuppressive therapy 7 days prior to start of study treatment.
10. Use of any live vaccines against infectious diseases within 4 weeks of initiation of study treatment.
11. Use of G-CSF and comparable, see protocol page 43/44 for details.

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):	16-08-2018
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Niet van toepassing
Generic name:	Niet van toepassing

Ethics review

Approved WMO

Date:	02-11-2017

Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-11-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-11-2017
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-11-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-12-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	16-02-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-06-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-07-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-08-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-11-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-11-2018
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	31-01-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-03-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-07-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-01-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	23-04-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-05-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-05-2020
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	EUCTR2017-000707-25-NL
ClinicalTrials.gov	NCT03172936
CCMO	NL61921.031.17