# An open label phase II study to evaluate the efficacy and safety of PDR001 in patients with well-differentiated advanced or metastatic non-functional neuroendocrine tumors of pancreatic, gastrointestinal (GI), or thoracic origin or poorly-differentiated gasteroenteropancreatic neuroendocrine carcinoma (GEP-NEC) who have progressed on prior treatment (CPDR001E2201)

Published: 09-01-2017
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Primary: To estimate the antitumor activity (assessed as overall response rate) of PDR001 as a single agent in patients with non-functional neuro-endocrine tumors (NET).Secondary: To estimate efficacy (duration of response) of PDR001. Safety and...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Malignant and unspecified neoplasms gastrointestinal NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON46949

**Source**
ToetsingOnline

**Brief title**
PDR001E2201. Phase II study of PDR001 in NET patients

## Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Endocrine neoplasms malignant and unspecified
- Respiratory tract neoplasms

**Synonym**
Neuroendocrin tumours of GI, pancreas and thorax origin

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** Neuro-endocrine tumors, Non-functional, PDR001

## Outcome measures

### Primary outcome

Overall response rate.

### Secondary outcome

Duration of response. Adverse events, additional efficacy parameters per

Resist, CgA and NSE, PK parameters, quality of life, immunogenicity.

# 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. In the mean time 11 early phase studies with PDR001 as a monotherapy or in combination with LAG525 (an anti-LAG3 antibody) are ongoing. By the end of March 2016, a total of 58 patients had been treated in the first in human study. No patient experienced a dose limiting toxicity and

the toxicity profile appears to be similar to that of marketed inhibitors of PD-1. The PK data support the use of flat dosing for PDR001 of 400 mg every 4 weeks for monotherapy studies.
Inhibitors of the PD-1/PD-L1 interaction are well tolerated and active across a range of cancer types.
In this phase II study the safety and efficacy of PDR001 will be assessed in neuro-endocrine tumors in the pancreas, GI-tract and chest.

## Study objective

Primary:
To estimate the antitumor activity (assessed as overall response rate) of PDR001 as a single agent in patients with non-functional neuro-endocrine tumors (NET).
Secondary:
To estimate efficacy (duration of response) of PDR001. Safety and tolerability, additional efficacy

## Study design

Multicenter phase II open-label non-comparative study.
PDR001 intravenous infusion 400 mg in 30 minutes (if indicated up to 2 hours) every 4 weeks.
The study treatment will be administered in cycles of 4 weeks.
Treatment until disease progression or unacceptable adverse reaction. Maximum duration of treatment 2 years.
Approx. 90 subjects. 3 cohorts of approx. 30 subjects (based on location of the primary tumor).

## Intervention

Treatment with PDR001.

## Study burden and risks

Risk: Adverse effects of PDR001.
Burden: Cycles of 4 weeks. Visits on day 1 of every cycle. Visit duration mostly 1-4 hours.
IV infusions of PDR001 on day 1 of every cycle (250 ml per occasion). Duration standard 0,5 hour (up to 2 hours is accepted).
Physical examination: once per cycle.
Blood tests (15ml/occasion): once per cycle.
Blood for biomarkers: 120 ml in total, PK 40 ml in total, immunogenicity 60 ml in total
ECG: every 12 weeks.
CT-/MRI scan: every 8-12 weeks.

Questionnaires EORTC QLQ-C30 and EQ-5D every 8-12 weeks.
Archival tumor tissue (if needed new biopsy).
Optional tumor biopsies during treatment and at disease progression.
Optional use of the remaining blood and tissue for future research.

# Contacts

**Public**
Novartis

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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

* Female and male patients * 18 years old.
* Pathologically confirmed, advanced (unresectable or metastatic):
- well-differentiated (G1 or G2) unresectable or metastatic non-functional neuroendocrine tumor of GI, pancreatic or thoracic (including lung and thymus) origin.
- poorly differentiated GEP-NEC based on local pathology report
* No active symptoms related to carcinoid syndrome during the last 3 months prior to start

* Criteria for the 4 cohorts (based on location of primary tumor): see protocol, page 35.
* Radiological documentation of disease progression while on/or after the last treatment, see protocol page 35/36 for details.
* At least one measurable lesion assessed by CT and/or MRI according to RECIST 1.1.
* ECOG performance status 0-1-2.
* Adequate contraception.
* Tumor biopsy material mist be provided for all patients for the purpose of biomarker analysis:
- well-differentiated (G1/2) NET: collected from the metastic site, not previously irradiated, preferably be taken within 6 months but not more than 24 months prior start study treatment
- poorly differentiated GEP-NEC: collected from the primary tumor of from metastartic site, not previously irradiated, taken not more tha 24 months prior start study treatment
Update Am2:
- life expectancy of at least 3 months

### Exclusion criteria

* Well differentiated grade 3 neuro-endocrine tumors; poorly differentiated neuro-endocrine carcinoma of any origin (other than GEP-NEC); including NEC of unknown origin, adenocarcinoid, goblet cell carcinoid, large cell neuro-endocrine carcinoma and small cell carcinoma.
* Pretreatment with interferon as last treatment prior to start of study treatment.
* Prior treatment for study indication with antibodies or immunotherapy, PRRT, systemische antineoplastic therapy, TKIs, PD-1 or PD-L1 directed therapy. Cryoablation, radiofrequency ablation, or trans-arterial chemo-embolization of hepatic metastases. See for details and washout periods protocol page 37.
* History of severe hypersensitivity reactions to other monoclonal antibodies which in the opinion of the investigator may pose an increased risk of a serious infusion reaction.
* Pregnancy, lactation, insufficient contraception for females of childbearing potential.
* Autoimmune disease that has required systemic treatment. Stable and adequate controlled endocrinopathies requiering replacement therapy are not considered as systemic treatment and therefore are allowed.
* Known history or current interstitial lung disease or nonb-infections pneumonitis
* Use of somatostatin analogs or any other medications administered to control active symtoms related to carcinoid syndrome during the last 3 months prior to start of study treatment

## Study design

### Design

Study phase: 2

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 19-07-2017 |
| Enrollment: | 4 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | PDR001 |
| Generic name: | PDR001 |

## Ethics review

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| Approved WMO Date: | 09-01-2017 |
| Application type: | First submission |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 13-04-2017 |
| Application type: | First submission |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 09-05-2017 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 19-06-2017 |

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| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 05-07-2017 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 13-12-2017 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 20-12-2017 |
| 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: | 22-02-2018 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 15-03-2018 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 06-07-2018 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |

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| Approved WMO Date: | 29-10-2018 |
| 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 | EUCTR2016-002522-36-NL |
| ClinicalTrials.gov | NCT02355069 |
| CCMO | NL60098.031.16 |