A phase II, multicenter, open-label study of EGF816 in combination with Nivolumab in adult patients with EGFR mutated non-small cell lung cancer and of INC280 in combination with Nivolumab in adult patients with cMet positive non-small cell lung cancer (CEGF816X2201C)

Published: 23-02-2015
Last updated: 21-04-2024

Primary: To assess 6 month PFS rate of Nivolumab in combination with EGF816 in EGFR mutated NSCLC patients and of Nivolumab in combination with INC280 in patients with cMET positive NSCLC patientsSecondary: 1: To assess clinical activity of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms benign (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON44688

Source
ToetsingOnline

Brief title
CEGF816X2201C

Condition

- Breast neoplasms benign (incl nipple)
- Respiratory tract neoplasms

Synonym

1 - A phase II, multicenter, open-label study of EGF816 in combination with Nivoluma ... 24-05-2025

non-small cell lung cancer (NSCLC); lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis Pharma B.V.
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: EGF816, INC280, Nivolumab, NSCLC

Outcome measures

Primary outcome

Progression free survival 6 months.

Secondary outcome

Other progression free survivals, overall response rate, disease control rate

and overall survival. Adverse events.

Study description

Background summary

Currently approved epidermal growth factor receptor tyrosine-kinase inhibitors (EGFR TKI) are effective in activated EGFR mutant non-small cell lung cancer (NSCLC), however nearly all patients develop resistance. cMET positive NSCLC patients progressing on chemotherapy fair prognostically worse than their non-cMET positive counterparts. Harnessing the immune system to treat patients with NSCLC represents a novel and exciting new treatment approach. The anti-PD-1 antibody Nivolumab has demonstrated response rates of up to 20% in patients with NSCLC and has been safely combined with several small molecules as well as chemotherapies.
In order to explore the hypothesis that concurrent treatment with an immune checkpoint inhibitor along with a targeted therapy is safe and may result in durable and sustained responses, Nivolumab will be combined with either the third generation EGFR TKI, EGF816, in EGFR T790M NSCLC patients who have developed resistance to EGFR TKI treatment or with the highly selective and potent c-MET inhibitor, INC280, in cMET positive (EGFR wild type) patients who

progressed on chemotherapy.

Study objective

Primary: To assess 6 month PFS rate of Nivolumab in combination with EGF816 in EGFR mutated NSCLC patients and of Nivolumab in combination with INC280 in patients with cMET positive NSCLC patients
Secondary: 1: To assess clinical activity of Nivolumab in combination with EGF816 and of Nivolumab in combination with INC280 as measured by other progression free survivals, overall response rate, disease control rate and overall survival. 2: To characterize the safety and tolerability of Nivolumab in combination with EGF816 and of Nivolumab in combination with INC280.

Study design

Multicenter phase II open-label study, with a safety monitoring cohort.
Study treatments:
* Nivolumab IV infusion every 2 weeks (3 mg/kg) plus EGF816 capsules once daily 150 mg.
* Nivolumab IV infusion every 2 weeks (3 mg/kg) plus INC280 capsules twice daily 400 mg.
Treatment until disease progression or unacceptable side effects. Patients who discontinue study treatment for any reason other than disease progression will be followed up for progression of disease and all patients will be followed for survival.
Approx. 100 patients (50 per treatment group).
Safety monitoring cohorts of 6-12 patients per treatment group with more intense monitoring.

Intervention

Treatment with nivolumab in combination with EGF816 or INC280.

Study burden and risks

Risk: Adverse effects of the combination of study drugs.
Burden: Cycles of 4 weeks. Cycle 1: 5 visits, cycle 2; 4 visits, from cycle 3 onwards: 2 visits. Duration mostly 1-4 hours. Some visits up to 8 hours.
2 infusions with nivolumab per cycle (approx. 200 ml).
Physical examination: cycle 1-2: 3 times, from cycle 3 onwards once/cycle.
Blood tests (5-40 ml/occasion): every visit.
Pulse oximetry: twice/cycle.
Pregnancy test: screening, once/cycle, 30 days after trial in blood. Up to 5 maanden after treatment in urine (possibly at home)
Tumor measurements: every 8 weeks for the 1st 12 cycles, every 12 weeks thereafter.

ECG: cycle 1: twice, from cycle 2 onwards once/cycle.
Tumorbiopsie: once and once optional.

Contacts

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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 of age.
* Advanced metastatic and/or unresectable NSCLC.
* Measurable disease.
* Group 1: confirmed T790M EGFR mutation.
* Group 2: confirmed c-MET positive.
* ECOG performance status 0, 1, 2.

Exclusion criteria

* Group 1: More than one prior line of EGFR TKI therapy.
* Group 2: Previous treatment with a c-MET inhibitor or HGFtargeting therapy.
* Prior treatment with PD1/PD-L1 targeting therapies.
* Patients who require emergent use of systemic steroids, emergent surgery and/or radiotherapy.
* Interstitial lung disease.
* Any active or history of autoimmune disease, hepatitis B virus or hepatitis C virus
* Prohibited co-medication: see protocol page 46.
* Pregnancy, lactation, inadequate contraception (males and females). See protocol page 30-31 for details.
* Group 2: GI impariment resulting in altered absorption of INC280

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2015
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	capmatinib
Generic name:	capmatinib
Product type:	Medicine

Brand name:	EGF816
Generic name:	EGF816
Product type:	Medicine
Brand name:	Opdivo
Generic name:	nivolumab

Ethics review

Approved WMO Date:	23-02-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-04-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-05-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-08-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-08-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-10-2015
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-11-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	20-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	25-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-09-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-10-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-02-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-07-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-03-2018

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-05-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-06-2018
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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2014□003731□20-NL
CCMO	NL51874.031.14