A phase II, multicenter, study of oral cMET inhibitor INC280 in adult patients with EGFR wild-type (wt), advanced nonsmall cell lung cancer (NSCLC) (CINC280A2201)

Published: 19-05-2015
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Primary: To evaluate the antitumor activity of INC280, as measured by overall response rate (ORR) as by a blinded independent review committee, by cohort.Secondary: Duration of response (DOR), ORR and DOR by investigator, time to response (TTR),...

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

Summary

ID

NL-OMON54800

Source
ToetsingOnline

Brief title
CINC280A2201 - GeoMETry Mono1

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
lung cancer; non-small cell lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: capmatinib, cMET, INC280, NSCLC

Outcome measures

Primary outcome

ORR by blinded independent review committee.

Secondary outcome

DOR, ORR and DOR by investigator, TTR, DCTR, PFS, OS, adverse events, PK

parameters.

Study description

Background summary

cMET dysregulation (amplification, overexpression, mutation) constitutes an oncogenic driver in several tumor types, including lung cancer. Currently, there is no approved therapy for tumors with cMET dysregulations and therefore there is a high unmet medical need to develop therapy capable of cMET inhibition for the treatment of these tumors.
INC280 is a highly potent and selective cMET inhibitor in biochemical and cellular assays and capable of blocking cMET activation. Overall, the emerging preclinical and clinical data suggest that INC280 may have a favorable benefit-risk ratio for the treatment of cMET dysregulated advanced lung cancer.
The primary objective of this study is to evaluate the antitumor activity of INC280 in patients with EGFR wild-type, advanced non-small cell lung cancer (NSCLC). The primary measure overall response rate as determined by a blinded independent review committee.

Study objective

Primary:
To evaluate the antitumor activity of INC280, as measured by overall response rate (ORR) as by a blinded independent review committee, by cohort.

Secondary:
Duration of response (DOR), ORR and DOR by investigator, time to response (TTR), disease control rate (DCTR), progression free survival (PFS), overall survival (OS), safety and tolerability, PK profile.

Study design

Multicenter phase II open-label 5 cohort study of INC280 monotherapy (800 mg twice daily, tablets).
Prescreening for cMET mutation and amplification. Cohorts based on cMET mutation / amplification status.
Treatment period until disease progression or unacceptable side effects.
Approx. 456 patients (69 per cohort 1a, 1b, 2, 3, 4 and 27 per cohort 5a, 5b and 7 and 30 in cohort 6).

Intervention

Treatment with INC280.

Study burden and risks

Risk: Adverse effects of INC280.
Burden: Cycles of 3 weeks. Cycle 1: 2 visits, cycle 2 onwards 1 visit. Duration mostly 2-4 hours.
Physical examination: Once per cycle.
Blood tests (5-35 ml/occasion): Once per cycle.
ECG: 5 visits in total (up to 5 ECGs per visit).
CT-/MRI-scan: every 6 weeks.
Questionnaires (EQ-5D-4L, QLQ-C30, LC13): every 6 weeks
Optional tumor biopsies: maximum of 3 and optional 20 mL blood for biomarkers.
Optional storage and 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

• Female and male patients >= 18 years of age.
• Stage IIIB or IV NSCLC.
• Histologically or cytologically confirmed diagnosis of NSCLC (see protocol page 42 for details):
• EGFR wild-type.
• ALK-negative rearrangement.
• Pre-treated Patients with cMET GCN>=6 and <10 (cohort 1a), Patients with cMET GCN>=10 (cohort 1b), GCN>=4 and <6 (cohort 2), GCN<4 (cohort 3), cMET mutations (cohort 4). Treatment naive patients with cMET GCN >= 10 (cohort 5a), cMET mutations (cohort 5b), Pre-treated patients (1 treatment line) with either cMET GCN >= 10 without cMET mutations or cMET mutations regardless of cMET GCN (cohort 6 = expansion group). Treatment naive patients with cMET mutations, regardless of cMET GCN (Cohort 7 = expansion group)
• For cohort 1-4 patients must have received one or two prior lines of systemic therapy for advanced/metastatic disease (stage IIIB or IV NSCLC). For cohort 5 patients must have received no prior lines of systemic therapy for advanced/metastatic disease (stage IIIB or IV NSCLC). See protocol page 42 for details.
• Measurable disease. See protocol page 42 for details.
• ECOG performance status 0-1.

Exclusion criteria

• Prior treatment with crizotinib, or any other cMET or HGF inhibitor.

• Characterized EGFR mutations that predict sensitivity to EGFR therapy.
• Characterized ALK-positive rearrangement.
• Symptomatic CNS metastases who are neurologically unstable or have required increasing doses of steroids within the 2 weeks prior to study entry.
• Clinically significant, uncontrolled heart diseases. See protocol page 44 for details.
• Thoracic radiotherapy to lung fields <= 4 weeks prior to starting INC280. For all other anatomic sites, radiotherapy <= 2 weeks prior to starting INC280. Palliative radiotherapy for bone lesions <= 2 weeks prior to starting INC280 is allowed. See protocol page 44 for details.
• Major surgery within 4 weeks prior to starting INC280. See protocol page 44 for details.
• Strong and moderate inhibitors of CYP3A4, strong inducers of CYP3A4, proton pump inhibitors.
• Unstable or increasing doses of corticosteroids, enzyme-inducing anticonvulsant. See protocol page 45 for details)
• Pregnancy, lactation, insufficient contraception for females of childbearing potential.
• Sexually active males unless they use a condom during intercourse.

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):	11-06-2015
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Capmatinib
Generic name:	Capmatinib

Ethics review

Approved WMO Date:	19-05-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-10-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	14-04-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-12-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	16-04-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-09-2019

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-02-2023
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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2014□003850□15-NL
CCMO	NL52842.056.15