A Phase IB/II, open label, multicenter study of INC280 administered orally in combination with gefitinib in adult patients with EGFR mutated, c-MET-amplified non-small cell lung cancer who have progressed after EGFR inhibitor treatment (CINC280X2202)

Published: 27-11-2014
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Primary objectives: 1) Phase Ib: To estimate the MTD or RP2D of INC280 in combination with gefitinib in NSCLC patients who have c-MET dysregulation. 2) Phase II: To estimate overall clinical activity of INC280 in combination with gefitinib in NSCLC...

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

Summary

ID

NL-OMON41765

Source
ToetsingOnline

Brief title
CINC280X2202

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
non-small cell lung cancer; lung cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: c-MET dysregulation, EGFR mutation, gefitinib, INC280

Outcome measures

Primary outcome

Dose-escalation: DLTs in 1st cycle.

Expansion: AEs.

Secondary outcome

Tumor response assessment as per RECIST v1.1. PK. Biomarkers in tumor tissue.

Study description

Background summary

c-MET amplification is a frequent molecular event that had been identified as a cause for acquired resistance to gefitinib and other epidermal growth factor receptor inhibitors (EGFRi) in EGFR mutated non small cell lung cancer (NSCLC). Nevertheless, patients may continue to derive benefit from EGFRi after disease progression through continuing inhibition of the EGFR pathway as reflected in the National Comprehensive Cancer Network (NCCN) Guidelines. In order to inhibit both aberrant pathways that drive EGFRi-resistant EGFR mutated NSCLC in the subset of cases with c-MET dysregulation, INC280 requires combination with the continued EGFRi treatment.
INC280 in a new anti-cancer drug in development and possesses potent inhibitory activity against the c-MET kinase.
Gefitinib (Iressa) is a potent and selective inhibitor of the EGFR tyrosine kinase, registered for the treatment of metastatic NSCLC..
Consequently, the purpose of this study will be to first investigate the safety and tolerability of INC280 in combination with gefitinib in a phase IB dose escalation part of the study at a constant dose of gefitinib as per its

prescribing information with increasing dose levels of INC280. Once the MTD/RP2D (recommended phase II dose) for the combination is established, this study will move on to a phase II part in order to investigate the clinical activity of the INC280/gefitinib combination in patients who progressed on gefitinib or erlotinib treatment. The phase II study is designed to be hypothesis generating for the design of a potential pivotal trial in this patient population.

Study objective

Primary objectives: 1) Phase Ib: To estimate the MTD or RP2D of INC280 in combination with gefitinib in NSCLC patients who have c-MET dysregulation. 2) Phase II: To estimate overall clinical activity of INC280 in combination with gefitinib in NSCLC patients with c-MET dysregulation.
Secondary objectives: 1) To determine safety and tolerability of INC280 in combination with gefitinib. 2) To estimate time dependent clinical activity of INC280 in combination with gefitinib. 3) To assess the pharmacodynamic effect of INC280 in combination with gefitinib. 4) To characterize the PK profile of INC280 and gefitinib in NSCLC patient population and to assess potential drug interaction between INC280 and gefitinib.

Study design

Open-label phase IB /II dose escalation and dose expansion study. Approximately 258 patients. Minimal 18 patients in the escaltion. 40 patients in the capsule cohort and 200 patients in the tablet cohort.
Screening for EGFR mutation and c-MET pathway dysregulation.
Determination of the MTD/RP2D of INC280 in combination with gefitinib 250 mg QD. At least 18 patients. Cycles of 4 weeks. Dose-escalation decision after 1 cycle.
After the MTD/RP2D been determined, patients will be enrolled to be treated with this dose.
Treatment until progression or unacceptable toxicity.

Intervention

Treatment with INC280 and gefltinib.

Study burden and risks

Risk: Adverse events of study medication.
Burden:
Cycles of 4 weeks.
Prescreening: tumor sample (either archival or fresh) for C-MET and EGFR status.
Screening visit, 4 visits during cycle 1 and 2. Thereafter 1 visit per cycle.
Duration 1,5-2 h. 1 visit with duration of 6-8 h (PK samples). 2 end of

treatment/study visits. Follow-up for survival (every 3 months).
Blood tests 10-20 ml/occasion.
Screening: Physical examination, blood tests, pregnancy test, ECG, tumor measurements, tumor biopsy.
Cycle 1: 4 times physical examination, 4 times blood tests, 3 times ECG, 1 tumor biopsy.
Cycle 2: 4 times physical examination, 4 times blood tests
Following courses: 1 physical examination, 1 blood draw, tumor measurements every 8 weeks.
End of treatment visit: Physical examination, blood tests, pregnancy test, ECG, tumor measurements (unless performed <30 days).
Pregnancy test every cycle.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* * 18 years of age.
* Confirmed c-MET pathway dysregulation (see protocol page 35-36 for details).
* EGFR mutated NSCLC patient who have developed acquired resistance to EGFR inhibitor treatment (see protocol page 35 for details).
* Must have discontinued any previous anti-cancer and investigational therapy (excluding gefitinib or erlotinib) for at least 28 days before study treatment administration.
* No more than 2 lines of chemotherapy and one line of gefitinib or erlotinib treatment.
* Must have discontinued any previous anti-cancer antibody treatment for at least 4 weeks before study treatment administration.
* Measurable disease as determined by RECIST version 1.1.
* ECOG performance status *2.

Exclusion criteria

* Previous treatment with a c-MET inhibitor or HGF-targeting therapy.
* Previous radiation therapy completed less than 4 weeks prior to dosing.
* History of cystic fibrosis.
* History of acute or chronic pancreatitis, surgery of pancreas or any risk factors that may increase the risk of pancreatitis.
* Pregnancy, breast feeding.
* Women of child-bearing potential not willing to use highly effective contraception.
* Sexually active males must use a condom during intercourse and should not father a child in the study period.

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):	05-04-2012
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	INC280
Generic name:	INC280
Product type:	Medicine
Brand name:	Iressa
Generic name:	gefitinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-05-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-07-2015
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-05-2016
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-03-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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; NCT01610336
EudraCT	EUCTR2011-002569-39-NL
CCMO	NL50563.042.14