A phase II study of erlotinib and sorafenib in patients with locally advanced and/or metastatic (stage IIIB or IV) Non-Small cell lung cancer (NSCLC) who have not received prior chemotherapy

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Primary:•Efficacy of combination of erlotinib and sorafenib as determined by the rate of no progression at 6 weeks.•Determination of the impact of concomitant administration of sorafenib on the pharmacokinetics (PK) of erlotinibSecondary:•Efficacy...

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

Summary

ID

NL-OMON31390

Source
ToetsingOnline

Brief title
phase II erlotinib-sorafenib in advanced NSCLC

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non small cell lung cancer

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Bayer,bedrijf

Intervention

Keyword: advanced NSCLC, erlotinib, phase II, sorafenib

Outcome measures

Primary outcome

No progression rate at 6 weeks

Secondary outcome

Response rate, disease control rate, duration of response, time to progression

or death, overall survival, safety.

Study description

Background summary

Therapeutic results of standard cytotoxic therapy for advanced non small cell lung cancer (NSCLC) are far from satisfactory: survival has reached a plateau at a median of 9-11 months in the recently published phase III trials. Therefore, clinical research of new treatment strategies is warranted. Several targeted agents have been introduced into clinical trials in NSCLC. Today, two agents, notably the EGFR-TKI erlotinib and the anti-VEGF monoclonal antibody bevacizumab have show clinically relevant activity in NSCLC either as a single agent in the relapse setting (erlotinib) or in conjuncture with chemotherapy in first line setting (bevacizumab). There is a strong preclinical rationale to pursue a strategy combining agents directed against the EGFR axis (including the RAS-RAF pathway) and the VEGF axis in NSCLC. Indeed, in NSCLC patients relapsing after platinum based chemotherapy, the combination of erlotinib and bevacizumab has shown activity comparable to standard chemotherapy in randomised phase II setting. There are several reasons to replace bevacizumab for sorafenib in this novel doublet. Sorafenib is a very potent inhibitor of the RAS-RAF pathway, but also affects several other pathways such as the VEGFR pathway. Sorafenib may prove to be particularly active against NSCLC because

the proliferation signaling of the RAS/RAF/MAPK/ERK pathway is increased due to an increase in K-RAS mutations. Sorafenib has shown activity against NSCLC cell lines and has clinically relevant single agent activity against platinum pretreated advanced NSCLC patients10. In addition, sorafenib is orally available and, in contrast to bevacizumab, is labeled for all histologies of NSCLC.

Study objective

Primary:
•Efficacy of combination of erlotinib and sorafenib as determined by the rate of no progression at 6 weeks.
•Determination of the impact of concomitant administration of sorafenib on the pharmacokinetics (PK) of erlotinib

Secondary:
•Efficacy of erlotinib and sorafenib as determined by
-the objective response rate and disease control rate
-duration of response
-time to disease progression or death
-survival
-safety of erlotinib and sorafenib

Study design

An open-label, multicenter, phase II study

Intervention

All patients will receive Erlotinib 150 mg od and Sorafenib 400 mg bid

Study burden and risks

Risks asociated with treatment of erlotinib and sorafenib. Phase I trials have shown no excess with respect to side effects when the two agents are combined.

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

Histologically advanced NSCLC
Normal organ function
ECOG PS 0-2
Age >18 yrs
Measurable disease

Exclusion criteria

History of cardiac disease
Symptomatic brain or leptomeningeal metastases
History of bleeding diasthesis

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2007
Enrollment:	48
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nexavar
Generic name:	sorafenib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tarceva
Generic name:	erlotinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-10-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-09-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2007-004625-14-NL
CCMO	NL19335.029.07