A parallel phase II study of Tarceva®(Erlotinib) in patients with advanced non-small cell lung cancer (Stage IIIB/IV) not pre-treated by chemotherapy including dose escalation to toxicity in current and former smokers

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To estimate the efficacy of erlotinib administered as a single agent to chemo-naïve NSCLC patients as determined by the non progression rate (NPR) at 8 weeks.

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

Summary

ID

NL-OMON30374

Source
ToetsingOnline

Brief title
Tarceva in NSCLC never smokers vs. smokers

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
1. non-small cell lung cancer, squamous cell lung malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Roche;sponsor;will finance the study

Intervention

Keyword: never-smokers, NSCLC, smokers, Tarceva

Outcome measures

Primary outcome

The primary efficacy variable is the non progression rate (NPR). The NPR is defined as the proportion of patients without progression (based on RECIST criteria) at 8 weeks after start of treatment, i.e. all patients with a response rating of Complete Response (CR), Partial Response (PR), or Stable Disease (SD) according to RECIST that is documented for at least 8 weeks from baseline.

Secondary outcome

Secondary efficacy parameters include overall response rate using RECIST criteria, response duration, time to progression, progression-free survival and overall survival.

Study description

Background summary

Never smokers with NSCLC appear to derive better clinical benefit (eg, higher response rateds, longer survival) from epidermal growth factor receptor (EGFR) inhibitors than former/current smokers. Current smokers were found to have as much as a 2-fold decrease in erlotinib trough plasma concentrations than former or never smoking patients, PK could contribute to the differences in efficacy and suggest higher doses may be required in current smokers. In the phase II setting, significant antitumour activity was demonstrated with first-line

erlotinib monotherapy. Erlotinib administered as single agent as first line treatment option in advanced NSCLC was well tolerated with mainley mild-to-moderate treatment-related AEs (rash and diarrhoea). Based on these results, erlotinib has potential as first-line treatment option in advanced NSCLC and further study in this setting is recommended.

Study objective

To estimate the efficacy of erlotinib administered as a single agent to chemo-naïve NSCLC patients as determined by the non progression rate (NPR) at 8 weeks.

Study design

This is an parallel, open-label, phase II, non-randomized study. Groups are defined by smoking status. This study will be performed at 11 centres within Europe. Approximately 44 patients will be enrolled in total. Histological tumour samples are mandatory and will be collected at screening. After successful completion of all screening procedures, patients will start on therapy with daily dosing. For the group of current/former smoker patients the starting dose will be 150 mg/day escalating up to a maximum of 300 mg/day according to the safety profile in order to determine the optimum dose in this population.Treatment will continue until PD, unacceptable toxicity or death. Subsequently, for a subset of 10 patients in both groups, a full PK assessment will be done. Minimal PK sampling will be done in all the other patients. PK sampling during study should be done at day 14 and day 42. Selected study centres will participate in the full PK sampling procedures. For all patients* safety and efficacy assesments will be scheduled as per the schedule of assesments (page 34, table 3 of the protocol)

Intervention

For the group of non-smoker patients, the daily dose will be 150 mg/day.
For the group of current/former smoker patients the starting dose will be 150 mg/day escalating up to a maximum of 300 mg/day according to the safety profile in order to determine the optimum dose in this population.Treatment will continue until PD, unacceptable toxicity or death.

Study burden and risks

Every patient will be treated for approximately 12 months followed by follow-up. During the treatment phase patients who entered the full PK group, will have up to 16 visits, these visits will involve about 25 hours in total.
30 bloodsamples will be taken (a cannule is optional) and 4 MRI/CT*s and one bronchoscopy assesments performed. The minimal PK group has approximately 10 visits, involving 12 hours and 20 bloodsamples(a cannule is optional) and 4

MRI/CT*s and one bronchoscopy assesments are performed. Major (rare) complications after a biopsy by bronchoscopy are low blood oxygen, pneumothrorax and arrhytmia. The most frequent side effects seen so far with erlotinib are in approximately 75% of patients rash, it generally improves without treatment (self-limiting). Other side effects are diarrhoea, fatigue, nausea ,vomiting and a dry skin. There may also be a risk of irreversible corneal lesions; this risk is increased in patients wearing contact lenses. Laboratory abnormalities were observed infrequently with erlotinib when used alone. Based on animal studies, there may also be a risk of side effects that involve your liver, kidneys, eyes, ovaries, or hair follicles. Because of the way erlotinib is metabolized (broken down by the body), there is a possibility of an interaction between erlotinib and a certain type of anti-coagulant (blood thinner). The long-term effects of erlotinib are unknown.

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

- Patients with histological documented, locally advanced or recurrent (stage IIIB and not amenable for combined modality treatment) or metastatic (Stage IV) NSCLC who have not received prior chemotherapy for advanced disease.
- Formalin-fixed, paraffin-embedded primary diagnosis lung tumour tissue samples (tissue blocks are preferred over slides) representative of the tumour and collected prior to starting erlotinib therapy will be provided to the co-ordinating investigator within 3 weeks of the patient starting erlotinib therapy. This Is A Mandatory Requirement For Study Entry
- No prior chemotherapy for advanced disease. Previous adjuvant treatment is permitted if patient relapsed * 1 year after the end of the chemotherapy.
- Measurable disease according to RECIST.
- Age 18 or greater.
- Able to comply with study and follow-up procedures.
- Patients must be able to take oral medication.
- Written (signed) Informed Consent (WIC) to participate in the study.
- ECOG performance status of 0 - 2.
- Life expectancy of at least 12 weeks.
- At least 4 weeks since any prior surgery or radiotherapy. Patients must have recovered (CTC < 1) from acute toxicities of any previous therapy.
- Granulocyte count > 1,500/mm3 and platelet count > 100,000/mm3; Haemoglobin * 9.0g/dl.
- Serum bilirubin within upper limit of normal (ULN), SGOT (AST) and SGPT (ALT) < 2.5 x ULN (or * 5 x ULN in case of liver metastases).
- Serum creatinine * 1.5 ULN or creatinine clearance * 60 ml/min.
- For all females of childbearing potential a negative pregnancy test must be obtained within 72 hours before starting therapy. Patients with reproductive potential must use effective contraception.
- Patients that either can be classified as never smokers or as current/former smokers according to the definitions in section 3.1 (note that all other smokers (e.g. cigar, pipe) will be excluded from study participation).

Exclusion criteria

1. Any unstable systemic disease including:
- active infection or serious underlying medical condition that would impair the ability of the patient to receive protocol treatment,
- uncontrolled hypertension,
- unstable angina,
- severe heart disease (NYHA stages III and IV heart failure, unstable angina, uncontrolled arrhythmia in particular)
congestive heart failure,
- history of myocardial infarction within the previous year,
- serious cardiac arrhythmia requiring medication,

- hepatic, renal or metabolic disease,
2. Any other malignancies within 5 years (except for adequately treated carcinoma in situ of the cervix or basal or squamous cell skin cancer).
3. Patients are excluded if they have clinical evidence of brain metastasis, or have brain metastasis or spinal cord compression that is newly diagnosed and/or has not yet been definitively treated with surgery and/or radiation; previously diagnosed and treated CNS metastases or spinal cord compression without evidence of stable disease (clinically stable imaging) for at least 2 months will also cause patients to be excluded.
4. Any diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of the study medication.
5. Previous treatment with any therapy which acts on the EGFR axis.
6. Patients unable to take oral medication, requiring intravenous alimentation, who have mal-absorption syndrome or any other condition affecting gastrointestinal absorption, or who have active peptic ulcer disease.
7. Nursing and/or pregnant women.
8. Any inflammatory changes of the surface of the eye.

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):	09-01-2006
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tarceva

Generic name:	erlotinib hydrochloride
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-07-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-09-2006
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-04-2009
Application type:	Amendment
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	EUCTR2005-004782-41-NL
CCMO	NL11276.029.06