A phase II study of carboplatin -paclitaxel with bevacizumab followed by the addition of erlotinib to bevacizumab beyond progression in patients with locally advanced and/or metastatic non-small cell lung cancer (NSCLC) who have not received prior systemic therapy.

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Primary objective: Efficacy of erlotinib plus bevacizumab subsequent to the combination of carboplatin, paclitaxel and bevacizumab as determined by the maximum achieved disease control rate (DCR, complete response, partial response, or stable...

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

Summary

ID

NL-OMON31631

Source
ToetsingOnline

Brief title
ULCN-0107 Bevacizumab plus erlotinib beyond progression

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
locally advanced lung cancer, metastatic lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: dit is een investiagtor initiated trial waarvoor een grant van Hoffmann-la Roche is gegeven om de studie uit te kunnen voeren,Hoffmann-La Roche

Intervention

Keyword: bevacizumab, erlotinib, NSCLC, phase II

Outcome measures

Primary outcome

Efficacy of erlotinib plus bevacizumab subsequent to the combination of

carboplatin, paclitaxel and bevacizumab as determined by the maximum achieved

disease control rate (complete response, partial response, or stable disease)

at 18 weeks

Secondary outcome

Efficacy of carboplatin, paclitaxel and bevacizumab as determined by PFS, DCR,

RR

Efficacy of bevacizumab and erlotinib as determined by DCR at 6, 12 and 27

weeks; PFS; RR

Overall survival

Safety profile of carboplatin, paclitaxel and bevacizumab and subsequent

bevacizumab and erlotinib

Determination of early response by FDG-PET

Study description

Background summary

Paclitaxel, carboplatin and bevacizumab demonstrated to be safe and effective in advanced NSCLC patients. In studies bevacizumab has been continued until progression. Preclinical data suggest rapid vascular re-growth in tumours after reversal of VEGF inhibition. These preclinical findings support studying the concept of continued use of VEGF inhibition in progressive patients. Further, preclinical studies have shown that VEGF and EGFR inhibitors can have additive effects and clinical trials have also produced promising data in second line therapy combining the anti-VEGF monoclonal antibody bevacizumab with the anti-EGFR antibody cetuximab or the EGFR tyrosine kinase inhibitor erlotinib. The combination increases benefit compared with either of these anti-EGFR agents alone. The toxicity profiles of bevacizumab and erlotinib are non-overlapping and the combination is more favourable when compared to current standard second line chemotherapy. In phase I, erlotinib 150mg/day p.o. plus bevacizumab 15mg/kg i.v. every 21 days was established as the phase II dose, although no true dose-limiting toxicities were observed. The most commonly reported adverse events were rash, diarrhea, and proteinuria, which were never more than mild to moderate.

Study objective

Primary objective:
Efficacy of erlotinib plus bevacizumab subsequent to the combination of carboplatin, paclitaxel and bevacizumab as determined by the maximum achieved disease control rate (DCR, complete response, partial response, or stable disease) at 18 weeks
Secondary objectives:
Efficacy of carboplatin, paclitaxel and bevacizumab as determined by PFS, DCR, RR
Efficacy of bevacizumab and erlotinib as determined by DCR at 6, 12 and 27 weeks; PFS; RR
Overall survival
Safety profile of carboplatin, paclitaxel and bevacizumab and subsequent bevacizumab and erlotinib
Determination of early response by FDG-PET

Study design

Open-label phase II study

Intervention

4 cycles (or less in case of progression) with Paclitaxel, Carboplatin and Bevacizumab. At (early) progression Bevacizumab 15 mg/kg i.v. q 21 days plus Erlotinib 150 mg/day orally

Study burden and risks

The burden related to study procedures is limited as most procedures are considered necessary in standard care. In the first three weeks in both the first line as second line treatment the visits are more frequent (4 extra visits including an venapunction) and radiological evaluation is more frequent compared to standard care during bevacizumab-monotherapy and in the first 18 weeks of second line treatment (resulting in an estimated 3 extra CT-Thorax per patient).
The favorable toxicity profile of the studied second line treatment compared to standard second line treatment can be considered beneficial to the participant.

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

- Advanced stage NSCLC (IIIB with malignant pleural effusion or stage IV) excluding squamous cell histology, with measurable or evaluable disease.
- No prior systemic therapy for advanced NSCLC, prior therapy for early stage disease with one regimen is acceptable if it was completed at least 6 months prior to study entry.
- Palliative radiotherapy to painful bony metastases will be permitted prior to study entry if completed prior to initiation of study treatment, and there are no residual sequelae of therapy such as bone marrow suppression.
- Life expectancy of at least 3 months.
- ECOG Performance status 0-1 (see appendix 2)
- Age 18 or higher.
-Female patients with reproductive potential must have a negative serum pregnancy test within 72 hours prior to start of study medication. All female patients of childbearing potential, and all male patients, must agree to use a medically acceptable method of contraception or agree to be abstinent throughout the treatment period and for 3 months after discontinuation of treatment
- Patients must have normal organ and marrow function

Exclusion criteria

- Prior systemic treatment for advanced NSCLC. One prior regimen (up to 4 cycles) of neoadjuvant or adjuvant therapy for early stage disease will be allowed if completed at least 6 months prior to study entry.
- Known brain metastases (in case of clinical signs or symptoms of brain metastases radiological evaluation is mandatory).
- Prior treatment with bevacizumab or erlotinib.
- History of allergic reactions or sensitivity attributed to compounds of similar chemical or biologic composition to bevacizumab or erlotinib.
- Current, recent (within 4 weeks of the first infusion of this study), or planned participation in any other experimental drug study.
- Concomitant chemotherapy, radiotherapy or investigational agents.
- Evidence of bleeding diathesis or coagulopathy.
- Use of full dose anti-coagulant agents.
- Pregnant (positive pregnancy test) or lactating women.
- Major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to start, anticipation of need for major surgical procedure during the course of the study.
- Minor surgical procedures, fine needle aspirations or core biopsies within 7 days prior to start.
- History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 6 months prior to start.
- Serious, non-healing wound, ulcer, or bone fracture.

- Lung carcinoma of squamous cell histology or any histology in close proximity to a major vessel, or with significant cavitation as assessed by treating investigator in consultation with an attending radiologist.
- History of hemoptysis (bright red blood of 2.5 ml or more).
- Significant co-morbidities including:
- No uncontrolled hypertension (systolic > 150 mmHg and/or diastolic > 100 mmHg)
- Unstable angina
- New York Heart Association (NYHA) Grade II or greater congestive heart failure
- History of myocardial infarction within 6 months
- History of stroke within 6 months
- Clinically significant peripheral vascular disease
- Patients diagnosed with a tracheo-oesophagal fistula
- Another active malignancy except for non-melanoma skin cancers in the last 5 years.
- Inability to comply with study and/or follow-up procedures.

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):	01-05-2008
Enrollment:	56
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	avastin
Generic name:	bevacizumab
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	carboplatin
Generic name:	carboplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	paxene
Generic name:	paclitaxel
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tarceva
Generic name:	erlotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-04-2008
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-06-2009
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2007-005523-15-NL
CCMO	NL19600.091.08