Phase I study of concurrent with involved-field thoracic radiotherapy for inoperable non-squamous cell lung cancer, followed by both concurrent and maintenance Bevacizumab

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Primary objectivesTo establish the safety and tolerability of1. two doses of bevacizumab 7.5 mg/kg administered every 3 weeks with concurrent thoracic radiotherapy to 66 Gy;2. concurrent (7.5 mg/kg) and maintenance (15 mg/kg) bevacizumab during, and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON30108

Source
ToetsingOnline

Brief title
Phase I study of Bevacizumab and thoracic radiotherapy for lung cancer

Condition

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

Synonym
lung cancer, non-squamous lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Bedrijf - Roche NL,Roche

Intervention

Keyword: avastin, combined modality, non-squamous cell lung cancer, radiation

Outcome measures

Primary outcome

Primary objectives

To establish the safety and tolerability of

1. two doses of bevacizumab 7.5 mg/kg administered every 3 weeks with

concurrent thoracic radiotherapy to 66 Gy;

2. concurrent (7.5 mg/kg) and maintenance (15 mg/kg) bevacizumab during, and

following, completion of thoracic radiotherapy to 66 Gy

Secondary outcome

Secondary objectives

1. Correlate all observed toxicity with dose-volume histograms of irradiated

normal organs.

2. Explore surrogate tumor end-points that may correlate with the efficacy of

combined treatment with anti-VEGF targeted therapy

3. Estimate the objective tumor response after radiotherapy and concurrent

bevacizumab based on RECIST criteria

Study description

Background summary

The treatment of choice in patients with locally-advanced non-small cell lung cancer is chemo-radiotherapy. However, novel measures are clearly needed to improve both survival and local control as median survival in patients treated by concurrent chemo-radiotherapy alone was 22.2 months, and the local failure rate of 22% [Albain 05]. The dismal long-term prognosis for these patients with stage III disease has prompted intensive efforts to find new therapeutic modalities that will provide survival improvements.

In randomized phase III clinical trials, the humanised anti-VEGF monoclonal antibody bevacizumab (Avastin) has shown a survival advantage in patients with metastatic lung, colo-rectal and breast cancer. Preclinical studies show that the combination of Avastin and radiation enhances radiation response and local tumor control.Safety data is patients undergoing thoracic radiotherapy and concurrent Avastin in a necessary step before incorporating this novel agent into phase II and III trials of chemo-radiation with Avastin.

Study objective

Primary objectives

To establish the safety and tolerability of
1. two doses of bevacizumab 7.5 mg/kg administered every 3 weeks with concurrent thoracic radiotherapy to 66 Gy;
2. concurrent (7.5 mg/kg) and maintenance (15 mg/kg) bevacizumab during, and following, completion of thoracic radiotherapy to 66 Gy

Secondary objectives

1. Correlate all observed toxicity with dose-volume histograms of irradiated normal organs.
2. Explore surrogate tumor end-points that may correlate with the efficacy of combined treatment with anti-VEGF targeted therapy
3. Estimate the objective tumor response after radiotherapy and concurrent bevacizumab based on RECIST criteria

Study design

A single-centre, open-label, non-comparative, dose-finding phase I trial of thoracic radiotherapy with bevacizumab and a stepwise (4-level) cohort design.Patients will receive 2 cycles of induction chemotherapy prior to radiotherapy and concurrent bevacizumab, which will commence 3 weeks after the

last administration of chemotherapy. Any cisplatin-based doublet combination will be accepted as an induction regime

Level 1: 66Gy (maximum permitted cord dose *32 Gy) + concurrent bevacizumab
Level 2: 66Gy (maximum permitted dose *36 Gy) + concurrent bevacizumab At least 3 patients will be treated at each level and each will be followed-up for at least 3 months before the next level.
Level 3: 66 Gy (maximum permitted cord dose *36 Gy) + concurrent Bevacizumab followed by maintenance bevacizumab until either disease progression or a maximum of 1 year
Level 4: 66 Gy (maximum permitted cord dose *40 Gy) + concurrent Bevacizumab followed by maintenance bevacizumab until either disease progression or a maximum of 1 year

Intervention

see study design (above)

Study burden and risks

During the radiotherapy, patients will receive 2 infusions of Avastin at intervals of 3 weeks, and Avastin will be repeated every 3 weeks after radiation for a maximum period of 12 months, in the absence of disease progression.

There are no preclinical data to suggest that the expected incidence of radiation-induced toxicities, mainly esophagitis and radiation pneumonitis, will be increased by the proposed combined treatment. On the other hand, the median survival of the study patients is less than 17.2 months despite high-dose chemo-radiotherapy and novel approaches are clearly indicated. As Avastin has been shown to improve survival in patients with metastatic non-small cell lung cancer, the relative risks with combined therapy is possible less that for agents without systemic activity.

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 aged 18 years or older with histologically- or cytologically-confirmed non-squamous cell carcinoma of the lung (NSCLC);Inoperable stages II*IIIB NSCLC, who have received no previous thoracic radiotherapy AND no chemotherapy or anti-cancer agents for at least 21 days ;WHO performance score of 0-2; acceptable pulmonary function as defined by a Fev1 of *30% and a DLCO of *40% of predicted; no use of anticoagulants.;Patients who are likely to be at low-risk for radiation pneumonitis (V20 < 35%).

Exclusion criteria

1. Mixed tumor types with small cell lung cancer or squamous cell carcinoma
2. Other serious diseases, such as heart failure, angina pectoris, myocardial infarction within the last 6 months, uncontrolled hypertension
3. Serious non-healing wound or ulcer.
4. ASAT and ALAT > 1,5 x UNL
5. alkaline phosphatase 5 x UNL
6. Evidence of bleeding diathesis or coagulopathy.
7. Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be assessed with the patient before registration in the trial.
8. Participation in other trial with investigational drug or treatment modality.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-11-2006
Enrollment:	25
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-09-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2007
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	EUCTR2006-003149-17-NL
CCMO	NL13724.029.06