Selective Pulmonary Artery Perfusion with carboplatin for the treatment of NSCLC: a phase I trial

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To determine toxicity of selective pulmonary artery perfusion (SPAP) for the treatment of non small cell lung cancer.

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON32894

Source
ToetsingOnline

Brief title
Selective Pulmonary Artery Perfusion

Condition

- Respiratory tract neoplasms

Synonym
lung cancer, non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: cardioth chir
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: carboplatin, chemotherapy, non-small cell lung cancer, Selective Pulmonary Artery Perfusion

Outcome measures

Primary outcome

Primary endpoint: toxicity (CTC criteria)

Secondary outcome

Secondary endpoint: radiologic response, downstaging, radical resection

Study description

Background summary

Cancer is the leading cause of death before the age of 85 years resulting in more than half a million deaths per year in the United States [ref 1 of the protocol, page 22]. In 2005, primary lung cancer was the second leading cancer type in the United States with approximately 190,000 new cases to be estimated for 2006. Among all cancer types, lung cancer has the highest death rate [2]. Lung cancer is usually treated by surgical resection and/or cytostatic drug administration depending on the disease stage. Stage I (a and b) and II NSCLC are currently treated by surgical resection and (neo-)adjuvant cytostatic therapy resulting in a 5-year survival of 75, 60 and 40% respectively [3]. However, adjuvant intravenous chemotherapy results in a 5-year survival benefit of 4-12% in patients eligible for surgery.
Patients suffering from stage IIIa and b NSCLC are treated intravenously using gemcitabine and a platin-derivate, e.g. cisplatin or carboplatin, resulting in an overall response of 40% and a 5-year survival of 20% [3]. However, infusion of carboplatin is dose-limited due to the presence of bone marrow suppression at higher doses and renal dysfunction.
Therefore, selective pulmonary artery perfusion (SPAP) has been developed as a new method of cytostatic drug delivery to the lungs for the treatment of lung cancer in order to achieve more effective down-staging of the tumour (T) and lymph node (N) status. Concomitantly, lung cancer is a systemic disease and therefore SPAP aims to achieve serum concentrations that are equivalent compared to intravenous administration [6-8].

Study objective

To determine toxicity of selective pulmonary artery perfusion (SPAP) for the treatment of non small cell lung cancer.

Study design

Phase 1, 4 levels:

Level 1 (n=3)
Cyclus 1 (3 weeks):
Day 1: gemcitabine (1250 mg/m2) and carboplatin (AUC 6) iv
Day 8: gemcitabine iv (1250 mg/m2)
Cyclus 2 (3 weeks): Day 1: gemcitabine iv (1250 mg/m2) and carboplatin SPAP (AUC 6, 15 minutes without BFO)
Day 8: gemcitabine iv (1250 mg/m2)
Restaging (at 8 weeks): CT, EUS, PET, V/Q, Lung function/DLCO, bronchoscopy
Surgery or radiotherapy
Toxicity determination (at 15 weeks): HRCT, Lung function/DLCO

Level 2 (n=3)
Cyclus 1 (3 weeks):
Day 1: gemcitabine (1250 mg/m2) and carboplatin (AUC 6) iv
Day 8: gemcitabine iv (1250 mg/m2)
Cyclus 2 (3 weeks): Day 1: gemcitabine iv (1250 mg/m2) and carboplatin SPAP (AUC 6, 15 minutes and 10 min. BFO)
Day 8: gemcitabine iv (1250 mg/m2)
Restaging (at 8 weeks): CT, EUS, PET, V/Q, Lung function/DLCO, bronchoscopy
Surgery or radiotherapy
Toxicity determination (at 15 weeks): HRCT, Lung function/DLCO

Level 3 (n=3)
Cyclus 1 (3 weeks):
Day 1: gemcitabine (1250 mg/m2) and carboplatin (AUC 6) iv
Day 8: gemcitabine iv (1250 mg/m2)
Cyclus 2 (3 weeks): Day 1: gemcitabine iv (1250 mg/m2) and carboplatin SPAP (AUC 6, 15 minutes and 20 min. BFO)
Day 8: gemcitabine iv (1250 mg/m2)
Restaging (at 8 weeks): CT, EUS, PET, V/Q, Lung function/DLCO, bronchoscopy
Surgery or radiotherapy
Toxicity determination (at 15 weeks): HRCT, Lung function/DLCO

Level 4 (n=3)
Cyclus 1 (3 weeks):
Day 1: gemcitabine (1250 mg/m2)and carboplatin (AUC 6) iv
Day 8: gemcitabine iv (1250 mg/m2)
Cyclus 2 (3 weeks): Day 1: gemcitabine iv (1250 mg/m2)and carboplatin SPAP (AUC 6, 15 minutes and 30 min. BFO)
Day 8: gemcitabine iv (1250 mg/m2)

Restaging (at 8 weeks): CT, EUS, PET, V/Q, Lung function/DLCO, bronchoscopy
Surgery or radiotherapy
Toxicity determination (at 15 weeks): HRCT, Lung function/DLCO

NB:
1. Gemcitabine 1250 mg/m2 i.v.: gemcitabine will be added to 250 mL of NaCl 0.9% and administered according to the current standard treatment protocol.
2. Carboplatin (AUC 6) i.v.: carboplatin will be added to 500 mL of glucose 5% and administered according to the current standard treatment protocol.
3. Carboplatin (AUC 6) SPAP: carboplatin will be added to 250 mL of glucose 5% and administered in 15 minutes according the technique as described in the introduction.

Intervention

Insertion of a balloon catheter into the left or right pulmonary artery after venous puncture in the groin. After insertion, the drug is infused; depending on the group, a balloon will be inflated after infusion during 10, 20 or 30 minutes; after infusion and/or balloon inflation, the catheter will be removed immediately.

Study burden and risks

A Medline search revealed two human studies evaluating pulmonary artery infusion of cisplatin (60 and 30 mg/m2), mitomycin (10 mg/m2) combined with navelbine (25 mg/m2) and one study evaluating doxorubicin (10-20 mg) [ref 9-11 protocol, page 22]. In total, 177 procedures are described in 74 patients. Pulmonary toxicity like pneumonitis or pulmonary fibrosis is not described. Regarding the lack of pulmonary toxicity, it is important to emphasize that pulmonary artery infusion was performed in lobar or segmental arteries which is in contrast to our studies in which infusion occurred centrally, proximal of the first side branches. The pulmonary distribution volume in our studies will be therefore larger than in the described studies in the literature suggesting that they even had higher lung concentrations than we will have. Furthermore, no significant histological toxicity was observed in our own animal studies [6-11].

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

Stage c3a en c3b NSCLC

Exclusion criteria

Other stages of NSCLC, age under 18 years old (however, NSCLC has never been described during childhood), patients who are mentally not able to chose whether to be involved in the study or not, pregnancy or lactation, severe comorbidity, uncontrollable infectious disease, Liver/kidney insufficiency; serum creatinine more than 130 µmol/l and urine creatinine clearance less than 60 ml/min, ALAT and ASAT more than 3 times normal

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2008
Enrollment:	12
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO

Date:	25-11-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2006-006348-71-NL
CCMO	NL25025.100.08