PeRsOnalized treatment fOr patients with pleural eFfusions due to malignant pleural mesothelioma or lung cancer in second or third line. An open label phase II study (Acronym: the PROOF study)

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The aim of this study is to evaluate the efficacy of a personalized drug profiling method using short-term cultures of malignant cells derived from the patient*s pleural fluid.

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

Summary

ID

NL-OMON40679

Source
ToetsingOnline

Brief title
Personalized treatment for patients with pleural effusions

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
mesothelioma and lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Lung cancer (NSCLC), Malignant pleural mesothelioma, Personalized treatment, Pleural effusions

Outcome measures

Primary outcome

The primary endpoint is accuracy of the drug profiling method, defined by the number of truly predicted responses, as a percentage of the total number of patients in the study.

Secondary outcome

Secondary endpoints include objective response rate (ORR), progression free survival (PFS), overall survival (OS), pulmonary function and frequency and severity of adverse events. Exploratory endpoints to identify potential biomarkers include genomic profiling, assessment of breath prints of Volatile Organic Compounds by E-nose.

Study description

Background summary

Prognosis of malignant pleural mesothelioma is extremely poor. There is no standard second line therapy for these patients. For metastatic NSCLC, the registrated third line therapy (erlotinib), is ineffective in the majority of these patients. We hypothesize that a personalized drug profiling method will allow a better prediction of responses and reduce unnecessary treatment toxicity.

Study objective

The aim of this study is to evaluate the efficacy of a personalized drug profiling method using short-term cultures of malignant cells derived from the patient*s pleural fluid.

Study design

In this open label phase II study, the choice of second or third line therapy will be determined by a personalized drug profiling method using short-term cultures, of primary tumour cells.

Intervention

Pleural fluid that is drawn for symptom relief, will be used to isolate tumor cells for short-term culture. A small scale drug screen will be performed within 3 weeks after isolation of tumor cells. If sample tumor cells are available, a large scale drug screen using the 101 anti-cancer compounds will be performed as well. Based on the in vitro results, an advise on both single agent and combination therapy will be provided by the committee of researchers. The treating physician will decide whether single agent or combination therapy is suitable for the patient and will determine which term therapy will be started. Patients will be treated according to chemotherapy protocols that are routinely used in our clinic and recorded in iProva. Response evaluation will be done according to modified RECIST.

Study burden and risks

Pleural effusion is usually drawned for symptom relief. The patient therefore don't need additional surgery. The collection of blood will - if possible - be combined with a regular blood collection which is required for the treatment. In about half of the patients it is not possible to do the test in the laboratory. So there is no guarantee that there will be a treatment proposal on the basis of the laboratory results. Furthermore, this research should show whether the laboratory result is indeed a good predictor for what the best follow-up treatment will be. So it is not sure if the predicted chemotherapy in the patient will show result.
All patients may experience any side effects of chemotherapy.

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 histologically or cytologically proven malignant mesothelioma or non small cell lung cancer that have a pleural effusion;
• Age > 18 years;
• At the time of pleural fluid drainage, patients must have completed:
For MPM: at least first-line chemotherapy with a platinum (cisplatin or carboplatin) and pemetrexed combination.
For NSCLC: at least first and second line therapy according to the local guidelines.
• At the start of study treatment, patients must have documented evidence of progressive disease.
• Measurable or evaluable disease.
• Ability to understand the study and give signed informed consent prior to beginning of protocol specific procedures.
• WHO performance status <= 2.
• Adequate organ function as evidenced by the following peripheral blood counts or serum chemistries at study entry:
o Hematology: Neutrophil count >= 1.5 x 109/l, Platelets >= 100 x 109/l, Hemoglobin >= 5.9 mmol/l.
o Hepatic function as defined by serum bilirubin <= 1.25 times the upper limit of normal (ULN), ALAT and ASAT <= 2.5 times the ULN, except for liver metastases then ALAT and ASAT < 5 times the ULN.

o Renal function as defined by serum creatinine <= 1.25 times ULN or creatinine clearance >= 50 ml/min (by Cockcroft-Gault formula).

Exclusion criteria

• Active uncontrolled infection, severe cardiac dysfunction or non-correctable bleeding tendency.
• Any identification of a driver mutation for which a registered treatment is available.
• Presence of symptomatic CNS metastases.
• Radiotherapy within 2 weeks prior to start of study treatment.
• Unstable peptic ulcer, unstable diabetes mellitus or other serious disabling condition.
• Concomitant administration of any other experimental drugs under investigation.
• Any non-resolved grade 3 or higher toxicity.
• For neurotoxicity any non-resolved grade 2 or higher toxicity

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):	01-06-2014
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	Pemetrexed

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Doxorubicin
Generic name:	Doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Hospira
Generic name:	Carboplatine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-06-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-07-2014
Application type:	First submission
Review commission:	METC NedMec

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	EUCTR2013-005621-24-NL
CCMO	NL47606.031.14