Onderzoek naar de gevoeligheid van tumorcellen uit pleuravocht voor verschillende chemotherapeutische middelen bij patiënten met een niet-kleincellig longcarcinoom of mesothelioom

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28874

Source
NTR

Brief title
PROOF

Health condition

Malignant pleural mesothelioma or metastatic NSCLC

Maligne longvlieskanker of
uitgezaaide longkanker (NSCLC)

Sponsors and support

Primary sponsor: Stichting Het Nederlands Kanker Instituut-Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF

Intervention

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 rates (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 and assessment of the accuracy of response evaluation by breath prints of Volatile Organic Compounds by SpiroNose.

Study description

Background summary

Summary study title: 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).

Principal Research Center: Netherlands Cancer Institute-Antoni van Leeuwenhoek Ziekenhuis.

Methodology: Open-label phase II

Scientific rationale: 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.

Primairy 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.

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.

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

Number of patients: 80 patients will be registrated. 60 patients with mesothelioma and 20 patients with NSCLC.

Study treatment:

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 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 objective

A personalized in vitro drug profiling method will allow a better prediction of responses and reduce unnecessary treatment toxicity.

Study design

Every 6 weeks untill progression, thereafter every 12 weeks.

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 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.

- Vinorelbine 25 mg/m2 x2q3w

- Gemcitabine 1250mg/m2 x2q3w

- Pemetrexed 500 mg/m2 q3w (max 1000 mg)

- Oxaliplatin 130 mg/m2 q3w

- Doxorubicin 60 mg/m2

- Cisplatin 75 mg/m2 q3w + Vinorelbine 25 mg/m2 x2q3w

- Cisplatin 75 mg/m2 q3w + Gemcitabine 1250 mg/m2 x2q3w

- Cisplatin 75 mg/m2 q3w + pemetrexed 500 mg/m2 q3w (max 1000 mg)

- Carboplatin AUC 5 + vinorelbine 25 mg/m2 x2q3w

- Carboplatin AUC 5 + gemcitabine 1250 mg/m2 x2q3w

- Carboplatin AUC 5 + pemetrexed 500 mg/m2 q3w (max 1000 mg)

- Oxaliplatin 100 mg/m2 q3w + vinorelbine 25 mg/m2 x2q3w (reduced dose oxaliplatin)

- Oxaliplatin 100 mg/m2 q3w + gemcitabine
1000 mg/m2 x2q3w (reduced dose oxali/gemci)

- Oxaliplatin 100 mg/m2 q3w + pemetrexed
500 mg/m2 xq3w (reduced dose oxaliplatin)

Contacts

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Eligibility criteria

Inclusion criteria

• Patients with histologically or cytologically proven malignant mesothelioma or non-small cell lung cancer that have a pleural effusion.

• Age >18 years.

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• Measurable or evaluable disease.

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• 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 type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2014
Enrollment:	80
Type:	Anticipated

Ethics review

Positive opinion

Date:	09-09-2014
Application type:	First submission

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
NTR-new	NL4624
NTR-old	NTR4775
Other	NKI-AVL : N14PLU

Study results

Summary results
N/A