NAC-PNP-study

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29356

Source
Nationaal Trial Register

Brief title
NAC-PNP-study

Health condition

NSCLC, non-small cell lung cancer, SCLC, small cell lung cancer, malignant mesothelioma, neuropathy due to cisplatin, niet kleincellig longcarcinoom, kleincellig longcarcinoom, mesothelioom, neuropathie door cisplatin

Sponsors and support

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Intervention

Outcome measures

Primary outcome

The main study parameter is the occurrence of peripheral neuropathy: therefore the NAC-arm and the placebo-arm will be compared regarding the peripheral neuropathy score (PNP-score) and the electrophysiological measurements.

Secondary outcome

Secondary parameters are the occurrence of differences in haematological pathology, creatinine clearance, liver chemistry and KPS, between the NAC-arm compared to the placebo-arm. Quality of Life will be assessed according to the EORTC QLQ-questionnaire. Differences in tumour response between the two groups will be compared.

Study description

Background summary

Background of the study:
Cisplatin (CDDP) and carboplatin are major compounds of chemotherapy in patients with non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC) and malignant mesothelioma. Cisplatin is associated with a number of side-effects, one of which is neurotoxicity. For a number of patients this neurotoxicity is a dose-limiting side-effect. At this point no measures are taken to prevent the occurrence of this neurotoxicity during treatment with cisplatin. Recent studies have shown that the association of anti-oxidants to treatment with cisplatin has a neuroprotective effect without loss of anti-tumour efficacy of cisplatin. One of these anti-oxidants is glutathione (GSH), this is a natural anti-oxidant that is synthesized in all cells, mainly in the liver and the muscles. This GSH plays a central role in the pathophysiology of cisplatin. We want to investigate the efficacy of N-acetylcysteine (NAC), which serves as a substrate for the synthesis of GSH, in the prevention of cisplatin-induced neurotoxicity. NAC has been shown to increase the GSH levels in the serum, it is also according to this principle that NAC is currently used in the treatment of acetaminophen-(paracetamol)-intoxications, where it replenishes the GSH-depletion of the liver.

Objective of the study:
The primary objective is to establish the neuroprotective efficacy of NAC against cisplatin-induced neurotoxicity. Mainly the sensory neuronal guidance will be assessed before and after treatment with cisplatin in a group of patients receiving NAC compared to a control-

group receiving placebo. The secondary objectives are establishing the protective effect of NAC regarding other cisplatin-induced side-effects such as haematological pathology (anaemia, leucopenia, thrombopenia, febrile neutropenia), loss of creatinine clearance and occurrence of liver-chemistry abnormalities. Secondary objectives include also establishing the effect on tumour response, clinical performance (Karnofski performance index) and quality of life.

Study design:
Monocenter, non-academical teaching hospital, double-blind randomized placebo-controlled study.

Study population:
Consecutive patients, who will receive at least 4 cycles of cisplatin in the treatment of NSCLC, SCLC and malignant mesothelioma, will be admitted, irrespective of the disease stage.
Inclusion criteria:
-diagnose is histologically or cytologically proven (NSCLC,SCLC), malignant mesothelioma (histologically)
-at least 4 cycles of cisplatin are planned
-adequate renal function (creatinine clearance as calculated by Cockroft-Gault method > 60 ml/min)
- Karnofski performance score > 60 %
-written informed consent
-patient must be able to comply with study measurements i.e. hospital visits for EMG and QoL assessments
-age ¡Ý 18 years
Exclusion criteria:
-patients with pre-existing neuropathy
-patients not willing to stop earlier prescribed NAC
-patients not willing to stop vitamins E and A above daily advisory dosage
-uncontrolled metastasis in the central or peripheral nervous system

Intervention (if applicable):
Patients will be randomized in a placebo-arm and a NAC-arm. They will receive oral study-medication (NAC or placebo) three times a day and they will receive intravenous study-medication every 3 weeks, each time 6 hours after the completion of the cisplatin-infusion.

Primary study parameters/outcome of the study:
The main study parameter is the occurrence of peripheral neuropathy: therefore the NAC-arm and the placebo-arm will be compared regarding the peripheral neuropathy score (PNP-score) and the electrophysiological measurements.

Secundary study parameters/outcome of the study (if applicable):
Secondary parameters are the occurrence of differences in haematological pathology, creatinine clearance, liver chemistry and KPS, between the NAC-arm compared to the placebo-arm. Quality of Life will be assessed according to the EORTC QLQ-questionnaire. Differences in tumour response between the two groups will be compared.

Nature and extent of the burden and risks associated with participation, benefit and group

relatedness (if applicable):
Burdens: Patients will have to take study-medication 3 times daily for the whole period of treatment. The other burden is the electromyographic (EMG) testing, which will normally take place 3 times during the course of the whole treatment, therefore patients will have to visit the hospital to be measured. To minimize this burden, the EMG-measurements will be planned on the same day, the patient has to visit the hospital for reasons regarding his/her regular chemotherapy-treatment. All other information will be obtained from the patients¡¯ files (blood samples, physic evaluations, etc) these are considered to be part of the routines of treatment. Patients will have to fill in Quality of Life questionnaires.
Risks: oral NAC is a well known drug, used for over thirty years, that is well tolerated even if dosed at 600 mg three times daily. For intravenous NAC, allergic reactions have been reported. There is also a theoretical risk, that NAC may reduce anti-tumour efficacy of cisplatin, this risk will be theoretically ruled out by appropiate dosing of NAC.
Benefits: NAC will possibly prevent the occurrence of neurotoxicity, improving quality of life. This may, in turn, result in less probability of dose-reductions and of pre-term arrest of treatment.

Study objective

Establishing efficacy of N-acetylcysteine (NAC) in preventing cisplatin-induced neuropathy.

Intervention

Patients will be randomized in a placebo-arm and a NAC-arm. They will receive oral study-medication (NAC or placebo) three times a day and they will receive intravenous study-medication every 3 weeks, each time 6 hours after the completion of the cisplatin-infusion.

Contacts

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Eligibility criteria

Inclusion criteria

1. Diagnose is histologically or cytologically proven (NSCLC,SCLC), malignant mesothelioma (histologically);

2. At least 4 cycles of cisplatin are planned.

3. Adequate renal function (creatinine clearance as calculated by Cockroft-Gault method > 60 ml/min);

4. Karnofski performance score > 60 %;

5. Written informed consent;

6. Patient must be able to comply with study measurements i.e. hospital visits for EMG and QoL assessments;

7. Age >= 18 years;

Exclusion criteria

1. Patients with pre-existing neuropathy;

2. Patients not willing to stop earlier prescribed NAC;

3. Patients not willing to stop vitamins E and A above daily advisory dosage;

4. Uncontrolled metastasis in the central or peripheral nervous system.

Study design

Design

Study type: Interventional

Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2008
Enrollment:	50
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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	NL1016
NTR-old	NTR1046
Other	: WP-07-148
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
there are no criteria set for the publication of the outcome of this study