Feasibility trial on combination of platinum doublets and hypofractionated radiotherapy for locally advanced stage non-small cell lung carcinoma

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To assess the safety of cisplatin doublets with hypofractionated radiotherapy (24 x2.75Gy).

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

Summary

ID

NL-OMON56676

Source
ToetsingOnline

Brief title
HYPOLAN

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
lung cancer, non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis

Source(s) of monetary or material Support: eigen afdeling

Intervention

Keyword: chemotherapy, hypofractionation, radiotherapy

Outcome measures

Primary outcome

To assess the safety of concurrent high dose chemotherapy with hypofractionated radiotherapy as defined by the rate of grade 5 treatment-related adverse events that occur during treatment and 3-month follow-up.

Secondary outcome

- The one-year disease control rate.

- Progression free survival

- Overall survival.

Study description

Background summary

Concurrent chemoradiotherapy is the standard treatment for locally advanced non-small cell lung carcinoma (NSCLC). Different chemotherapy and radiation regimens have been advocated but in general, cisplatin-doublets are deemed standard of care. Decreasing the overall treatment time of irradiation is thought to increase the efficacy. Extensive experience is available on the combination of daily-low dose cisplatin in combination with hypofractionated radiotherapy. However, no data is available on the safety of cisplatin doublets and hypofractionated radiotherapy

Study objective

To assess the safety of cisplatin doublets with hypofractionated radiotherapy (24 x2.75Gy).

Study design

Patients presenting with locally advanced NSCLC will be consented to participate in this phase 2 trial that evaluates the concurrent treatment of Cisplatin (Day 1: 75mg/m2) and Pemetrexed (Day 1: 500mg/m2 for non-squamous) or Etoposide (Day1-3 100mg/m2 for squamous), 3-weekly regimens, together with radiotherapy (24 daily fractions of 2.42 Gy to the mediastinal lymph nodes with an integrated boost of 2.75 Gy to the primary tumour). An interim analysis is planned following the first cohort of 25 patients to assess safety. Period to strict stopping rules have been formalized:

Intervention

Cisplatin (Day 1: 75mg/m2) and Pemetrexed (Day 1: 500mg/m2 for non-squamous) or Etoposide (Day1-3 100mg/m2 for squamous), 3-weekly regimens, together with radiotherapy (24 daily fractions of 2.42 Gy to the mediastinal lymph nodes with an integrated boost of 2.75 Gy to the primary tumour)

Study burden and risks

Concurrent chemoradiotherapy is a demanding treatment with a high rate of grade 3-4 side effects and a small risk of treatment-related death. The current standard is either low-dose cisplatin regimen with hypofractionated radiotherapy (24 fractions of 2.75 Gy in 24 days) for the NKI-AVL or a cisplatin-doublet with a 6-weekly irradiation schedule (30 fractions of 2 Gy). The standard dose 3-weekly chemotherapy regimens cause higher rates of systemic side effects but will be limited by a total of two cycles. This is supported by the RTOG 9410-trial , in which patients were treated with 2 cycles of cisplatine and vinblastine and randomized to a sequential or concurrent radiotherapy schedule. Patients treated with a concurrent schedule showed a significant better 5-year overall survival. A second argument is that the hypofractionated radiotherapy may cause an increase of the acute pulmonary and esophageal toxicity. bBy limiting the number of courses to a total of two, we expect that these side effects will be tolerable.

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

1. Provision of signed, written and dated informed consent prior to any study specific procedures
2. Male or female aged 18 years or older
3. Cytological or histological proven NSCLC stage III or inoperable stage II (cT1*3*3N0-1), according to the 8th edition of the AJCC staging, with a clinical indication for concurrent chemo-irradiation.
4. Patients with locoregional recurrent lung tumor following surgery or a second primary cancer are eligible, unless a pneumonectomy was performed.
5. Minimum required laboratory data
a. Adequate bone marrow reserve: absolute neutrophil (segmented and bands) count (ANC) *1.5 x 109/L, platelets * 100 x 109/L, and hemoglobin * 5.5 mmol/L.
b. Hepatic:
i. Serum bilirubin * 1.5 times the upper limit of normal (× ULN); alkaline phosphatase (AP), aspartate aminotransferase (ASAT), and alanine aminotransferase (ALAT) * 3.0 × ULN.
ii. This does not apply to patients with confirmed Gilbert*s syndrome (persistent or recurrent hyperbilirubinaemia that is predominantly unconjugated in the absence of evidence of haemolysis or hepatic pathology) who will be allowed in consultation with their physician.
c. Renal: GFR * 60 ml/min; if below this threshold a creatinine clearance (CrCL) can be calculated based on the original weight based Cockcroft and Gault formula and should be * 45 ml/min.

Exclusion criteria

1. WHO*performance status * 2
2. FEV1 and DLCO < 35 % of the age- and sex*adjusted normal value
3. Patients with grade 3 dyspnea or worse at baseline (according to CTCAE version 4.03)
4. Prior radiotherapy to the thorax.
5. Participation in another clinical study with an investigational product during the last 4 weeks.
6. Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study or the follow-up period of an interventional study
7. Recent major surgery within 4 weeks prior to entry into the study (excluding the placement of vascular access) that would prevent administration of chemotherapy.
8. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the patient to give written informed consent
9. Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow*up schedule; those conditions should be discussed with the patient before registration in the trial
10. Female patients who are pregnant, breast-feeding or male or female patients of reproductive potential who are not employing an effective method of birth control
11. Any condition that, in the opinion of the investigator, would interfere with evaluation of the chemoradiotherapy or interpretation of patient safety or study results

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	cisplatin
Generic name:	cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Eposin
Generic name:	Etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	pemetrexed
Generic name:	pemetrexed
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-11-2016
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-04-2017
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2016-003790-18-NL
ClinicalTrials.gov	NCT02947113
CCMO	NL57625.031.16