A randomized phase III study of adjuvant chemotherapy with or without low-molecular weight heparin in completely resected non-small-cell lung cancer patients with high-risk for recurrence: NVALT- 8B.

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The primary aim of the study is to investigate whether adding Nadroparin to adjuvant chemotherapy in patients in the poor prognostic group (i.e. high SUV) prolongs recurrence-free survival.

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

Summary

ID

NL-OMON35584

Source
ToetsingOnline

Brief title
NVALT-8B

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non-small cell lung cancer

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Eli Lilly,Farmaceutische industrie,GlaxoSmithKline

Intervention

Keyword: adjuvant chemotherapy, high-risk, LMWH, NSCLC

Outcome measures

Primary outcome

The main endpoint is recurrence-free survival.

Secondary outcome

Secundary end-points are overall survival, dose intensity of subsequent cycles,

quality of life, toxicity, health economics. Exploratory endpoints are analysis

of blood and tumor samples for prognostic markers, genomics/proteomics.

Study description

Background summary

The use of adjuvant chemotherapy and especially cisplatin in combination therapy in patients with completely resected early-stage NSCLC improves recurrence-free and overall survival. In this study we combine cisplatin with a potent and least toxic drug pemetrexed. Subgroup analyses suggested that not all patients benefit from chemotherapy, but how to select patients for treatment is still not clear. In this study we select patients by FDG-PET in a good and a poor prognosis group using FDG avidity as measured by the standardized uptake value (SUV). Several studies suggested that treatment with low-molecular weight heparin (LMWH) improves survival in cancer patients. The hypothesis of this study is that in patients with resected NSCLC and high SUV (poor prognosis group) adding LMWH to four cycles of adjuvant chemotherapy will improve the recurrence-free survival rate.

Study objective

The primary aim of the study is to investigate whether adding Nadroparin to adjuvant chemotherapy in patients in the poor prognostic group (i.e. high SUV) prolongs recurrence-free survival.

Study design

This is a randomized multicenter phase III study. Patient with a high SUVof the primary tumor prior to surgery will be randomised to four cycles of pemetrexed and cisplatin with or without nadroparin for 16 weeks in order to improve the recurrence-free survival rate in these patients. A total of 600 patients will be entered in the study (300 patients in each arm) in 3 years. The follow up will continue for 2 years and 3 months further, at the end of which a total of 243 events would be observed allowing the comparison (alpha=0.05 two-sided log-rank test.) of the curves by treatment arm with 80% power to detect a true difference of 60% versus 70% at 3 years, or HR=0.70.

Intervention

Within 4-6 weeks after surgery all patients will receive 4 cycles of pemetrexed (500 mg/m2) and cisplatin (75 mg/m2) on day 1 every 3 weeks. Patients in de nadroparin arm will receive nadroparin s.c. daily for 16 weeks, 2 weeks therapeutic dose en 14 weeks half-therapeutic dose.

Study burden and risks

Treatment of these patients consists of cisplatin based adjuvant chemotherapy for 4 cycles. After treatment the follow-up of patients will be every 8 weeks for the first 2 years and thereafter every 3 months till 5 years after surgery. Patients in the nadroparin arm will receive nadroparin s.c. daily for 16 weeks. No additional toxicity is expected. The duration of the treatment is 16 weeks and the duration of the study is about 5 years.

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 resectable NSCLC
- SUVmax >= 10
- Age >= 18 years
- WHO Performance score <= 2 before chemotherapy.
- Adequate organ function before administration of chemotherapy, including:
Adequate bone marrow reserve: ANC >= 1.5 x 109/L, platelets >= 100 x 109/L.
Hepatic: bilirubin <= 1.5 x ULN, AP, ALT, AST <= 3.0 x ULN.
Renal: calculated creatinine clearance >= 60 ml/min based on the Cockroft and Gault formula.
INR < 1.5
- Patients must sign and date a written Independent Ethics Committee approved informed consent form.

Exclusion criteria

- Patients with stage IA NSCLC
- Prior chemotherapy or radical radiotherapy for NSCLC.
- Any unstable systemic disease (including active infection, uncontrolled hypertension, unstable angina, congestive heart failure, myocardial infarction within the previous year, severe cardiac arrhythmia requiring medication, hepatic, renal or metabolic disease).
- Concomitant treatment with any other experimental drug under investigation.
- Inability to interrupt aspirin or other nonsteroidal anti-inflammatory agents for a 5-day period (8 day period for long-acting agents such as piroxicam).
- Inability or unwillingness to take folic acid, vitamin B-12 supplementation or

dexamethasone.
- History of any active malignancy (other than NSCLC) unless treated more than 3 years with curative intent and no recurrence, except non-melanoma skin cancer or in situ cervical cancer.
- Pregnancy
- Men and women of child-bearing potential not using effective means of contraception for 6 months after treatment has been completed
- Indication for anticoagulant treatment.
- Any contraindication listed in the labeling of nadroparin.
- Documented history of heparin-induced thrombocytopenia with UFH or LMWH
- Current active bleeding or judged to be as high risk of bleeding;

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2007
Enrollment:	600
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fraxiparin
Generic name:	nadroparin

Ethics review

Approved WMO Date:	21-09-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-07-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-07-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-09-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2007-002608-16-NL
CCMO	NL16517.042.07