Long-term treatment for cancer patients with deep vein thrombosis or pulmonary embolism - a randomized open label study

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

Summary

ID

NL-OMON39493

Source
ToetsingOnline

Brief title
Longheva

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Embolism and thrombosis

Synonym
venous thrombosis / clot

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Leo Pharma,LeoPharma

Intervention

Keyword: anticoagulants, cancer, venous thrombosis

Outcome measures

Primary outcome

The primary efficacy outcome is symptomatic recurrent VTE, i.e. the composite of recurrent DVT and fatal or non-fatal PE. The primary efficacy analysis is based on the time to the first symptomatic recurrent VTE event. The principal safety outcome is major bleeding.

Secondary outcome

Not applicable.

Study description

Background summary

Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), represents a major cause of morbidity and mortality in cancer patients. The risk of VTE is increased several-fold in patients with cancer with incidences ranging between 4% and 20%. Treatment of VTE aims at preventing recurrent events, including potentially fatal PE, which in turn could reduce the morbidity, use of health care resources and, above all, mortality for cancer patients. Recently, randomized clinical trials and prospective cohort studies in cancer patients with acute VTE have shown that low-molecular-weight heparin (LMWH) is more effective in preventing VTE recurrences at a comparable bleeding risk as compared to oral anticoagulants. In the large CLOT study, dalteparin treatment was associated with a 50% reduction in recurrent VTE compared to Vitamin K antagonists (VKA). The guidelines of the American Society of Clinical Oncology and the American College of Chest Physicians, and also the recently published Dutch guideline of

the CBO all advice LMWH for acute and long-term treatment in cancer patients with acute VTE. Generally, after six months of LMWH, indefinite anticoagulant therapy is recommended for patients with active cancer, such as those with metastases or receiving chemotherapy, because of the greater risk for recurrent VTE. For most patients, this means lifelong anticoagulant therapy. The relative benefits and risks of continuing LMWH beyond 6 months versus switching to oral VKA are unknown and therefore remain a clinical judgment in the individual patient.
Therefore, there is an urgent need for a randomized trial that directly compares LMWH and VKA as extended anticoagulant treatment in cancer patients to assess which has the best risk-benefit ratio.

Study objective

The primary efficacy objective is to evaluate whether LMWH is superior to VKAs in the long-term treatment of symptomatic VTE in cancer patients who completed 6 to 12 months of anticoagulant treatment. Two aspects are important: the efficacy with which it prevents recurrent DVT/PE and the bleeding risk.

Study design

This is a multicenter, randomized, open, superiority trial for efficacy.

Cancer patients with confirmed DVT or PE who have completed 6-12 months of treatment with LMWH are eligible for this trial. After randomization, patients will be allocated to VKA or LMWH. The treatment duration will be 6 months. Allocation to treatment will be done by block randomization via a web based application and will be stratified by country.
All outcomes will be evaluated by a central, blinded, independent adjudication committee. Adjudication results will be the basis for the final analysis.
An independent data and safety monitoring board will monitor the patient*s safety during the study and give recommendations to the executive committee.

For all patients, contacts are scheduled at regular time intervals. Including the screening/randomization visit, 4 visits and one phone call are planned. Patients who are randomized but who did not receive study treatment or did discontinue anticoagulant treatment prematurely will at least be seen at the end of the respective treatment periods. During all contacts, the treatment and the clinical course of the patient will be evaluated using a contact report. Patients with suspected efficacy outcomes or bleeding will undergo confirmatory testing. All outcomes are adjudicated by the central independent adjudication committee.

Intervention

Patients will be treated for 6 months with either LMWH or VKA. The type of LMWH

or VKA used, is up to preferences of the local physician and the local guidelines. In case of treatment with VKA, INR values will be monitored. A target INR of 2.5 will be used. LMWH will be used in 2/3 of normal doses (conform the treatment regime in the CLOT study).

Study burden and risks

There is no additional risk associated with participation, because the decision to give long-term (sometimes life long) anticoagulation has already been made prior to participation in the study. Doctors and patients can then choose between LMWH and VKA, based on the current literature there is no preference for one of them. This study only dictates whether LMWH or VKA should be given. Participation will not interfere with the oncological treatment.
The burden of this study is minimally. Next to the screening/randomization visit, there are only 3 visits and 1 phone call. Visits will take maximally 30 minutes (probably much less) and will probably be interwoven with a standard clinical care.
Information from this study will benefit future patients with cancer and PE or DVT and an indication for long-term anticoagulant treatment.

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. Patients with cancer and confirmed PE or DVT of the leg who have been treated for minimally 6 and maximally 12 months with therapeutic doses of anticoagulants, i.e. LMWH or VKA or a new anticoagulant in a trial
2. Written informed consent
3. Indication for long-term anticoagulant therapy (e.g. because of metastasized disease, chemotherapy)

Exclusion criteria

1.* 18 years of age or below the legal age of consent as per country specific regulations
2. Indications for anticoagulant therapy other than DVT or PE
3. Any contraindication listed in the local labeling of enoxaparin, dalteparin, tinzaparin, nadroparin, warfarin, acenocoumarol or fenprocoumon
4. Childbearing potential without proper contraceptive measures, pregnancy or breastfeeding
5. Life expectancy of less than 3 months

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	18-01-2010
Enrollment:	220
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	clexane
Generic name:	enoxaparin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	fragmin
Generic name:	dalteparin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	fraxiparin or fraxodi
Generic name:	nadroparin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	marcoumar
Generic name:	phenprocoumon
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	sinthrom
Generic name:	acenocoumarol
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-09-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2010

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-09-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2009-015336-15-NL
ClinicalTrials.gov	NCT01164046
CCMO	NL29462.018.09

Study results

Date completed:	15-11-2013
Actual enrolment:	10

Summary results
Trial is onging in other countries