TropicALL study; Thromboprophylaxis in Children treated for Acute Lymphoblastic Leukemia with Low-molecular-weight heparin: a randomized controlled trial

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Main objective:To assess the efficacy of thromboprophylaxis with high prophylactic dose LMWH as compared with standard care without systemic thromboprophylaxis in children treated for primary ALL during asparaginase treatment.Secondary objectives:1...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON44520

Source
ToetsingOnline

Brief title
TropcALL study

Condition

- Leukaemias
- Embolism and thrombosis

Synonym
Leukemia; bloodcancer. Venous thromboembolism; clot of blood.

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Kinderoncologie Nederland
Source(s) of monetary or material Support: ZonMw,KIKA fonds

Intervention

Keyword: Acute Lymphoblastic Leukemia, Children, Low-molecular-weight heparin, Thromboprophylaxis

Outcome measures

Primary outcome

Incidence of symptomatic objectified VTE during childhood ALL treatment in the intervention and standard arm during asparaginase treatment.

Secondary outcome

1. Incidence of major bleeding in the intervention and standard arm during asparaginase treatment.

2. Incidence of the clinically relevant non-major bleeding and minor bleeding in the intervention and standard arm during asparaginase treatment.

3. Incidence of composite of asymptomatic and symptomatic objectified VTE during childhood ALL treatment in the intervention and standard arm during asparaginase treatment.

4. Identification of clinical risk factors and hematological biomarkers in consecutively included patients with and without VTE; to increase insight in the pathogenesis of coagulation disorders during ALL treatment, and to establish a risk model for VTE

Study description

Background summary

Venous thromboembolism (VTE) often complicates the treatment of acute lymphoblastic leukemia (ALL), particularly during asparaginase therapy.

Study objective

Main objective:
To assess the efficacy of thromboprophylaxis with high prophylactic dose LMWH as compared with standard care without systemic thromboprophylaxis in children treated for primary ALL during asparaginase treatment.

Secondary objectives:
1. To assess the safety of thromboprophylaxis using high prophylactic dose LMWH as compared with standard of care without systemic thromboprophylaxis in children treated for newly diagnosed ALL, by assessment of the incidence of major bleeding during asparaginase treatment.
2. To identify clinical risk factors or hematological biomarkers in ALL patients with and without symptomatic objectified VTE; to increase insight in the pathogenesis of coagulation disorders during ALL treatment and to establish a risk model for VTE.

Study design

A national, multi-centre, randomized controlled, open-label trial.

Intervention

Intervention-arm:
In the intervention arm, high prophylactic dose LMWH (nadroparin) is subcutaneously injected daily, adjusted to actual body weight with 85 IU anti-Xa/kg with a maximum of 5700 IU anti-Xa daily. Target anti-Xa level: 0.3-0.4 IU/ml).

Standard of care-arm:
The comparator treatment in the standard of care control arm is no systemic thromboprophylaxis, i.e. no intervention, which is the current standard during childhood ALL treatment. Placebo injections will not be applied.

Study burden and risks

The route of administration is by subcutaneous injections; by self-administration or by administration by their parents / caretakers or nurses. The burden is that patients will have to receive or administer subcutaneous injections for the entire duration of asparaginase therapy. Pain of subcutaneous injections can be relieved by using anesthetic creme (EMLA

creme) or by using insuflon, a subcutaneous catheter.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

a. Written informed consent for TropicALL randomisation has been given
b. Newly diagnosed patients with T-lineage or precursor-B lineage ALL (patients with mature B-ALL are not eligible)
c. Age between * 366 days and < 19 years
d. Diagnosis ALL confirmed by DCOG laboratory

e. Patient should be treated in a Dutch Childhood Oncology Centre

Exclusion criteria

a. Patients who are already being treated with anticoagulation upon screening (for other indications)
b. Patients with a heparin allergy (or for one of its components), a recent history (within 6 months) of heparin-induced thrombocytopenia (HIT) or any other contraindication listed in the local labeling of LMWH
c. Patients with active bleeding or high risk for bleeding contraindicating anticoagulant therapy (Thrombocytopenia is not an exclusion criterion)
d. Patients with renal insufficiency (glomerular filtration rate (GFR) < 30 ml/min/1.73m2)
e. Patients with hepatic disease which is associated with coagulopathy leading to a clinically relevant bleeding risk
f. Patients with stage 2 hypertension defined as blood pressure confirmed > 99th percentile + 5 mmHg
g. Patients with any condition that, as judged by the investigator, would place the patient at increased risk of harm if he/she participated in the study.
h. Patients who are included in the ALL-11 IVIG study
i. Patients with Ph-positive ALL (documented presence of t(9;22)(q34;q11) and/or of the BCR/ABL fusion transcript). These patients will be transferred to the EsPhALL protocol in induction according to the guidelines of the EsPhALL protocol.

Study design

Design

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

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	354
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Fraxiparin
Generic name:	Nadroparin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-11-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-05-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2014-003303-30-NL
CCMO	NL50440.078.14