Long-term outcome after heparin plus edoxaban versus heparin plus vitamin K antagonists for acute deep vein thrombosis and pulmonary embolism

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON42861

Source
ToetsingOnline

Brief title
Hokusai post VTE

Condition

- Other condition
- Pulmonary vascular disorders
- Embolism and thrombosis

Synonym
embolism, thrombosis

Health condition

kwaliteit van leven

Research involving
Human

Sponsors and support

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

Intervention

Keyword: DOAC, Post thrombotic syndrome, Quality of Life, Vitamin K antagonist

Outcome measures

Primary outcome

The primary outcome among the DVT group is the cumulative incidence of PTS in patients with an acute DVT treated with heparin plus edoxaban versus heparin plus warfarin. PTS is defined as a Villalta total score of >=5 or the presence of a venous ulcer. Among the PE patients, the primary outcomes are Quality of Life (SF-36 and PembQoL) at least 2 years after the index PE.

Secondary outcome

Secondary study outcomes are the QOL of patients with PTS compared to patients without PTS and the incidence of PTS based on the patient-reported Villalta compared to the original Villalta scale score.

Among the PE patients, the secondary study outcome is the feasibility of pro-active case-finding of CTEPH in Hokusai post VTE study selected patients with acute PE by use of a recently derived risk stratification score based on clinical variables and detailed assessment of index CTPA scans.

Study description

Background summary

Post thrombotic syndrome (PTS) and chronic thromboembolic pulmonary hypertension (CTEPH) are long-term complications of deep vein thrombosis (DVT) and pulmonary embolism (PE), respectively. For development of PTS, it is known that poor quality treatment with vitamin K antagonists (VKA) is a risk factor. Direct oral anticoagulants (DOACs) have a more stable pharmacologic profile than VKA. We hypothesize that treatment of venous thromboembolism (VTE) with the direct oral anticoagulant (DOAC) edoxaban leads to improved thrombus resolution and thereby less long-term sequelae, translating into better quality of life and a lower incidence of both PTS and CTEPH, compared to treatment with heparin followed by VKA.

Study objective

To assess the long-term PE-related Quality of Life and to assess the cumulative incidence of PTS in patients with acute DVT, treated with heparin plus edoxaban in comparison to patients treated with heparin plus warfarin. Furthermore, the feasibility of pro-active case-finding of CTEPH will be evaluated in selected patients with acute PE by use of a recently derived risk stratification score, based on clinical variables and detailed assessment of index computed tomography pulmonary angiography (CTPA) scans.

Study design

This investigator-initiated cohort study includes patients who participated in the Hokusai venous thromboembolism (VTE) trial. The Hokusai VTE trial was a randomized, double-blind, non-inferiority trial that compared the efficacy and safety of heparin (enoxaparin or unfractionated heparin) followed by edoxaban with heparin (enoxaparin or unfractionated heparin) followed by warfarin (target INR 2-3) in patients with acute, symptomatic VTE. A subset of centers that participated in the Hokusai VTE trial will be invited to collect follow-of previously enrolled patients at least 2 years after the index VTE. Patients with an index DVT will be asked to complete the VEINES-QOL questionnaire, and to assess the venous disease-specific quality of life the Villalta score will be calculated. The objectively and subjectively obtained Villalta score will be compared. Among patients with an index PE, the QoL will be assessed by the validated generic (SF-36) and pulmonary embolism specific (PEmbQoL) questionnaires. Patients diagnosed with both PE and DVT at index will be examined for PTS and will be asked the complete all questionnaires. In addition, the CTEPH risk stratification score will be assessed in a substudy among 1000 HOKUSAI-PE patients of which detailed CTPA scans are already available, and selective follow-up of high-risk patients will be performed with

echocardiography in centers that are willing to participate in the substudy (target n= 250).

Patients of selected centres will be requested to enrol in this study. Patients will be invited by the participating centres. For Hokusai DVT patients, the single hospital visit will included an examination of the affected leg and patients are asked to fill out 2 questionnaires. Hokusai PE patients will be asked to only complete the questionnaires. When patients are identified as a high risk patient for CTEPH according to the CTEPH risk stratification score, additional follow-up will be performed with echocardiography and standard care for CTEPH might follow.

Study burden and risks

All VTE patients will be asked to visit the hospital on one occasion for physical examination and to complete one, two or three QoL questionnaires. For PE patients that are classified as having a high risk of developing CTEPH, additional echocardiography will be performed. No serious risks are associated with echocardiography, but false positive or incidental findings can be regarded as a burden to patients. The study has some potential benefits. When CTEPH is diagnosed, before end stage right ventricular dysfunction has occurred, it may be curable by a surgical intervention.

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 from centers that participated in the Hokusai VTE trial and where implementation of this study is feasible.

Exclusion criteria

Inability for follow-up due to geographic or logistic reasons, or death.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-04-2017
Enrollment:	255
Type:	Actual

Ethics review

Approved WMO Date:	21-10-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-09-2017
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
ClinicalTrials.gov	NCT00986154
CCMO	NL58725.018.16