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EXCOA-CVT study: the benefit of EXtending oral antiCOAgulation treatment after acute Cerebral Vein Thrombosis

Submission date
14/02/2014

Recruitment status
No longer recruiting

Registration date
10/04/2014

Overall study status
Completed

Last Edited
28/05/2024

Condition category
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Cerebral vein and dural sinus thrombosis (CVT) is a rare type of cerebrovascular disease (conditions that develop as a result of problems with the blood vessels inside the brain). It most often affects young people and with potentially disabling or fatal consequences. Patients suffering a CVT are likely to be at increased risk of having further blood clots in the brain or in different parts of the body. Oral anticoagulation treatment (medicine that reduces the ability of the blood to clot) is given to prevent such recurrences, although there is a risk of severe bleeding. The optimal duration of anticoagulation after a CVT is unknown and based on the doctors preference or expert consensus. Our goal is to improve the therapeutic use of anticoagulation after the acute phase of an episode of CVT, by comparing a short (3-6 months) versus a long (12 months) treatment approach for the prevention of blood clot recurrences.

Who can participate?
Adults (age over 18 years) with a confirmed CVT (diagnosed less than 1 month ago) and able to start oral anticoagulation.

What does the study involve?
Before the study starts, each of the participating medical centres will be asked whether they have a preference for any of the two treatment options. If so, they will follow their preferred treatment policy. Centres with no preference will be given the alternative to adopt one of the options or to be randomly allocated to one of the two treatment policies: short (3-6 months) or long-term (12 months) oral anticoagulation. Patients will be treated according to the treatment approach initially allocated to their centre. The treating physicians will be responsible for decisions about type of oral anticoagulant, medication adjustments, inpatient or outpatient management during the assigned study period. Patients included in the study will have follow-up appointments at 6, 12 and 24 months from the date of entry. Information about recurrent symptomatic CVT, other symptomatic venous or arterial blood clots, bleedings or any other major incident will be evaluated and recorded at every follow-up visit.

What are the possible benefits and risks of participating?
Those taking part on the study will benefit from a structured diagnostic examination, careful follow-up and the possibility of the best treatment approach. In addition, there should be improvements in treatment for future patients with CVT. The main risk of anticoagulation therapy is bleeding. However, this is preventable by close monitoring and medication adjustment. Furthermore, the current medical consensus is that the benefits of anticoagulant treatment after the acute phase of CVT outweigh the risks. The main doubt is for how long this treatment is advantageous.

Where is the study run from?
This study is part of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT2) project, which involves near 100 centres in more than 20 countries worldwide. It has been set up by the Clinical Neurology Research Unit of the Molecular Medicine Institute (Lisbon, Portugal) in collaboration with the Hospital de Santa Maria (Lisbon, Portugal).

When is the study starting and how long is it expected to run for?
It is anticipated that recruitment will start in March 2014. Participants enrolled on the study will be followed up for a period of 2 years. The study is expected to end in March 2023.

Who is funding the study?
Funding has been provided by grants from the AstraZeneca Foundation, Faculty of Medicine (University of Lisbon) and from the Hospital de Santa Maria North of Lisbon Medical Centre.

Who is the main contact?
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Contact information

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
A multicentre, multinational study with a randomised cluster allocation design comparing the efficacy and safety of short (3-6 months) versus long-term (12 months) oral anticoagulation for the prevention of venous thromboembolic events after an episode of cerebral vein thrombosis

Acronym
EXCOA-CVT

Study objectives
Due to the risk of thromboembolic recurrence, oral anticoagulation is recommended after the acute phase of cerebral vein thrombosis (CVT). The optimal duration of this treatment is unknown. The majority of these recurrences occur during the first year, although the absolute risk of recurrence is low. Extended oral anticoagulation could prevent a recurrence, but it can also increase the risk of major bleeding.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical Committee - Faculty of Medicine (University of Lisbon) and Hospital de Santa Maria (Lisbon, Portugal), 01/06/2011

Study design
Multicentre multinational prospective study with a cluster allocation design for the therapeutic approach

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cerebral vein thrombosis

Interventions
Before the study starts, each of the participating centres will be asked whether they have a preference for any of the policy treatment options. If so, they will follow their preferred policy. Centres with no preference will be given the alternative to adopt one of the policies or to be randomly allocated to one of the policy treatment options. Patients will follow a treatment of short-term (3-6 months) or long-term (12 months) oral anticoagulation according to the approach initially allocated to their centre, as soon as their acute clinical situation is stable and not more than 1 month after the CVT diagnosis. The total follow-up time will be 24 months.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Any confirmed fatal or nonfatal venous thromboembolic event. The primary outcomes will be measured at 6, 12 and 24 months.These are the compulsory timepoints. However, we also suggest a phone interview at 18 months.

Key secondary outcome(s))
1. Recurrent CVT: any new neurological symptom with a new thrombus or occlusion (partial or total) of a cerebral vein or dural sinus and confirmed by repeated conventional CT venography, MRI combined with MR venogram, conventional angiography or surgery, following established diagnostic criteria.
2. Deep vein thrombosis (lower or upper limbs, pelvic or abdominal): acute, symptomatic proximal deep-vein thrombosis of the legs, arms or of any abdominal vein, objectively verified with the use of compression ultrasonography or venography of leg veins or arm veins, CT angiography/venography, MRI combined with angiography/venogram, conventional angiography or at surgery.
3. Pulmonary embolism: acute, symptomatic pulmonary embolism objectively verified with the use of ventilation-perfusion
lung scanning, angiography or spiral computed tomography of pulmonary arteries.
4. Arterial thrombotic event (stroke, acute MI, acute arterial limb ischaemia, death proven to be secondary to an arterial vascular event)
5. All thrombotic events (arterial and venous)
6. Death proven to be secondary to a vascular event (arterial or venous), sudden unexplained death (<24 h), nonvascular and death of unknown aetiology

The secondary outcomes will be measured at 6, 12 and 24 months.These are the compulsory timepoints. However, we also suggest a phone interview at 18 months.

Completion date
01/01/2024

Eligibility

Key inclusion criteria
1. Patients with acute symptomatic and radiologically confirmed cerebral vein thrombosis (CVT)
2. Age ≥ 18 years at entry
3. CVT must have been diagnosed in <1 month before inclusion

4. The patient must be clinically stable and able to stop parenteral anticoagulation in order to initiate oral anticoagulation
5. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1030

Key exclusion criteria
1. Systemic life-threatening or major bleeding while on anticoagulants during the acute phase of CVT or during the 6 months prior to randomisation (intracranial bleeding due to inclusion CVT is not an exclusion criteria)
2. General contraindications for anticoagulant therapy
3. Need for prolonged treatment with antiplatelet drugs, non-steroidal anti-inflammatory drugs or other drugs/diseases that interfere significantly with anticoagulant therapy or with INR
4. Life expectancy < 2 years due to a pre-existing condition (including any malignancy)
5. Childbearing potential without adequate contraceptive measures, pregnancy or breastfeeding
6. Known allergy to study medications
7. Other conditions judged by the investigator to be an absolute indication for prolonged oral anticoagulation such as recurrent CVT, venous thromboembolism (VTE) after CVT or first CVT with antiphospholipid syndrome or known severe thrombophilia (antithrombin, protein C or protein S deficiency, homozygous factor V Leiden or prothrombin G20210A mutation or combined abnormalities)

Date of first enrolment
01/03/2014

Date of final enrolment
01/01/2024

Locations

Countries of recruitment
United Kingdom

Austria

Belgium

Brazil

Denmark

Finland

France

Germany

Greece

India

Italy

Mexico

Netherlands

Norway

Poland

Portugal

Slovakia

Slovenia

Spain

Sweden

Switzerland

Study participating centre
Unidade Neurológica de Investigação Clínica do Instituto de Medicina Molecular
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Sponsor information

Organisation

Institute of Molecular Medicine (Instituto de Medicina Molecular) (Portugal)

ROR
https://ror.org/01c27hj86

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
AstraZeneca Foundation (USA)

Funder Name
Faculty of Medicine, University of Lisbon (Portugal)

Funder Name
Hospital de Santa Maria - North of Lisbon Medical Centre (Portugal)

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/10/2018	24/04/2019	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes