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Extended AntiCoagulation Treatment for venous thromboembolism (VTE)

Submission date	Recruitment status	[X] Prospectively registered
22/07/2010	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/09/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
05/03/2021	Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2101-022119-20

Protocol serial number
1

Study information

Scientific Title

Extended anticoagulation treatment for venous thromboembolism (VTE): a prospective multicentre randomised controlled trial

Acronym
ExACT

Study objectives
This study will primarily investigate the role of extending treatment with oral anticoagulation for those patients with raised d-dimer levels prior to discontinuing treatment and will study the impact of this management on both recurrence of thrombosis and development of post-thrombotic syndrome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Prospective multicentre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Venous thromboembolism (VTE)

Interventions
Patients will be randomly allocated to either continue warfarin (Group W) for a further 2 years or to discontinue treatment (Group O).

Visit 1:
Patients will be interviewed and their medical notes reviewed. Data collected will be:
1. Concomitant medications
2. Smoking status
3. Alcohol consumption
4. Medical history
5. Body mass index (BMI)
6. INR data (therapeutic control in terms of percentage time in range from the start of their treatment)
7. Family history of VTE

A heparinised venous sample of blood will be taken for a d-dimer test on a point-of-care device (Cobas h 232, Roche diagnostics) and then sent to a central laboratory to be frozen and stored for d dimer testing at the end of the study.

All patients will be clinically examined for signs and symptoms of post thrombotic syndrome (PTS) using a validated clinical scoring system (the Villalta scale) and will also complete the VEINES quality of life score as well as EQ 5D which allows the measurement of broad aspects of quality of life.

Patients randomly allocated to Group W will be followed-up through their usual oral anticoagulation service provided in terms of warfarin management and the anticoagulation clinic lead will be asked to extend their clinic visits for a further 2 years.

Patients randomly allocated at this point to Group O will undergo a further d-dimer test 1 month after cessation of treatment. Again both researcher and patient will be blinded to this result.

Visits 3 - 7:
All patients randomised (Groups W and Group O) will be reviewed every 6 months for 2 years in total to assess evidence of VTE recurrence, clinical assessment of PTS, and measurement of d-dimer (again patient and researcher are blinded to these results).

All patients will be asked to complete the VEINES-QOL/Sym a validated disease specific, quality of life score, and EQ 5D, questionnaires at the start of the study and at the 6 monthly reviews.

If a patient in Group O (off warfarin) has their warfarin restarted by their GP during the study period, the patient will be removed from the study.

The total duration of treatment and follow-up in all arms of the trial is 2 years.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oral anticoagulation

Primary outcome(s)
Number of recurrent thrombotic events between those showing a positive d-dimer on treatment and those showing a positive d-dimer who receive no treatment, measured every 6 months for 2 years.

Key secondary outcome(s))
Measured every 6 months for 2 years:
1. Severity of PTS between groups
2. Bleeding events
3. INR control in terms of percentage time in range
4. Optimal cut off on a d-dimer result -
5. Costs of d-dimer and subsequent extended treatment with anticoagulation
6. Cost effectiveness
7. Information on the types of patient who potentially benefit from extended warfarin treatment, age and gender
8. Patient quality of life

Completion date
30/09/2015

Eligibility

Key inclusion criteria
1. Aged 18 years or over, either sex
2. Diagnosis of first unprovoked proximal deep vein thrombosis (DVT) or pulmonary embolism (PE)
3. On treatment with anticoagulants
4. Have completed 3 - 6 months of anticoagulant therapy (target 2 - 3)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
281

Key exclusion criteria
1. Patients under the age of 18 years
2. Patients with another indication for long term warfarin therapy, e.g., atrial fibrillation
3. Patients with a diagnosis of first unprovoked proximal DVT or PE who are no longer on anticoagulation therapy
4. Patients with a high risk of bleeding as evidenced by any of the following:
4.1. Patients with a previous episode of major bleeding where the cause was not effectively treated
4.2. Known thrombocytopaenia with a platelet count of less than 120 x 10^9 /L
4.3. Known chronic renal failure with a creatinine of more than 150 umols/L (1.7 mg/dl) or estimated glomerular filtration rate (eGFR) less than 30
4.4. Known chronic liver disease with a total bilirubin of more than 25 umols/L (1.5 mg/dl)
4.5. Active peptic ulcer
4.6. Poor compliance with, or control of, anticoagulation therapy during initial treatment (International Normalised Ratio [INR] control less than 50% time in range)
4.7. Patients requiring dual antiplatelet therapy (e.g., aspirin and clopidrogel)
5. Patients with a vena cava filter in place
6. Patients who have had a ddimer test performed within 2 months of potential enrolment other than for evaluation for suspected recurrent VTE that was not confirmed
7. Patients whose GP expects their life expectancy to be less than 5 years

8. Patients unable to attend follow up visits due to geographic inaccessibility
9. Patients participating in a competing investigation
10. Patients with known antiphospholipid syndrome or known deficiency
11. Patients with a diagnosis of active cancer
12. Patients unwilling to give consent

Date of first enrolment
30/09/2010

Date of final enrolment
30/09/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Primary Care Clinical Sciences
Birmingham
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Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (NIHR) (UK) - Programme Grant for Applied Research (PGfAR) (ref: RP-PG-0608-10073)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	27/11/2019	02/01/2020	Yes	No
Results article	results	01/05/2020	05/03/2021	Yes	No
Protocol article	protocol	09/03/2013		Yes	No