

Extended AntiCoagulation Treatment for venous thromboembolism (VTE)

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

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 $120 \times 10^9 /L$
 - 4.3. Known chronic renal failure with a creatinine of more than 150 $\mu\text{mol}/L$ (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 $\mu\text{mol}/L$ (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 clopidogrel)
5. Patients with a vena cava filter in place
6. Patients who have had a d-dimer 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

United Kingdom

B15 2TT

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