Feb 25, 2020

Start or STop Anticoagulants Randomised Trial (SoSTART) after spontaneous intracranial haemorrhage

Rustam Al-Shahi Salman[1], Martin S. Dennis[1], Kasia Adamczuk[1], Karen Innes[1], Ruth Fraser[1], Jonathan Drever[1], Lynn Dinsmore[1], Carol Williams[1], Steff Lewis[1], Philip M. White[2], David E. Newby[1], Gregory Y.H. Lip[3], Adrian Parry-Jones[4], Dan Lasserson[5], Colin Oliver[6], Joanna Wardlaw[1], John Norrie[1]

[1]University of Edinburgh, [2]University of Newcastle-upon-Tyne, [3]University of Liverpool, [4]University of Manchester, [5]University of Birmingham, [6]The Stroke Association

1 Works for me dx.doi.org/10.17504/protocols.io.bcw4ixgw

Rustam Al-Shahi Salman
University of Edinburgh

ABSTRACT

Primary research question

For adults surviving spontaneous (non-traumatic) symptomatic intracranial haemorrhage with persistent/paroxysmal atrial fibrillation/flutter (AF), does starting full treatment dose oral anticoagulation (OAC) result in a beneficial net reduction of all serious vascular events compared with not starting OAC?

Trial design

Investigator-led, multicentre, randomised, open, assessor-masked, parallel group, clinical trial of investigational medicinal product (CTIMP) prescribing strategies. We plan for a pilot phase, followed by a safety phase.

Objectives

Pilot phase: ~30 hospital sites keep screening logs and recruit at least 60 participants >24 hours after spontaneous symptomatic intracranial haemorrhage with AF and a CHA2DS2-VASc score ≥2 to determine the acceptability and feasibility of recruiting the target sample size in a definitive trial in an acceptable timescale.

Safety phase: ~60 hospital sites will recruit at least 190 participants to determine whether the risk of recurrent symptomatic intracranial haemorrhage is sufficiently low (non-inferior) to justify a definitive trial.

Eligibility criteria

Inclusion: Spontaneous symptomatic intracranial haemorrhage, AF and a CHA2DS2-VASc score ≥2.

Exclusion: Patient age <18 years. Symptomatic intracranial haemorrhage within the last 24 hours. Brain imaging that first diagnosed the intracranial haemorrhage is not available. Intracranial haemorrhage is exclusively due to trauma or haemorrhagic transformation of ischaemic stroke. Patient or their doctor is certain about whether to start full dose OAC. Intention to implement the allocated treatment strategy for <1 year. Patient is not registered with a general practitioner. Patient is pregnant, breastfeeding, or of childbearing age and not taking contraception. Lactose intolerance. Patient and carer unable to understand spoken or written English. Previously randomised in SoSTART.

Brain magnetic resonance imaging (MRI) sub-study: MRI must be done after intracranial haemorrhage but before randomisation. Sub-study participants must not have contraindications to MRI.

Setting

Recruitment in secondary care (inpatient and outpatient services in stroke, general internal medicine, medicine of the elderly, cardiology, neurology and neurosurgery) with follow-up in primary and secondary care.

Randomisation

Central, web-based randomisation, with 1:1 allocation of intervention: comparator, using a minimisation algorithm.

Intervention

Start long-term (≥1 year) full treatment dose OAC (either a non-vitamin K antagonist direct oral anticoagulant [DOAC] or vitamin K antagonist if a DOAC cannot be used), chosen by the patient's physician before randomisation.
Comparators Do not start OAC (standard clinical practice without OAC may include antiplatelet drug(s) or no antithrombotic drugs).

Outcome measures

Pilot phase: The proportions of eligible patients who are recruited, unsuitable, or decline to participate; the acceptability of the trial protocol to investigators and patients; and the rate of recruitment per site.

Safety phase: Primary outcome: Recurrent, symptomatic, spontaneous intracranial haemorrhage. Exploratory outcomes: All symptomatic serious vascular events (i.e. major adverse cardiac or cerebrovascular events [MACCE]) including non-fatal stroke and spontaneous subdural haemorrhage, non-fatal myocardial infarction, vascular death, sudden death, or death of unknown cause. Individual symptomatic vascular events. Individual types of fatal events. Dependence according to the modified Rankin Scale.

Follow up

At least one year after randomisation, using annual questionnaires to participants and their GPs, including review of any medical records and brain imaging relating to outcomes.

Sample size

We plan to recruit at least 60 participants in a pilot phase and at least 190 participants in a safety phase (12% equivalence margin in the outcome of symptomatic intracranial haemorrhage, 1-sided p=0.025 and power 90%).

EXTERNAL LINK

http://www.SoSTART.ed.ac.uk

THIS PROTOCOL ACCOMPANIES THE FOLLOWING PUBLICATION

Sponsor number AC16141, EudraCT number 2016-004121-16, REC number 17/SS/0082, ClinicalTrials.gov Identifier NCT03153150, Version number 6.0, 23 January 2020

ATTACHMENTS

2020_01_23_SoSTART protocol _v 6.0.pdf