Professional summary

www.RESTARTtrial.org

REstart or STop Antithrombotics Randomised Trial

SUMMARIES

Professional summary

Primary research question	For adults surviving spontaneous (non-traumatic) intracerebral haemorrhage (ICH) who had taken an antithrombotic (i.e. anticoagulant or antiplatelet) drug for the prevention of vaso-occlusive disease before the ICH, does a policy of starting antiplatelet drugs result in a beneficial net reduction of all serious vascular events compared with a policy of avoiding antiplatelet drugs?
Trial design	Investigator-led, multicentre, randomised, open, assessor-blind, parallel group, clinical trial of investigational medicinal product (CTIMP) prescribing strategies.
Setting	UK National Health Service (NHS) secondary care (inpatient and outpatient services in stroke, neurology and neurosurgery) and primary care.
Eligibility criteria	**Inclusion:** Patient age ≥18 years. Spontaneous primary or secondary ICH. Patient had taken antithrombotic drug(s) for the prevention of vaso-occlusive disease before ICH onset. Randomisation more than 24 hours after ICH onset. Patient and their doctor are uncertain about whether to start or avoid antiplatelet drugs. Patient is registered with a general practitioner (GP). Brain imaging that first diagnosed the ICH is available. Participant or representative consent. **Exclusion:** ICH due to preceding trauma or haemorrhagic transformation of ischaemic stroke. Patient is taking an anticoagulant drug following ICH. Patient is pregnant, breastfeeding, or of childbearing age and not taking contraception. Patient and carer unable to understand spoken or written English. **Brain magnetic resonance imaging (MRI) sub-study:** MRI done after ICH but before randomisation**.** No claustrophobia. MRI not contraindicated.
Randomisation	Central, web-based randomisation system using a minimisation algorithm, with 1:1 treatment allocation to which central research staff are masked.
Interventions	Start antiplatelet drug(s) (one or more of aspirin, clopidogrel, or dipyridamole, chosen by patient's physician pre-randomisation) *vs.* avoid antiplatelet drug(s).
Outcome measures	**Primary outcome:** recurrent symptomatic ICH **Secondary outcomes:** symptomatic haemorrhagic events; symptomatic vaso-occlusive events; symptomatic stroke of uncertain type; other fatal events; modified Rankin Scale score; adherence to antiplatelet drug(s).
Follow up	*Central:* annual postal or telephone questionnaires to participants and their GPs. *Local:* medical records and any brain imaging relating to outcomes. *Administrative data:* Flagging and the GP Clinical Practice Research Datalink (CPRD).
Power	Given that the annual recurrence rate of ICH may be 1.8-7.4% and there may be a 1-4-fold relative increase in this risk on antiplatelet drugs, this trial will have 90% power to detect a doubling of an annual ICH rate of 4.5% or 93% power to detect a quadrupling of an annual rate of 1% over two years at the 5% level. This trial will also provide adequately precise estimates of the rates of all serious vascular events to inform the design of a trial with the power to assess net clinical benefit.
Statistical methods	Hazard ratio after randomisation, adjusted for baseline covariates included in the minimisation algorithm.
Sample size	Recruitment began on 22 May 2013 and the target sample size is at least 720 participants in the main trial (at least 550 in the MRI sub-study).