

# Ongoing Trials ESC Hamburg 2011

**OAID2**

**Subject area/topic: Ongoing Trial**

**The Efficacy of Cerebrolysin in Patients With Acute Ischemic Stroke**

The study investigates the clinical efficacy and safety of a 7-day course of therapy with daily intravenous administration of 60 mL Cerebrolysin based on a comparison with Placebo in patients with acute ischemic stroke. 60 patients will be randomized in this trial in 2 parallel groups, one receiving Cerebrolysin, the control group receiving Placebo. Study drug will be given once daily by intravenous infusion for 7 consecutive days. Acetylsalicylic acid will be given orally, twice daily throughout the study duration of 90 days as basic treatment. The clinical observation period for each patient will be 3 months and will include four clinical evaluation visits at Baseline (day 1) and on study days ,7, 30 and 90.this study will be completed three months later (february 2011). Primary Outcome Measures: •Modified Rankin Scale : 90 days after start of treatment •Barthel Index : 90 days after start of treatment •NIH Stroke Scale : 90 days after start of treatment

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## OAID4

### Subject area/topic: Ongoing Trial

#### THE INTERVENTIONAL MANAGEMENT OF STROKE (IMS) III TRIAL: AN ONGOING PHASE III TRIAL

**BACKGROUND AND PURPOSE:** The IMS I and II pilot trials showed that the combined intravenous (IV) and intra-arterial (IA) approach to recanalization may be more effective than standard IV rt-PA (Activase®) alone for moderate-to-large ischemic strokes with a similar safety profile. Therefore, the primary objective of this NIH-funded, Phase III, randomized, multi-center, open-label clinical trial is to determine whether a combined IV/IA approach to recanalization is superior to standard IV rt-PA alone when initiated within three hours of acute ischemic stroke onset. **METHODS:** A projected 900 subjects with moderate-to-large ischemic strokes between ages 18-82 will be enrolled at over 50 centers in the United States, Canada, Australia and Europe. Subjects will be randomized in a 2:1 ratio (IV/IA : IV). The IV rt-PA alone group will receive the full standard dose of rt-PA intravenously over an hour. The combined IV/IA group will receive a lower dose of rt-PA over 40 minutes followed by immediate angiography. If an appropriate thrombus is identified, treatment will continue with either the Merci® Retriever or the Penumbra System™ thrombus-removal device, infusion of rt-PA and delivery of low-intensity ultrasound at the site of the occlusion via the EKOS® Micro-Infusion Catheter (in US only), or infusion of rt-PA via a standard micro-catheter. Additional new devices will be evaluated as they become clinically available. The choice of IA strategy will be made by the treating neurointerventionalist. The primary outcome measure is a modified Rankin Score of 0-2 at 3 months. The primary safety measure is mortality at 3 months and symptomatic ICH within 36 hours. **CONCLUSIONS:** The IMS III Trial will test the safety, feasibility, and potential efficacy of a combined IV/IA approach to recanalization. As of December 1, 2010, 458 subjects had been randomized. **TRIAL CONTACT INFORMATION:** Program Manager, Judith Spilker, spilkeja@ucmail.uc.edu, 513-558-4350. Administrative Coordinator, Rose Beckmann, beckmare@ucmail.uc.edu, 513-558-3907. <http://www.ims3.org>

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## OAID6

### Subject area/topic: Ongoing Trial

#### VAST: Vertebral Artery Stenting Trial

**Background:** Twenty to 30 percent of all transient ischaemic attacks (TIA's) and ischaemic strokes involve tissue supplied by the vertebrobasilar circulation. In about a quarter of the patients atherosclerotic stenosis  $\geq 50\%$  of the vertebral artery accounts for vertebrobasilar stroke or TIA. The risk of recurrent vascular events in patients with vertebral artery stenosis is uncertain and revascularisation is not frequently performed. Treatment of vertebral artery stenosis by percutaneous transluminal angioplasty has been introduced as an attractive treatment option. The safety and benefit of stenting as compared with best medical therapy alone remains to be elucidated in a randomised clinical trial. **Objectives:** The primary aim of the Vertebral Artery Stenting Trial (VAST; ISRCTN29597900) is to assess whether stenting for symptomatic vertebral artery stenosis  $\geq 50\%$  is both feasible and safe. A secondary aim is to assess the rate of new vascular events in the territory of the vertebrobasilar arteries in patients with symptomatic vertebral artery stenosis  $\geq 50\%$  on best medical therapy with or without stenting. **Design:** This is a randomised, open clinical trial, comparing best medical treatment with or without vertebral artery stenting in patients with recently symptomatic vertebral artery stenosis. The trial will include a total of 180 patients with TIA or non-disabling ischaemic stroke that may be attributed to vertebral artery stenosis of at least 50%. The primary outcome is any stroke, vascular death, or non-fatal myocardial infarction within 30 days after start of treatment. Secondary outcome measures include any stroke or vascular death during follow-up and the degree of (re)stenosis after one year. As of January 2011, a total of 66 patients have been included. **Funding:** Netherlands Heart Foundation, grant number 2007B045.

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## OAID7

### Subject area/topic: Ongoing Trial

Lipoprotein- associated phospholipase A2 serum mass correlated with cognitive impairment in small vessel stroke and white matter disease. A possibility or not? A preliminary report.

**Objective** Lipoprotein- associated phospholipase A2 (Lp-PLA2) has been known to be an independent predictor of cardiovascular disease. There has also been some evidence of its potential role in identifying those individuals at risk of developing dementia. Our objective is to examine to what extent Lp-PLA2 contributes to cognitive impairment in small vessel stroke and white matter disease. **Methods** In this five-year on going study 45 subjects of a mean age 71 years (25 female and 20 male) with acute cerebrovascular disorders due to small vessel stroke, as well as an equal and comparable, in terms of age and gender, control sample, were included. Patients were evaluated upon hospital admission by the Canadian Neurological Scale, Clinical Dementia Rating Scale and the Mini-Mental State Examination . All subjects were re-examined one month later and from then on in three month intervals. Lp-PLA2 mass was measured by immunoassay (ELISA) for quantitative determination using BIOTEK analyzing technology. Blood samples were obtained during the first three hours of symptom onset. **Results** A multiple logistic regression model was employed in order to determine the associations of Lp-PLA2 with cognitive decline. The first month of the study showed no association. A year later the levels of Lp-PLA2 mass seem to present a weak correlation. After adjusting for coronary heart disease, hypertension, atrial fibrillation, diabetes mellitus, hyperlipidemia, alcohol consumption, smoking and statin treatment, patients with a larger burden of white matter hyperintensities and elevated Lp-PLA2 mass had a greater degree of cognitive impairment and worse outcome. Another issue which has surfaced is the high mean levels of Lp-PLA2 mass in the control group. Is it coincidence or a reality in Greek patients? This is currently being investigated. **Conclusion** Lp-PLA2 mass serum levels seem to be related to cognitive deficits, but further studies are needed to elucidate this issue.

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## **OAID10**

### **Subject area/topic: Ongoing Trial**

#### **ASPIS - Austrian Polyintervention Study to Prevent Cognitive Decline after Ischemic Stroke**

**Background:** Cognitive impairment after stroke is a considerable burden to stroke survivors and their caregivers. Prevalence of post-stroke dementia was found up to 32%, and is 4-6 times higher than in stroke-free persons. Current research suggests that treatment should be individualized as well as multifactorial. Aim of this study is to test whether intensive polyinterventional therapy including life style modification can reduce the risk of cognitive decline in stroke patients compared to a group of stroke patients receiving standard care. **Methods:** This Phase IV clinical trial is designed as a multicenter, randomized, observer-blind, parallel group clinical study with 200 acute ischemic stroke patients divided into two groups. Group one receives intensive control and motivation for better compliance with medication, regular blood pressure measurements, diet changes, regular physical activity and cognitive training. Group two obtains stroke care according to standard guidelines. The primary outcome variable is cognitive decline at 24 months after randomization, detected by a series of tests including speed of mental processing, executive functions, working memory, memory and spatial constructive functions, and ADAS-cog. Secondary outcome variables include MMSE, NIHSS, Modified Rankin Scale, Barthel Index, Quality of Life, Depression, vascular events and all cause mortality. **Progress:** At January 2011 three centers in Lower Austria participate in this study. In late 2011 all 200 patients will be recruited and the 24 months follow up checks will be finished in late 2013. Supported by a Grant from the Life Science Krems GmbH

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## OAID11

**Subject area/topic: Ongoing Trial**

### **OPTIMISING THE UTILISATION OF ANTITHROMBOTIC THERAPY FOR STROKE PREVENTION IN AF: DEVELOPMENT AND EVALUATION OF A COMPUTERISED ANTITHROMBOTIC RISK ASSESSMENT TOOL (CARAT)**

**Background:** Appropriate risk:benefit assessment is at the core of safety concerns regarding the use of antithrombotics. The aim of this study was to develop and evaluate a novel computerised antithrombotic risk assessment tool (CARAT) to aid decision-making regarding appropriate selection of therapy in elderly patients with atrial fibrillation (AF). **Methods:** Phase 1: Development of CARAT was based on algorithms (previously developed & trialled) which facilitate systematic patient review by assessing various factors impacting on treatment selection. Phase 2: CARAT was evaluated and modified through an iterative process, canvassing clinicians' perspectives on its usability and practicality. Phase 3: CARAT was applied to a small cohort of elderly patients to further test the feasibility and clinician satisfaction with the tool, prior to clinical trial. **Results:** Interim results indicate that ~70% of surveyed clinicians (cardiologists, haematologists, geriatricians; n=27) find CARAT to be useful and are "satisfied" with its: clinical inputs (variables); risk assessments and scoring; treatment recommendations; and technical application. However, geriatricians are 3 times more likely to disagree with CARAT recommendations than cardiologists. Phase 3 is currently underway; interim results indicate that the CARAT is useful in facilitating systematic patient review and risk assessment. This study is in progress. **Conclusion:** The CARAT is an efficient tool for assisting clinicians in decision-making regarding the use of antithrombotic therapy in elderly patients with AF. The impact of CARAT on prescribing decisions and patient outcomes will be tested in the next phase of this study.

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## OAID12

### Subject area/topic: Ongoing Trial

#### Pilot Study of Stem Cells in Stroke [PISCES]

**Background:**The CTX0E03 neural stem cell line is conditionally immortalized, originally derived from human fetal cortical neuro-epithelium that has been manufactured to clinical grade standard fulfilling Good Manufacturing Practice requirements. This cell line, in animal studies, has demonstrated in-vivo survival, migration, neuronal proliferation and differentiation resulting in improved functional outcome. The PISCES trial is a “first in man” safety trial.

**Aim:** To investigate the safety profile of intra-cerebral implantation of CTX0E03 (Neural Stem Cells product; ReNeuron Ltd. UK); a secondary aim is to explore indices of neurological function. **Methods:** Open label, single site, ascending dose, Phase 1 clinical trial. Over a 1.5 year period, 12 male patients with stable disability (NIHSS >6, mRS >1) who suffered ischemic MCA territory stroke 6 months to 5 years previously, will be recruited. Four groups of 3 patients each will receive 2, 5, 10 and 20 million cells respectively, implanted in the putamen by stereotaxic injection. Follow up will be for 2 years with clinical (NIHSS, mRS, BI, MMSE, EuroQoL) and radiological data (MRI, MRS, fMRI, DTI) gathered at 1, 3, 6, 12 and 24 months post implantation.

Protocol includes rigorous safety monitoring and reporting of adverse events with independent board review. Primary endpoints are safety factors including adverse events, neurological deterioration, or mortality. Secondary endpoints are the assessments of functional outcome at 24 months. Extended follow up for further 8 years will be offered to every patient. Each patient will also be followed on the NHS Central Register for life. **Conclusions:** PISCES trial will test the safety, feasibility and potential efficacy biomarkers of the CTX0E03 neural stem cells in stroke patients. **Status:** As of 30 Jan 2011, two patients have received the stem cells with no cell related adverse events observed. **Register:** ClinicalTrials.gov NCT01151124

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## OAID14

### Subject area/topic: Ongoing Trial

**The Stroke Oxygen Study (SO2S):** a multi-centre, prospective, randomised, open, blinded-endpoint study of routine oxygen supplementation during the first 72 hours after a stroke

**Introduction** Hypoxia after stroke is common, often missed, and associated with worse outcome. Oxygen supplementation could prevent hypoxia and related brain damage and lead to better recovery from the stroke. However, a small clinical study of short-term fixed dose oxygen supplementation did not show overall benefit. Oxygen supplementation may interfere with mobilization and thus affect early rehabilitation. Since hypoxia is most likely to occur at night, restricting routine supplementation to night time may be better than continuous oxygen or no routine oxygen. Current guidelines on oxygen supplementation are not based on evidence from clinical trials and differ between countries and organizations. **Aims:** To determine if patients benefit from routine oxygen supplementation after stroke. To establish whether nocturnal oxygen supplementation is as effective as, or more effective than, continuous oxygen supplementation. **Method** **Inclusion criteria:** Patients with a clinical diagnosis of acute stroke who have no clear indication for and no clear contraindication against oxygen treatment are recruited within 24 h of hospital admission. **Intervention for first 72 hours:** 1. No routine oxygen supplementation 2. Oxygen per nasal cannula over night either 3L/min (if baseline oxygen saturation is 93% or below) or 2L/min (if baseline oxygen saturation is >93%) 3. Oxygen (as in 2) continuously (day and night) **Assessments:** 1 week by the local investigator (clinical examination, complications, compliance and NIHSS) 3, 6, and 12 months via postal questionnaire sent out by the trial centre (mRS, Barthel Index, EuroQuol, Nottingham EADL). **Study size:** 6,600 subjects **Results Progress (31.3.11):** 82 centres open, 3029 patients recruited. [www.so2s.co.uk](http://www.so2s.co.uk) Funded by the NIHR Research for Patient Benefit programme.

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## OAID15

### Subject area/topic: Ongoing Trial

Third International Stroke Trial (IST-3). A large-scale randomised trial of thrombolytic therapy for patients with acute ischaemic stroke ISRCTN ISRCTN25765518

**Background.** Current regulatory approvals permit the use of thrombolysis in a highly selected subset of patients with acute ischaemic stroke. **Objective.** To determine whether a wider variety of patients can benefit from treatment than is possible under the current approvals. **Design.** IST-3 is a randomised controlled, trial of iv rt-PA (0.9mg/kg), with a PROBE (Prospective, Randomised, Open, Blinded Endpoint) design. **Eligibility.** acute ischaemic stroke, assessed and able to start treatment within 6 hours of onset, CT (or MR) scan has excluded intracranial haemorrhage. Details at [www.ist3.com](http://www.ist3.com). Patient inclusion is by (telephone or a secure website to) a rapid centralised randomisation system balancing on key prognostic factors. Treatment is allocated after the baseline data have been recorded and cross-checked. Brain imaging (CT or MR) must be repeated after treatment (at 24-48hrs). In centres where pre-treatment perfusion or angiography are routine, these scans are collected as well the plain CT or MR scans. Baseline and follow-up CT/MR images reviewed by 'blinded' expert panel. Perfusion and angiography data are processed centrally. In all centres, follow-up is conducted by centralised (blinded) postal or telephone questionnaire, independently of the clinician treating the patient. **Outcome measures:** primary outcome is survival free of death or dependence at six months. **Planned subgroup analyses:** effect of: age, stroke severity, time to randomisation, blood pressure, CT appearances, perfusion or angiographic findings (where available) on the risks and benefits of treatment. **Sample size** With 3100 patients, the trial could detect a 4.7% absolute difference in the primary outcome. **Trial Status:** A total of 2178 patients had been recruited by 4th April 2011. Results will be reported at ESC (May 2012)

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## OAID16

### Subject area/topic: Ongoing Trial

**CLOTS 3 - A randomised trial to establish the effectiveness of Intermittent Pneumatic Compression to prevent post stroke deep vein thrombosis (DVT)**

**Introduction:** About 10% of immobile patients with stroke will develop a proximal DVT detectable on compression duplex ultrasound in the first month. The CLOTS trials 1&2 established that graduated compression stockings (GCS) do not reduce the risk of post stroke DVT. Anticoagulation, with heparins or low molecular weight heparin, reduce the risk of DVT but this benefit is largely offset by a three fold increased risk of bleeding. Intermittent Pneumatic Compression (IPC) is effective in surgical patients. Small RCTs in stroke suggest it is feasible in stroke patients although there are insufficient data to justify its routine use. The CLOTS trial 3 aims to test IPC in immobile stroke patients. **Methods:** These are based on those of the CLOTS 1 & 2. Immobile patients admitted to hospital within 3 days of an acute stroke can be randomised into the trial. Simple baseline data are collected via telephone or the web and the patient is randomised to Routine care + IPC or Routine care alone. The primary outcome is the presence of DVT in the popliteal vein or more proximal vein detected on either Duplex ultrasound or venography within 30 days of randomisation. Patients have a screening Duplex ultrasound of both legs between Day 7 and Day 10 and between Day 25 and Day 30. Data are collected at hospital discharge to monitor compliance and to identify in hospital complications, deaths and length of stay. At six months we establish patient's place of residence, functional status, current antithrombotic medication regimen and the quality of life. **Conclusions:** Funding has been obtained from the NHS R&D Health Technology Assessment Board. The main phase of the trial started on 1st April 2010 and will include at least 70 UK centres and enrol over 2500 patients. The trial has already recruited 1044 patients in 58 centres. The trial has been adopted by the UK Stroke Research Network.

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## OAID17

### Subject area/topic: Ongoing Trial

#### Hypothermia for Acute Ischaemic Stroke Trial - Edinburgh

**Introduction:** Hypothermia is a candidate treatment for acute ischaemic stroke based on efficacy in animal studies and in other neurological conditions. Cooling is probably most efficacious with temperatures of 34°C or below, but such temperatures may not be tolerated well by awake patients on a stroke unit. The aim of HAIST-UK is to compare the feasibility and safety of surface cooling to 35°C or 33°C, started within 6 hrs after the onset of acute ischaemic stroke and maintained for either 12 hrs or 24 hrs. This study is part of the EuroHYP network of trials looking into the development of hypothermia as a therapeutic tool in ischaemic stroke. **Methods:** 24 eligible patients will be randomised to: Control = standard care, A = 35°C for 12 hrs, B = 33°C for 12hrs, C = 35°C for 24hrs or D = 33°C for 24hrs. In all patients randomised to hypothermia, cooling will be initiated by the intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 mins, followed by surface cooling using the Arctic Sun device. Shivering and discomfort will be prevented and if necessary treated with intravenous pethidine. At the end of the cooling period patients will be warmed at 0.3°C/hr until the oesophageal temperature is 36°C after which the device will be disconnected. **Trial Objectives:** • to compare the safety, feasibility and tolerability of hypothermia at various depths and duration • to identify which peripheral temperature measurement (oesophageal, rectal, bladder or tympanic) best reflects brain temperature as measured by MRI spectroscopy • to identify which panel of biomarkers, mRNA or DNA may be suitable for incorporation into a larger trial • to assess the effect on infarct volume using CT or MRI at baseline and at day 7 • to assess the effect on stroke severity as measured by mRS, NIHSS and BI at baseline, 1 and 3 months **Conclusions:** HAIST-UK which is funded by CHSS has commenced enrolment and is among a number of pilot studies aiding the design of a definitive Phase III trial.

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## OAID18

### Subject area/topic: Ongoing Trial

#### Preventive Antibiotics in Stroke Study (PASS)

**Rationale:** Stroke is a leading cause of mortality worldwide resulting around 6,000,000 deaths annually. Infections occur in 40% of patients and are a strong and independent predictor of a poor outcome. As shown in a recent meta-analysis, preventive antibiotic therapy lowers the infection rates after stroke. However, a sufficient large phase-III-RCT evaluating its effect on clinical outcome has not been performed yet. Ceftriaxone, an off-patent antibiotic, has a broad defence against the bacteria that cause the most common infections after stroke. **Aim:** To investigate whether the preventive use of ceftriaxone improves functional outcome in patients with stroke. **Design:** We will conduct a multicentre prospective, randomised, open-label, blinded endpoint trial of standard care with additional preventive ceftriaxone treatment and compare it with standard care without preventive ceftriaxone. **Study:** Adult patients with stroke (ischaemic and haemorrhagic), with an onset of symptoms within 24 hours before presentation and with a score  $\geq 1$  on the National Institutes of Health Stroke Scale are included. A total of 3200 patients will be randomly assigned into two groups of 1600 patients. The treatment group receives standard care plus ceftriaxone at a dose of 2000 mg, given every 24 h intravenously for four-days; the control group will receive standard care. **Outcomes:** Primary endpoint is the functional outcome at a three-month follow-up on the modified Rankin Scale (mRS), dichotomised as a favourable (0–2) or unfavourable (3–6) outcome. Secondary outcome measures will be death rate at discharge and three-months, infection rate during hospital admission, length of hospital admission, volume of post-stroke care, total use of antibiotics during follow-up, functional outcome using the ordinal scoring range of the mRS, and quality-adjusted life years and costs. **Study Proceedings:** Medical ethical approval was obtained in May 2010. The first inclusion was on 4 July 2010. At time of submission of this abstract, 267 patients were included. Up-to-date statistics are available at [www.passamc.nl](http://www.passamc.nl) Website [www.passamc.nl](http://www.passamc.nl) Trial registration ISRCTN-number: 66140176

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## OAID19

### Subject area/topic: Ongoing Trial

#### Japan Statin Treatment Against Recurrent Stroke (J-STARS)

**【Background】** In Japan, it is still unclear if hyperlipidemia is a risk factor of recurrent stroke or not in the ischemic stroke patients, though inhibition of HMG-CoA reductase could decrease the incidence of coronary heart disease and first occurrence of stroke in Japanese patients with hypercholesterolaemia (MEGA Study (Lancet 368: 1155, 2006)). In SPARCL (NEJM 355: 549, 2006), high dose of atorvastatin (80mg per day) was shown to decrease the overall incidence of strokes in the patients with stroke or TIA. The neuroprotective mechanism beyond cholesterol-lowering effects could be expected to attenuate cerebrovascular inflammation and atherosclerosis. The present study hypothesizes if treatment with low dose of pravastatin prevents recurrent stroke in Japanese patients with ischemic stroke with safety. **【 Study Design and Patients】** In this open label, randomized, prospective, blinded-endpoint study, patients who aged 45 to 80 years, had serum-total-cholesterol levels of 180-240mg/dl and had histories of non-cardiogenic infarction within 1 to 36 months after stroke were applied, from March 2004 to February 2009. They were assigned randomly to pravastatin (10mg/day) group or non-pravastatin group. The mean duration of follow-up will be 5.5 years. This study is registered at Clinical Trials.gov, number NCT00221104. **【 Outcome Endpoint】** The primary endpoint is cerebrovascular events including TIA. **【Analysis】** Independent Data and Safety Monitoring Board will perform the interim analysis in 2011. The final analysis will be performed by employing Kaplan-Meier survival method, log-rank test and Cox proportional hazard model. **【Trial Status】** A total of 1578 patients were recruited from 123 centers by the end of February 2009, and have been in the process of follow-up for 3.2 years of the mean duration. Mean age 66.2 years; male 68.9%. 25.4% atherothrombotic infarction, 64.2% lacunar infarction. Present status of the trial will be presented at the meeting.

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## OAID21

### Subject area/topic: Ongoing Trial

Cooling in intracerebral hemorrhage (CINCH) trial: a randomized German-Austrian clinical study

**Background:** Intracerebral hemorrhage (ICH) accounts for up to 15% of all strokes and is frequently associated with poor functional outcome and high mortality. So far, there is no clear evidence for a specific therapy, apart from general stroke unit or neurointensive care and management of secondary complications. Promising experimental and pilot clinical data support the use of therapeutic hypothermia (TH) after ICH. This trial will investigate whether TH improves survival rates and reduces cerebral lesion volume after large ICH compared to conventional treatment. **Methods:** The Cooling in Intracerebral Hemorrhage (CINCH) trial is a prospective, multicenter, interventional, randomized, parallel, two-arm (1:1) phase II trial with blinded endpoint adjudication. **Enrolment:** 50 patients (age: 18 to 65 years) with large (25 to 64 ml on CCT), primary ICH of the basal ganglia or thalamus within 6 to 18 hours after symptom onset are randomly allocated to TH for 8 days or conventional temperature management. In the TH-group a target temperature of 35.0 °C is achieved by endovascular catheters and followed by slow controlled rewarming. Data analysis is based on the intent-to treat population. The primary outcome measure of the study is the development in total lesion volume on CCT (ICH plus perihemorrhagic edema on day 8±0.5 and day 11±0.5 after ICH) and the mortality after 30 days. Secondary endpoints are the in-hospital mortality, mortality and functional outcome (modified Rankin Scale and Barthel-Index) after 90 and 180 days. Safety measures include any adverse events associated with TH. **Discussion:** Since there are no clear evidence-based therapies for patients with large ICH new promising approaches are desperately needed, but need evaluation in randomized controlled trials. TH investigated in this randomized controlled trial as a strategy against perihemorrhagic edema and potential neuroprotective method in ICH might directly influence future therapy of large ICH.

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## OAID22

### Subject area/topic: Ongoing Trial

#### Fluoxetine or Control Under Supervision (FOCUS): A randomised controlled trial

**Background.** New treatments are urgently needed to reduce the huge burden of disability and dependency after stroke. Selective serotonin reuptake inhibitors stimulate neurogenesis, are neuroprotective and have effects on the adrenergic system. The FLAME Trial (n=118) demonstrated that fluoxetine improved motor recovery and reduced dependence. These promising results need to be confirmed in a much larger group of patients. **Aims.** We aim to determine whether fluoxetine 20mg daily for 6 months, started at 2-15 days after stroke onset in patients with persisting neurological deficits, reduces dependency at 6 months and whether any benefits persist to 12 months. **Methods.** This multicentre UK, randomised placebo-controlled trial will recruit 3000 patients. Eligible patients will be randomised by a central web-based system, thus ensuring allocation concealment. Local follow-up at discharge (for inpatients) or one month (for outpatients) and then at 7 months will assess adverse effects and adherence to the trial medication. Central follow-up at 6 months and 12 months will collect data on our primary outcome (modified Rankin scale, mRs) and our secondary outcomes (survival, health related quality of life, mood, fatigue, overall level of recovery (Stroke Impact Scale), new clinical diagnosis of depression and resource use). Based on a sample size for a binary outcome, a trial of 3000 (1500 per group) will provide greater than 90% power ( $\alpha = 0.05$ ) to detect a 5.5% absolute increase in proportion of patients with a mRs of 0-2 (i.e. independent) (odds ratio = 1.30). We are harmonising assessments with the AFFINITY (Assessment of fluoxetine in stroke recovery) investigators to allow future joint analyses. **Potential impact.** Our trial will tell us whether this simple, inexpensive treatment, with very few serious side effects improves overall recovery in a broad range of patients after stroke.

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## OAID23

### Subject area/topic: Ongoing Trial

#### The Enhanced Control of Hypertension ANd Thrombolysis strokeE StuDY (ENCHANTED): rationale and progress update

**Background:** ENCHANTED aims to address 3 questions in patients eligible for i.v. rtPA in ischaemic stroke: (i) does low-dose (0.6 mg/kg) provide equivalent benefits to standard-dose (0.9 mg/kg) rtPA; (ii) does rapid blood pressure (BP) lowering (140-150 mmHg systolic target) improve outcomes compared to guideline recommended BP control (180 mmHg systolic target); and (iii) does adding rapid intensive BP lowering to rtPA reduce the risk of symptomatic intracerebral haemorrhage (sICH)? We report progress in establishing this independent, international, multicentre study. **Methods:** 2-linked, optional randomised, open, blinded endpoint (PROBE), controlled trials, with central internet randomisation of patients fulfilling local criteria for rtPA and have uncertainty over [a] 'rtPA dose' and/or [b] 'BP control' using i.v. agents via standardised protocols for early (<30 mins) and sustained (72 hrs) systolic BP target (140-150 mmHg) versus a higher systolic BP target (<180 mmHg) in the control group. Brief follow-up data are collected 5 times: 24 and 72 hours, and 7 (or hospital discharge if sooner), 28 and 90 days. If the primary 90-day 'poor' outcome (death and any disability [mRS score 2-6]) in patients who receive standard-dose rtPA is 50%, a sample size of 3300 (1650 per group) for each trial arm provides >90% power (one-sided  $\alpha$  0.025) to detect: non-inferiority of low-dose rtPA; superiority of intensive BP lowering (2-sided  $\alpha$  0.05); and  $\geq$ 80% power to detect 40% reduced symptomatic ICH and >90% to detect >26% reduced any ICH from any treatment. **Results:** The study has commenced as a start-up phase across 50 sites in Australia, China, Singapore and Korea during 2011. A Project Grant application is currently under review with the NHMRC of Australia for funding support during 2012-1016. **Conclusions:** Low-dose rtPA and early intensive BP lowering could provide more affordable and safer treatments in the management of acute ischaemic stroke all over the world.

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## OAID24

**Subject area/topic: Ongoing Trial**

### **MR CLEAN - MULTICENTER RANDOMIZED CLINICAL TRIAL OF ENDOVASCULAR TREATMENT FOR ACUTE ISCHEMIC STROKE IN THE NETHERLANDS (NTR1804)**

**Rationale:** Ischemic stroke is often caused by embolic occlusion of proximal intracranial arteries. The effect of intravenous alteplase is limited in these patients. Endovascular treatment increases the likelihood of recanalization, but the effect of treatment and functional outcome is not certain. **Aim:** The main purpose of the Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands (MR CLEAN) is to assess the effect on functional outcome and safety of endovascular treatment in these patients. **Design:** MR CLEAN is a pragmatic phase III multicenter randomized clinical trial with blinded outcome assessment. The intervention contrast is endovascular treatment with thrombolytics (urokinase or alteplase) and/or mechanical thrombectomy versus no endovascular treatment. The choice of endovascular treatment modality for each patient is left to the discretion of the local investigator and treating physicians. Background medical management is delivered according to national standards and guidelines. It may include intravenous alteplase within the first 4.5 hours after onset. **Outcomes:** The primary outcome is the score on the modified Rankin scale (mRS) 90 days after inclusion in the study. Secondary outcomes are the NIHSS score at 24 hours, vessel patency, infarct size, and the occurrence of major bleeding. The randomization will be stratified for use of intravenous alteplase, planned treatment modality (intra-arterial thrombolysis, mechanical thrombectomy or both) treatment center and stroke severity. The effect of treatment will be estimated by means of the ordinal logistic regression (shift analysis). In total, 500 patients will be included in the trial. **Discussion:** MR CLEAN is a pragmatic trial. Inclusion of patients will take 4 years and has started in December 2010. As of April 2010, 3 of 14 participating centers are active and 10 patients have been included.

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## OAID26

### Subject area/topic: Ongoing Trial

The benefit of EXtending oral antiCOAgulant treatment after acute Cerebral Vein Thrombosis (EXCOA-CVT) – a cluster randomised study

**Background.** After a cerebral vein thrombosis (CVT) there is an increased risk of further venous thromboembolic events (VTEs). Current guidelines suggest oral anticoagulation for 3 to 12 months after a first episode of CVT, depending on event-related features and thrombophilic characteristics. These recommendations are extrapolated from studies on extracerebral vein thrombosis, which may be inaccurate, since the risk of thrombotic recurrence is different. **Method.** As part of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT2) project, the EXCOA-CVT is a prospective study with a cluster randomised allocation design that aims to compare a policy of short (3 months) versus long term (12 months) oral anticoagulation in the prevention of VTEs after an episode of CVT. The study population will consist of consecutive adult subjects with confirmed CVT. Participating centres are asked whether they have preference for any of the policy treatment options and centres with no preference will be randomly allocated for one of the two options. Eligible patients will be treated according to the approach allocated to their centre as soon as their acute clinical situation is stable and not more than 1 month after the CVT diagnosis. Subjects with conditions judged by the investigator to be an absolute indication for prolonged oral anticoagulation, such as recurrent CVT, VTE after CVT or first CVT with antiphospholipid syndrome or known severe thrombophilia will be excluded. Follow-up will be performed at 6, 12, 18 (telephone-interview) and 24 months from the date of entry. The primary efficacy outcome is any symptomatic and confirmed VTE (recurrent CVT or other systemic VTE) or death associated with venous thromboembolism. Primary safety endpoints include bleeding events, classified as major/minor and according to the site of bleeding, and death from any cause.

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## OAID27

### Subject area/topic: Ongoing Trial

**ICTUS Study: International Citicoline Trial on acUte Stroke.** A multicenter, prospective, randomized, double-blind, placebo-controlled study (Update at 2nd May 2011)

**Background:** Citicoline is a safe drug approved in some countries for the treatment of acute ischemic stroke. The drug has shown some evidence of efficacy in a data pooled analysis, based on four clinical trials performed in USA with oral citicoline given within 24 hours from symptoms onset.

**Purpose:** To confirm the results obtained in the data pooled analysis. **Design:** Multicenter, randomized (under minimization), double-blind, placebo-

controlled trial, based on a sequential analysis (triangular model). **Sample**

**Size:** The study will follow a sequential analysis, with the first approach to test the efficacy with 1000 patients. The upper limit has been established in 2600 patients. This design has 80% power to establish a treatment effect of

1.26 (common odds ratio). **Active Centers:** 24 centers in Spain, 8 in Portugal and 9 in Germany **Study Population:** Male or female, <sup>3</sup> 18 years old, treated

within 24 hours of symptoms onset, with a measurable focal neurological deficit lasting for a minimum of 60 minutes. **Baseline NIHSS score**  $\geq 8$ , with a neuroimage compatible with the diagnosis of acute ischemic stroke and

symptoms referable to MCA territory. **Pre-stroke mRS**  $\leq 1$ . Signed informed consent is mandatory. **Interventions:** Patients will be randomized in a 1:1 ratio

to receive either citicoline or placebo. **Citicoline forms:** 1000 mg ampoules (4 cc) and 500 mg tablets. **Daily dosage:** 1000 mg/12 h i.v. during the first three days and orally from the fourth day until the end of the 6 weeks treatment

period. **Outcome Endpoints:** Primary end-point will consist in a global score test combining three measures of success evaluated 12 weeks after treatment on the basis of intention-to-treat criteria: neurological (NIHSS)  $\leq 1$ ), disability (MRS  $\leq 1$ ), and activities of daily life (BI  $\geq 95$ ), averaged using a Global Test.

**Secondary endpoints:** Results of the single scales at week 12. Formal training and certification in the use of mRS and NIHSS are mandatory. **Trial Status:**

2047 valid patients included in the study by 2nd May 2010.

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## OAID28

### Subject area/topic: Ongoing Trial

#### Secondary Prevention of Small Subcortical Strokes (SPS3)

**Background** Small subcortical strokes (S3) also known as lacunar strokes account for about 25% of all brain infarcts, are usually due to cerebral small artery disease which predisposes to vascular dementia. Over 2 million S3 survivors in US are at high risk of stroke recurrence and subsequently vascular dementia; millions more suffer subclinical S3 and cognitive decline caused by the intrinsic disease of the small penetrating cerebral arteries. No previous randomized trials have focused on secondary prevention after S3 or subcortical TIA, optimal target levels of BP control after stroke and their relationship to cognitive decline, or prevention of stroke and dementia in HA.

**Objectives** Determine: if the combination of Aspirin 325 mg/d+Clopidogrel 75 mg/d is more efficacious than Aspirin 325 mg/d alone AND whether intensive BP lowering (systolic <130 mmHg) is superior to usual hypertension management (systolic between 130-149 mmHg) in reducing stroke recurrence, cognitive decline and major vascular events in patients with symptomatic S3 or subcortical Transit Ischemic Attack (TIA).

**Methods** SPS3 is a randomized multicenter international clinical trial. Patients are assigned in a factorial design to 2 interventions: a. Aspirin 325 mg/d vs. Aspirin 325 mg/d+Clopidogrel 75 mg/d. (double-blinded). b. Two targets of systolic BP, “usual” (130-149 mmHg) vs. “intensive” (<130 mmHg). (open-label with blinded event assessment). Patients with symptomatic, MRI documented S3/subcortical TIA within the prior 6 months and without carotid stenosis or major cardiac sources of embolism are included in the study. Follow-up every 3 months for a mean of 3.5 yrs. Outcomes Recurrent stroke (primary), cognitive decline, major vascular events and death.

**Trial Status** Recruitment was finalized on April 2, 2011 with a total of 3020 patients included from 8 countries. The study will be completed on April 2012. Sponsorship National Institute of Health of United States/NINDS. Registry # NCT00059306. Grant # U01 NS38529. <http://www.sps3.org> PI Oscar Benavente, MD. Professor of Neurology, University of British Columbia, Vancouver, Canada. Contacts Oscar.Benavente@ubc.ca; Hartr@uthscsa.edu

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## OAID29

### Subject area/topic: Ongoing Trial

#### Field Administration of Stroke Therapy – Magnesium (FAST-MAG) Phase 3 Trial

FAST-MAG is a multicenter, randomized, double-blind, placebo-controlled phase 3 trial to demonstrate whether paramedic-initiated intravenous magnesium sulfate within 2 hours of symptom onset improves the longterm functional outcome of hyperacute stroke patients Planned enrollment: 1700 patients Participating Sites: 355 rescue vehicles and up to 65 receiving hospitals in Los Angeles and Orange Counties in California, USA Target Population: Ambulance-arriving patients with hyperacute stroke, both cerebral infarction and intracerebral hemorrhage Funding: NIH-NINDS Award U01 NS44364 Inclusion Criteria: 1) Suspected stroke identified by the Los Angeles Prehospital Stroke Screen (LAPSS), 2) Age 40-95, inclusive, 3) Last known well time < 2 hours of treatment initiation, 4) Deficit present for ≥ 15 minutes Exclusion Criteria: 1) Coma, 2) Rapidly improving neurologic deficit, 3) Pre-existing neurologic, psychiatric or advanced systemic disease that would confound outcome evaluations, 4) SBP<90 or>220, 5) Severe renal dysfunction, 6) Severe respiratory distress 7) 2nd or 3rd degree heart block w/o pacemaker, 8) Major head trauma in last 24h, 9) Recent stroke within prior 30d, 10) No individual available to provide consent/assent Intervention: Paramedic field loading dose: 4 grams magnesium sulfate over 15m or matched placebo in the ambulance on route, followed by hospital maintenance dose: 16 grams Mg over 24h or matched placebo Primary Endpoint: Modified Rankin Scale 3 months post stroke, Cochran-Mantel-Haenszel test to detect shift in distribution over all 7 strata. Study Progress: As of 5/3/2011 there were 1255 out of 1700 subjects enrolled (74%). Subject characteristics are a mean age of 69, 42% female, median NIHSS 9, and median time to study drug initiation 46 minutes with 73% receiving treatment in <1 hour. Final diagnosis of enrolled subjects was cerebral ischemia in 73%, intracerebral hemorrhage in 24% and stroke mimic in 3%.

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## OAID30

### Subject area/topic: Ongoing Trial

High ABCD2 score is rather predictive for ischemic origin of transient neurological attack than for risk of recurrence

**Background:** The ABCD2 score is a clinical tool for emergency physicians to triage patients with suspected transient neurological attack (TIA) for urgent evaluation due to the risk of recurrent stroke. We assessed the correlation of the score with ischemic origin of symptoms and recurrent stroke risk in our outpatient TIA clinic. **Methods:** ABCD2 scoring and TIA work-up was performed on 200 consecutive patients with suspected TIA. Three months follow-up was completed in 99.5%. **Results:** 116 (58%) patients had confirmed TIA or minor stroke. 84 patients (42%) were diagnosed as having other transient neurological attacks (TNA). Patients with TIA had significantly more often an ABCD2 score  $\geq 4$  than patients with TNA ( $p=0.002$ ). The proportion of patients with TIA increased with each ABCD2 point from 1 to 7: 28% ( $n=18$ ), 50% ( $n=50$ ), 56% ( $n=55$ ), 68% ( $n=37$ ), 74% ( $n=19$ ), 90% ( $n=10$ ), and 100% ( $n=1$ ), respectively. 60% of patients with an ABCD2 of 0 ( $n=10$ ) were also diagnosed as TIA. Recurrent TIA/stroke occurred in 4 patients with initial ABCD2 score of 3, 3, 4, and 5, respectively. **Conclusions:** Patients with ABCD2 score  $\geq 4$  points are more likely to have TIA than patients with ABCD2 score  $< 4$  points. However, low ABCD2 score does not exclude TIA. Recurrent events similarly occurred in patients with low or intermediate ABCD2 score, indicating that factors not included in the ABCD2 score determine short term risk of stroke recurrence.

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## **OAID31**

### **Subject area/topic: Ongoing Trial**

#### **Kidney Disease and Stroke Recurrence**

Patients with kidney disease (KD) have higher risk of stroke regardless of hypertension or diabetes. KD is quantified by impaired filtration of creatinine (creatinine-based glomerular filtration rate –GFR-) and cystatin-C (cysC), or by glomerular leak of albumin (alb). Variations of these renal markers after stroke are unknown. Analyzing the relationship between KD and stroke may guide preventative strategies. Hypothesis: Renal function changes after stroke; abnormal renal function increases risk of stroke recurrence.

**Objectives:** Determine renal function variability after stroke; compare baseline and one year values. Analyze relationship between renal function and stroke recurrence. **Design:** Prospective cohort, pilot. 50 subjects admitted to Mayo Clinic Hospital Arizona with primary stroke; follow up 18 months. Cr (mg/dl) on admission and discharge; cysC (mg/L), Alb (mg/L) and GFR (ml/min) at discharge and 12 months. Telephone interview at 1, 6, 18 months. Visit at 12 months. Patient change in renal biomarkers and change in kidney function will be summarized and tested for statistical significance using paired t-test and McNemar's test respectively. **Trial status:** 50 subjects enrolled, qualifying event 44 ischemic. 18 female, mean age 69.4, mean admission Cr 1.0, mean markers at discharge Cr 1.0, cysC 0.9, GFR 85.3. Nine subjects completed 12 month follow-up.

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## OAID32

### Subject area/topic: Ongoing Trial

#### Efficacy of Nitric Oxide in Stroke (ENOS) Trial - A Prospective Randomised Controlled Trial in Acute Stroke

**Rationale:** Acute hypertension is associated with a poor outcome after stroke. No large trials have assessed the effect of altering BP during the acute phase of stroke on outcome. We are testing whether nitric oxide, a multimodal molecule given as glyceryl trinitrate (GTN), is safe and effective in improving outcome after acute stroke. Furthermore, around half of all patients admitted with acute stroke are taking antihypertensive therapy immediately prior to the stroke. No data exist as to whether it is beneficial or safe to stop or continue this treatment during the acute phase. **Design:** ENOS is a prospective, international, multicentre, randomised, parallel-group, blinded, controlled trial. 3,500 - 5,000 ischaemic or haemorrhagic stroke patients with systolic BP 140-220 mmHg, and within 48 hours of onset will be included. Subjects will be randomised to 7 days of single-blind treatment with transdermal GTN or control. Those patients taking prior antihypertensive therapy will also be randomised to continue or temporarily stop this for 7 days. ENOS is conducted over a secure internet site. The primary outcome is modified Rankin Scale at 90 days which is carried out by a blinded assessor. The analysis will be by intention to treat. **Trial status:** As at 28th April, 2011, 2294 patients had been recruited from 128 centres (Australia, Canada, China, Egypt, Hong Kong, India, Italy, Malaysia, New Zealand, Philippines, Poland, Republic of Ireland, Romania, Singapore, Spain, Sri Lanka and UK). More centres welcome to join. **Funding:** The Medical Research Council. **Contact information:** <http://www.enos.ac.uk> , E-mail: [enos@nottingham.ac.uk](mailto:enos@nottingham.ac.uk), Telephone: +44 (0)115 82 31770

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## OAID33

### Subject area/topic: Ongoing Trial

**PODCAST: Prevention Of Decline in Cognition After Stroke Trial: a factorial randomised trial of blood pressure and lipid lowering**

**PODCAST Investigators, Sandeep Ankolekar, Lynn Stokes, Philip MW Bath Stroke Trials Unit, Institute of Neuroscience, University of Nottingham, UK**

**Rationale: Stroke and dementia are common, economically costly to society, and devastating to patients and their family. Elevated BP and cholesterol are common after stroke and may be associated with increasing cognitive decline. Although BP-lowering post-stroke may reduce cognitive decline, there is little evidence to date that lipid lowering is effective in preventing cognitive decline. Critically, it is unknown whether BP and cholesterol should be lowered intensively, or moderately as per current guidelines. The aim of the proposed trial is to determine if intensive BP and/or lipid lowering therapy after stroke is better in preventing cognitive decline, compared to current guideline treatment. Design: PODCAST is a prospective, randomised, open-label, blinded end-point, controlled, partial factorial, phase IV trial. The start up phase will assess feasibility of the study over 3 years in 600 patients. The main phase will then assess the efficacy of intensive treatment in a further 2,800 patients over 8 years in total. The target SBP is <125 mm Hg for the intensive BP lowering group and <140 mm Hg for the guideline group. For the intensive lipid lowering group the target LDL-C is <2 mmol/L and <3 mmol/L for the guideline group. The primary outcome is Addenbrooke's Cognitive Examination. Secondary outcomes include quality of life, vascular events, functional outcome, depression and death. Trial Status: The trial has Ethics and NHS RD approvals and has commenced recruitment in September 2010. Funding: The start-up phase is funded jointly by The Stroke Association UK and Alzheimer's Society UK. Contact Information: Website: <http://www.podcast-trial.org/> E-mail: [podcast@nottingham.ac.uk](mailto:podcast@nottingham.ac.uk) Telephone: +44 (0) 115 8231671**

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## OAID34

### Subject area/topic: Ongoing Trial

#### Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke (TARDIS).

Safety and tolerability of clopidogrel when added to aspirin and dipyridamole in high risk patients with recent ischaemic stroke: a randomised controlled trial

**Rationale:** The risk of recurrence is greatest immediately after stroke or TIA. Existing prevention strategies (antithrombotic, lipid/blood pressure lowering, endarterectomy) reduce, not abolish, further events. Dual antiplatelet therapy – aspirin & clopidogrel (AC) for IHD, aspirin & dipyridamole (AD) for stroke, is superior to aspirin monotherapy. We hypothesise that triple antiplatelet therapy (ACD) will be superior to AD in patients at high-risk of recurrence, providing bleeding does not become excessive.

**Design:** TARDIS is a multicentre, parallel-group, prospective, randomised, open-label, blinded-endpoint, controlled trial. In the start-up phase, we will assess over 3 years the safety, tolerability and feasibility of intensive therapy (ACD) versus guideline therapy (AD) given for 1 month in 750 patients with acute stroke/TIA. The main phase will then assess the safety and efficacy of ACD in up to 3500 patients. The primary outcome is ordinal stroke (fatal/severe non-fatal/mild/TIA/none) at 90 days. Secondary outcomes include death, MI, vascular events, function, bleeding, serious adverse events; sub-studies will assess cerebral emboli and platelet function.

**Trial Status:** The trial started in April 2009. As of 5th May, 2011, 405 patients have been recruited from 44 centres within the UK Stroke Research Network.

**Funding:** The British Heart Foundation

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## OAID35

### Subject area/topic: Ongoing Trial

**EuroHYP-1: European, multicentre, randomised, assessor-blinded, phase III clinical trial of hypothermia plus best medical treatment versus best medical treatment alone for acute ischaemic stroke**

**Background:** In animal studies modelling ischaemic stroke, cooling to 35°C reduced infarct size by about one third, and cooling to 34°C by around 45%. Cooling also improves outcome in patients with hypoxic-ischaemic brain injury after cardiac arrest. Cooling awake patients with ischaemic stroke to 35°C has been shown feasible and safe, but whether this improves functional outcome has not yet been tested in an adequately-sized randomised clinical trial. **Aim:** To determine whether systemic cooling to a target temperature of 34 to 35°C, started within 6 hours of symptom onset and maintained for 24 hours, improves functional outcome at 3 months in patients with acute ischaemic stroke. **Methods:** This is an assessor-blinded, randomised, phase III, multicentre, international clinical trial with masked outcome assessment in 1500 awake adult patients with acute ischaemic stroke and a score on the NIH Stroke Scale of 6 to 18. Cooling will be initiated within 6 hours of symptom onset with an intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 to 60 minutes, followed by surface or endovascular cooling to 34 to 35°C, maintained for 24 hours. Patients will receive intravenous thrombolysis with alteplase if indicated. The primary outcome measure will be the common odds ratio of improvement on the modified Rankin Scale (mRS) at 90 days as analysed with multiple ordinal logistic regression (shift analysis). Raters will be blinded to treatment allocation. Secondary outcome measures include death and dependency (mRS >2) at 90 days, infarct volume, quality of life, and serious adverse events. A trial with 750 patients per arm has 90% power to detect a 7% absolute improvement at the 5% significance level. **Status and funding:** Unconditional grant by W. Hacke, Heidelberg, (from Max Jarecki and Mihara awards 2009) for an FP7 grant application, which was prioritised by DG research in April 2011. Financial support by the universities of Copenhagen, Edinburgh, Erlangen, Helsinki, Malmo, and Utrecht. Patient enrolment is planned to start in 2012.

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## OAID36

### Subject area/topic: Ongoing Trial

National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health, Stroke Common Data Elements (CDEs): Version 1.0 Available for Use

**Background:** To assist investigators conducting studies and increase data sharing among researchers, the NINDS CDE Team convened a Working Group of experts to develop CDEs with accompanying documentation specific to adult and pediatric stroke clinical research. **Methods:** The Stroke CDE Working Group divided into nine subgroups to identify and define elements for specific domains. Recommendations were developed during regular teleconferences and were released in August 2010 for a one-month period of public comment. During the public comment period, comments were invited from multiple expert groups worldwide, including the European Stroke Organization, the Stroke Societies of Japan, Korea, Australia, and Canada, and the World Stroke Organization. Based on public feedback, the WG finalized Version 1.0 of the Stroke CDEs which was published on the NINDS CDE Web site (<http://www.commondataelements.ninds.nih.gov/>) in December 2010. Version 1.0 includes the following:

- Catalog of over 600 stroke-specific CDEs with detailed specifications including definitions and code values;
- Approximately 25 standardized instruments with recommendations for use;
- Several case report form (CRF) templates and procedural manuals to guide the use of the CDEs.

**Results:** The poster presentation will provide an update about Version 1.0 of the Stroke CDEs including:

- Details on how the Stroke CDEs may be used by a clinical study;
- Explanation of trainings available to research team members about how to navigate the Web site and pick and choose CDEs from it; and
- Outline of the next steps to ensure the Stroke CDEs are continuing to meet the needs of stroke researchers.

**Conclusions:** The Stroke CDEs will undergo periodic reviews and updates from experts in the field to ensure the CDEs remain useful tools. The NINDS encourages research teams to use the Stroke CDEs and share feedback about them with the NINDS CDE Team to better inform this ongoing review process.

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## OAID38

### Subject area/topic: Ongoing Trial

**COOLIST: COOLing for Ischaemic Stroke Trial A phase II randomised clinical trial**

**Background:** Cooling to 32 - 34°C improves outcome in patients with post-anoxic encephalopathy after cardiac arrest. Animal studies strongly suggest that cooling also improves outcome after ischaemic stroke, being efficacious at temperatures of 35°C or below. Lower temperatures are associated with a greater benefit. The feasibility of surface cooling to temperatures of 35°C or below in patients with acute ischaemic stroke has not been evaluated systematically in awake patients admitted to a stroke unit. **Aim:** To compare the feasibility and safety of surface cooling to 34, 34.5, and 35°C, started within 4.5 hours after the onset of acute ischaemic stroke and maintained for 24 hours, in awake patients on a stroke unit. **Methods:** A randomised, open, multi-centre, phase II clinical trial, comparing three different surface cooling strategies with standard treatment in 84 awake adult patients with acute ischaemic stroke and a score on the NIH Stroke Scale  $\geq 6$ , admitted to a stroke unit. The trial consists of two phases. First, 48 patients will be randomised to conventional treatment or to surface cooling to 34, 34.5 or 35°C maintained for 24 hours (n = 12 in each group). Second, 36 patients will be randomised to conventional treatment or to one of two surface cooling strategies selected from the first phase (n = 12 in each group). The primary outcome measure is feasibility: the number of patients that has successfully completed the treatment strategy they had been assigned to. Secondary outcome measures include safety and the score on the modified Rankin scale at three months. The trial is scheduled to start in June, 2011. Registerend as NTR2616 and supported by the Netherlands Heart Foundation (2010B239) **Expected results:** This study will provide adequate information on the feasibility and safety of different surface cooling strategies on a stroke unit. It should facilitate the design of a large pragmatic phase III trial of surface cooling for acute ischaemic stroke.

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## OAID39

### Subject area/topic: Ongoing Trial

#### A Very Early Rehabilitation Trial (AVERT): Ongoing Phase III Trial Efficacy & Cost Effectiveness Study

**Background:** Getting patients out of bed very early after stroke (<24 hours) may be an important component of effective stroke unit care. Within a multi-centre, single blind, randomized controlled trial, we hypothesize that VEM will reduce death and disability and be cost effective. **Methods:** Medically stable patients within 24 hrs of stroke are included. Patients with severe premorbid disability and comorbidities are excluded. Randomisation is stratified by site and stroke severity. Intervention is delivered by a nurse/physiotherapist, commences with 24 hours and continues for a maximum of 14 days. Control group patients receive standard care. Primary outcome is modified Rankin Scale at 3 months. Sample size is 2104 patients (n=1052 per group). Analyses will be intention to treat. **Trial status:** Recruitment commenced July 2006. 32 hospitals are participating in Australia, New Zealand, Malaysia, Singapore and the United Kingdom. At May 2011, 958 patients (6% all strokes) have been recruited. Major exclusions (i) patients admitted > 24 hours after stroke (40%) and (ii) admitted after hours/ weekends (25%). Participants aged 70(13) years, 47% with moderate-severe stroke. 889 patients have completed 3 month follow up with 8 drop outs. **Conclusion:** The Data Monitoring Committee has met 6 times and no safety issues have been identified.

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## **OAID40**

### **Subject area/topic: Ongoing Trial**

**Acute Stroke and Dysphagia. Reduced risk of pneumonia and death with transdermal Scopolamine. A randomized controlled trial.**

Dysphagia and pneumonia are both prevalent after stroke. Patients with stroke and dysphagia have increased risk of pneumonia which is associated with early mortality. Aspiration probably also occurs because of difficulties in swallowing normal amounts of saliva. Hence, reduction of salivation may contribute to reduced aspiration of salivation and subsequent pneumonia. Dysphagia in acute stroke often improves rapidly after hemispheric strokes, therefore the reduction of saliva is most useful during the first two weeks. Transdermal Scopolamine, an anticholinergic drug, is used to reduce saliva in patients with sialorrhea. In this study we hypothesise, that treatment with Scopolamine during the first two weeks after an acute stroke in patients with dysphagia, reduces the risk of pneumonia and death. We are conducting a randomized placebo controlled trial with transdermal Scopolamine in the interventional group and a placebo patch in the control group. The sample size is calculated to 117 patients in each arm. Primary outcomes are differences in proportion of any lung infection or mortality during the first three months. Secondary outcome measures are differences in neurological deficits, disability and health related quality of life.

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## OAID41

### Subject area/topic: Ongoing Trial

#### Desmoteplase in Acute Ischaemic Stroke: Status Update on The DIAS Clinical Trial Programme

Desmoteplase is a novel, highly fibrin-specific thrombolytic agent in phase III of clinical development. In comparison to rt-PA, it has high fibrin selectivity, an absence of neurotoxicity, and no apparent negative effect on the blood-brain barrier. The safety and efficacy of desmoteplase is studied in the DIAS Clinical Trial Programme. Three studies are completed (DEDAS, DIAS and DIAS-2). Two large randomised, double-blind, placebo-controlled, phase III trials are ongoing at >200 sites worldwide (DIAS-3 & DIAS-4, n=800, NCT00790920 & NCT00856661). In Europe, the following countries participate: Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Italy, Netherlands, Poland, Spain, Switzerland, and the UK. The objective of DIAS-3 and DIAS-4 is to evaluate the efficacy and safety of a single IV bolus of 90 µg/kg desmoteplase given 3-9 h after onset of ischaemic stroke (NIHSS 4-24, age 18-85 y). Patients are selected with occlusion or high-grade stenosis (TIMI 0-1) in proximal cerebral arteries as assessed by MRA or CTA. An independent data review by the Data Monitoring Committee in February 2011, revealed no safety issues. In the USA, to support patient recruitment and retention, a DIAS trial network (hub-spoke model) has been implemented that consists of both tertiary and community-based acute stroke centres managed by regional hub directors. In Japan, a randomised, double-blind, placebo-controlled, dose-escalation Phase II trial is ongoing (DIAS-J; NCT01104467). Its primary objective is to evaluate the safety and tolerability of desmoteplase 70 and 90µg/kg 3-9 h after ischaemic stroke onset in Japanese patients (n=48). Desmoteplase is the only thrombolytic agent in late stage development for acute ischaemic stroke, despite the fact that there is a high unmet need. Therefore, the results of the DIAS clinical trial programme will be important for physicians and patients that are in need for a safer and effective treatment in a time-window up to 9 hours.

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## **OAID42**

### **Subject area/topic: Ongoing Trial**

**A Survey and feasibility RCT of pre discharge home visits for patients with a stroke**

**Background** Pre-discharge home visits for stroke patients are a common component of occupational therapy (OT) practice. The purpose of these visits is to facilitate a safe discharge home and to ease the transition of care from hospital to the community. The UK 2006 National Sentinel Stroke Audit reported that 73% of patients admitted to a stroke unit had a home visit before discharge. However, there is a paucity of evidence in terms of outcomes for patients and the clinical and cost effectiveness of these visits is not known.

**Aim** We are conducting a feasibility randomised controlled trial of pre-discharge OT home visits in Derby, which aims to investigate outcomes and establish criteria for home visits for stroke patients. As part of this trial we wish to identify current practice and opinions of OTs providing in-patient stroke care. This will highlight any national differences in practice and place the findings of our RCT in context. This will also help us to implement the findings of the research into practice. **Methods** **Survey:** Audit of home visit practice across stroke services in England. Interviews will be conducted at a location to suit the informants, or via telephone to their place of work. Questionnaires will be sent by email and post to occupational therapists at their work address. **Feasibility RCT:** A cohort group and randomised controlled trial in patients who have had a stroke and who are transferred to the Stroke Rehabilitation Unit (Derby Royal Hospital). Patients will receive either: No visit (Pre discharge hospital assessment and advice only) or a Home Visit (A pre-discharge home assessment visit will be conducted). The primary outcome measure is the Nottingham Extended Activities of Daily Living (NEADL) at one month. Results Interviews of experts and senior OTs have taken place. A questionnaire for use in all English stroke centres is being prepared. The feasibility RCT is ongoing, 50 patients have been recruited into the RCT and 28 into the cohort group.

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**OAID43**

**Subject area/topic: Ongoing Trial**

**Strings of Pearls Initiative (PSI) – Cerebrovascular Diseases Pearl**

**Introduction** The String of Pearls Initiative is a unique partnership between the eight university medical centers (UMCs) in the Netherlands. First established in 2007 by the Netherlands Federation of University Medical Centers (NFU), in this initiative clinical data and biomaterials is gathered from all participating UMCs to promote the advance of science, to improve treatment and encourage the development of new products. PSI is focusing on eight different disease entities, its pearls: cerebrovascular diseases, diabetes, hereditary colorectal cancer, inflammatory bowel disease, leukaemia, neurodegenerative diseases, renal failure and rheumatoid arthritis. The Cerebrovascular diseases (CVA) Pearl has been designed to create an extensive database in which clinical data and biomaterials are gathered uniformly to perform large-scale stroke research with a focus on genetics. In the Netherlands, 41,000 people suffer from stroke each year. Moreover, stroke is the first leading cause of disability in the western world. Epidemiological and genetic research in stroke based on extensive sample size is limited. Prevention and treatment strategies may be improved by this high quality large-scale research. **Methods** All eight UMCs participate in the CVA Pearl. All consecutive patients with cerebral infarction, intracerebral and subarachnoid hemorrhage or venous sinus thrombosis are included prospectively in the CVA Pearl. Data on vascular risk factors, clinical symptoms, laboratory tests, radiological examinations, genetic material (DNA), therapy and prognosis is collected and stored. **Results** Currently, clinical data and biomaterials of 929 patients are present in the PSI database. **Conclusion** The CVA Pearl is a unique database in which clinical data and biomaterial of patients with stroke is uniformly gathered. This dataset will be used for epidemiological and genetic research and will contribute to better understanding, prevention and treatment of cerebrovascular diseases.

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## OAID44

### Subject area/topic: Ongoing Trial

#### Platelet Transfusion in Cerebral Haemorrhage (PATCH)

**Background** Hematoma volume is one of the most important outcome predictors in intracerebral hemorrhage (ICH). At least 38% of patients suffer from hematoma growth which occurs mainly in the first 6 hours. If patients are selected carefully, outcome may be improved by limiting hematoma growth. The use of antiplatelet treatment (APT) seems to be a risk factor for the development of hematoma growth as well as poor outcome. **Objective** To investigate whether platelet transfusion in patients with ICH, who are using antiplatelet agents, improves outcome by preventing hematoma growth.

**Design** PROBE design: Prospective, Randomized, Open treatment, Blinded Endpoint evaluation

**Inclusion criteria** - Age  $\geq$  18 years - Spontaneous, non-traumatic supratentorial ICH confirmed by CT scan - GCS score 8-15 - Antiplatelet treatment in the week preceding ICH - Treatment can start  $\leq$  6 hrs after onset of symptoms - Treatment can start  $\leq$  1½ hrs after CT - Pre-stroke mRS score 0 or 1

**Exclusion criteria** - Suspected epidural, subdural, aneurysmal or AVM hematoma - Surgical evacuation planned  $\leq$  24 hrs - Intraventricular extension - Previous transfusion reaction - Use of Vitamin K antagonists (Warfarin) in the previous 5 days - Known thrombocytopenia  $<$   $100 \times 10^9 / l$  - History of coagulopathy - Previously legally incompetence - Death appears imminent

**Sample size** Outcome is assessed with the mRS, a score of 4 or more is defined as poor outcome. If poor outcome is reduced from 0.70 to 0.50, 95 patients are required in each group, totalling 190 patients.

**Outcome measure** Primary outcome Poor outcome mRS 4-6 at 3 months

**Main secondary outcome** - Hematoma growth  $<$  24 hrs - Complications of platelet transfusion (thrombotic complications and transfusion reaction) - Predictive value of the CTA "spot sign" regarding primary outcome - Predictive value of the CTA "spot sign" regarding hematoma growth - Patient's functional health using the full ordinal scoring range of the mRS at 3 months

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## OAID45

### Subject area/topic: Ongoing Trial

The Sleep Apnea cardioVascular Endpoints (SAVE) study: 1000 patients recruited

**Background:** Despite increasing evidence of a link between obstructive sleep apnea (OSA) and cardiovascular (CV) disease, well powered randomised controlled trials (RCT) of OSA therapy focussed on hard CV endpoints are lacking. **Methods:** SAVE is an international, multicentre RCT of CPAP therapy plus standard care versus standard care alone in 5000 patients with established CV disease and co-existing moderate-severe OSA to be followed-up over several years. Patients with a history of coronary artery disease or stroke/TIA who screen positive for OSA using a home monitoring device (Apnealink), are randomised following their satisfactory completion of a 1-week run-in phase of unblinded sham-CPAP. **Results:** To date, over 1000 patients (179 Australia/NZ, 819 China, and 13 India) have been recruited from 63 sites. On average, 2-3 patients are screened for OSA for 1 patient to be randomised. Half (53%) of patients have a history of a stroke/TIA. CPAP adherence at 6 and 12 months is high, at 4.2+0.13 (n=287) and 3.9+0.16 (n=166) hours/night, respectively. The clinical network is currently being expanded to the United Kingdom, Spain, USA and Brazil. **Conclusions:** There has been widespread acceptance of the need for the SAVE trial by clinicians. Recruitment is increasing and CPAP adherence is high, reassuring us of the feasibility and quality of the study. **TRIAL CONTACT INFORMATION:** Global Study Director Dr Emma Heeley info@savetrial.org ph +61299934561. <http://www.savetrial.org>

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## OAID46

### Subject area/topic: Ongoing Trial

#### Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT2): progress update on the largest clinical trial in ICH

**Background:** INTERACT2, an international, open, randomised, controlled trial, aims to establish the effectiveness of early intensive blood pressure (BP) lowering treatment in acute intracerebral haemorrhage (ICH), the most serious and least treatable form of stroke. **Methods** A target of 2800 patients with ICH, elevated systolic BP (150-220 mmHg) and capacity to receive intensive BP lowering treatment within 6 hours of onset are being included from 100+ sites worldwide. Simple electronic data collection procedures are used and patients are centrally randomly assigned to intensive (target systolic <140 mmHg) or conservative (target systolic <180 mmHg) BP management using routine blood pressure lowering agents. Vital status and disability is assessed at 28 and 90 days. CT digital images are analysed centrally. The trial is registered (ACTRN1260800036239, NCT00716079, ISRCTN73916115). **Results** Since late 2008, over 1900 patients have been randomised from Australia, China, Europe, India, Pakistan, Argentina and Chile at the end of April 2011, including 315 patients from 35 European centers (3 in Austria, 1 Belgium, 1 Finland, 13 France, 7 Germany, 5 Italy, 1 Portugal, 3 Spain, and 1 Switzerland). Quality parameters are encouraging with a BP separation of 19 mmHg between groups at 1 hour. The clinical network has expanded with sites in United Kingdom and Norway to boost recruitment of non-Chinese patients. **Conclusions:** Europe is making a significant contribution to INTERACT2. Recruitment and quality parameters indicate the study is on schedule to achieve its key objectives.

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## OAID47

### Subject area/topic: Ongoing Trial

#### Optimising the Analysis of Cognition Collaboration (OA-Cog)

**Rationale:** Over 800,000 people suffer with dementia in the UK. The evidence base for the treatment of cognitive decline and dementia is small. One reason for this may be that the measures used to assess cognition in clinical trials are not sensitive to change and/or the analyses used are suboptimal. OA-Cog aims to identify the most efficient cognitive measurement and analysis technique for cognition data and dementia in randomised controlled trials. Sample size in clinical trials is an important issue. A reduced sample size will allow trials to be conducted faster and use fewer resources. OA-Cog aims to assess the implication of choosing particular methods of analysis and also adjusting for baseline prognostic factors on sample size. **Design:** Chief investigators of randomised controlled trials with cognitive assessments are asked to share individual patient data from their trials. Variables requested include baseline prognostic factors, treatment group, cognitive measures (e.g. Mini Mental State Examination (MMSE), Alzheimer's Disease Assessment Scale cognitive subscore (ADAS-cog)) and other outcome measures (e.g. death, dementia). Data are then analysed using various endpoints (e.g. mean MMSE score at end of trial, MMSE score as a gradient over time) and statistical methods (e.g. Wilcoxon rank-sum test, repeated measures ANOVA) in order to identify the most efficient. **Trial Status:** As of 20th April 2011, data from 16 clinical trials, with a total of 36911 patients have been shared. The OA-Cog project is currently seeking further clinical trial data. **Contact Information:** E-mail: [cheryl.hogg@nottingham.ac.uk](mailto:cheryl.hogg@nottingham.ac.uk) Telephone: +44 (0) 115 823 1670

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## OAID48

### Subject area/topic: Ongoing Trial

#### Thrombolysis Or Anticoagulation for Cerebral venous Thrombosis (TO-ACT trial)

**Background** Endovascular thrombolysis (ET), with or without mechanical clot removal, may be beneficial for a subgroup of patients with cerebral venous sinus thrombosis (CVT), who have a poor prognosis despite treatment with heparin. Published experience with ET is promising, but only based on case series. **Objective** The objective of the TO-ACT trial is to determine if ET improves the functional outcome of patients with a severe form of CVT. **Methods** The TO-ACT trial is a multi-centre, prospective, randomized, open-label, blinded endpoint (PROBE) trial. Patients are eligible if they have a radiologically proven CVT, a high risk of poor outcome (defined by presence of one or more of the following: mental status disorder, coma, intracranial hemorrhagic lesion, or thrombosis of the deep cerebral venous system) and if the responsible physician is uncertain whether ET or standard treatment is better. 164 patients will be included. **Intervention** Patients are randomized to receive either ET or standard treatment (therapeutic doses of heparin). ET consists of local application of rt-PA or urokinase within the thrombosed sinuses. Mechanical clot removal, such as thrombosuction, is allowed, but not mandatory. **Outcomes** The primary endpoint is the modified Rankin score (mRS) at 12 months, with a score  $\geq 2$  defined as poor outcome. Secondary outcomes are 6 months mRS, mortality and recanalization rate. Principal safety outcomes are major intra- and extracranial hemorrhagic complications. Results will be analyzed according to the "intention-to-treat" principle. Blinded assessors not involved in the treatment of the patient will assess endpoints with standardized questionnaires. **Further information** Trial started April 2011. Investigators who are interested and would like to participate please e-mail us at [to-act@amc.nl](mailto:to-act@amc.nl)

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## OAID49

### Subject area/topic: Ongoing Trial

#### DUTCH ACUTE STROKE TRIAL (DUST) Prediction of functional outcome with CT-perfusion and CT-angiography

**Background** In acute ischemic stroke, risk assessment of poor functional outcome is necessary to weigh the potential benefits and side effects of treatment. Clinical parameters and non-contrast CT (NCCT) at admission are of limited value in predicting natural stroke outcome. Moreover, still relatively few patients receive intravenous thrombolysis (IVT), as most present later than the accepted 4.5 hours time window. CT perfusion (CTP) and CT angiography (CTA) are easily accessible and can potentially predict outcome and benefit or harm of IVT or thrombectomy. **Objectives** The primary aim of the DUST is to assess the additional prognostic value of combined CTP and CTA parameters to baseline patient criteria and NCCT. A secondary aim is to identify the best CTP and CTA indicators of functional outcome after ischemic stroke in a prediction model for improving therapy selection. **Design** This is a prospective multi-centre observational cohort study. The trial will include 1500 patients with stroke symptoms of less than 9 hours duration and no hemorrhage on NCCT. All patients will undergo NCCT, CTP and CTA on admission. If possible patients will undergo follow-up imaging (NCCT alone or combined with CTP and CTA) at 72 hours after onset. **Outcome** The primary outcome measure is the modified Rankin Scale score at 3 months. Among the secondary endpoints are infarct size, vessel recanalization, symptomatic and asymptomatic hemorrhage on follow-up imaging. **Trial status** Recruitment of patients started in June 2009. Currently, 14 centers are participating in the trial and 500 patients have been included so far. The mean age of the included patients was 68 years and 54% was male. In total, 52% of the patients received IVT. The trial is funded by The Netherlands Heart Foundation and NutsOhra.

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**OAID50**

**Subject area/topic: Ongoing Trial**

**Update of the SPEED Trial: A Study of the Penumbra Early Evacuation Device**

**Background:** The Penumbra System is an aspiration-based mechanical thrombectomy device for the revascularization of large vessel occlusion in acute ischemic stroke. We report results of a proof of concept study to assess the extent to which a reperfusion catheter with a larger internal diameter (0.054 inch) affects aspiration efficiency and speed, as well as accessibility and safety of the System. It is designed to increase aspiration efficiency, address large clot burden in proximal vessels and leverage existing aspiration technology. **Methods:** The 054 SPEED Trial is a retrospective case review of 74 patients with large vessel occlusion in the brain who were treated with the Penumbra System 054 catheter at 11 international centers. The main inclusion criteria were presentation within 8 hours of symptom onset and an occlusion of a treatable cerebral vessel. The primary endpoints were time of aspiration and rate of complete revascularization as measured by the TIMI scale (TIMI $\geq$ 2). Results from the Penumbra Pivotal and POST trials that utilized the smaller catheters (0.026 to 0.041 inch) were used as the historical controls. **Results:** Stroke severity with a median baseline NIHSS of 18 (range: 11-25) was high. All 74 patients presented with an occlusion graded TIMI 0 or 1 in the target vessel. The target vessel was the ICA in 24%, the MCA in 70% and the vertebrobasilar system in 5%. Time to recanalization was reduced to a median of 18 min. compared to 45 min. in the Pivotal Trial. Successful recanalization with TIMI 2 and 3 was attained in 92% compared to 87%. Procedure and device related SAE occurred in 5.4% (no change). **Conclusion:** Increasing the internal diameter of the Penumbra Reperfusion Catheter to 0.054 inch can enhance aspiration efficiency and speed, leading to a shorter aspiration time and a more complete revascularization without affecting accessibility or safety. Its effectiveness in large clot burden reduction points to a role as frontline therapy.

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## **OAID51**

### **Subject area/topic: Ongoing Trial**

#### **AXIS 2: AX200 for the treatment of ischemic stroke**

**Background:** AX200 (Granulocyte colony stimulating factor, G-CSF) is pre-clinically one of the best characterized drug candidates for the treatment of acute stroke. A phase IIa study (AXIS) showed that AX200 is safe over a broad dose range and well tolerated in stroke patients. Exploratory analysis of clinical outcome measures showed signs of efficacy. **Objective:** The primary objective of AXIS-2 is to assess efficacy of AX200 compared to placebo in patients suffering from acute ischemic stroke. **Methods:** AXIS-2 is designed as a European multicenter, randomized, double blind, placebo controlled phase II study. The target sample size is 328 patients randomized. Primary endpoint of the study is the improvement on mRS compared to placebo after 90 days. Further endpoints include the NIHSS, Barthel Index, infarct size reduction, mortality and safety parameters. Main inclusion criteria are ischemic stroke in the MCA territory, treatment within 9h, baseline NIHSS 6 – 22, age 18 - 85y, initial infarct size (DWI) >15ccm. **Results/Conclusion:** The study is currently ongoing in 53 sites in 7 countries (Germany, Spain, Czech Republic, Slovakia, Poland, Belgium and Austria). More than 80% of patients have been randomized in the study and the results are expected by end of 2011.

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## OAID52

### Subject area/topic: Ongoing Trial

**Double-Blind, Placebo Controlled, Randomized, Multicenter Study to Investigate Chinese medicine NeuroAiDTM Efficacy on Stroke Recovery (CHIMES Study) : Study Update to April 2011 CHIMES Investigators**

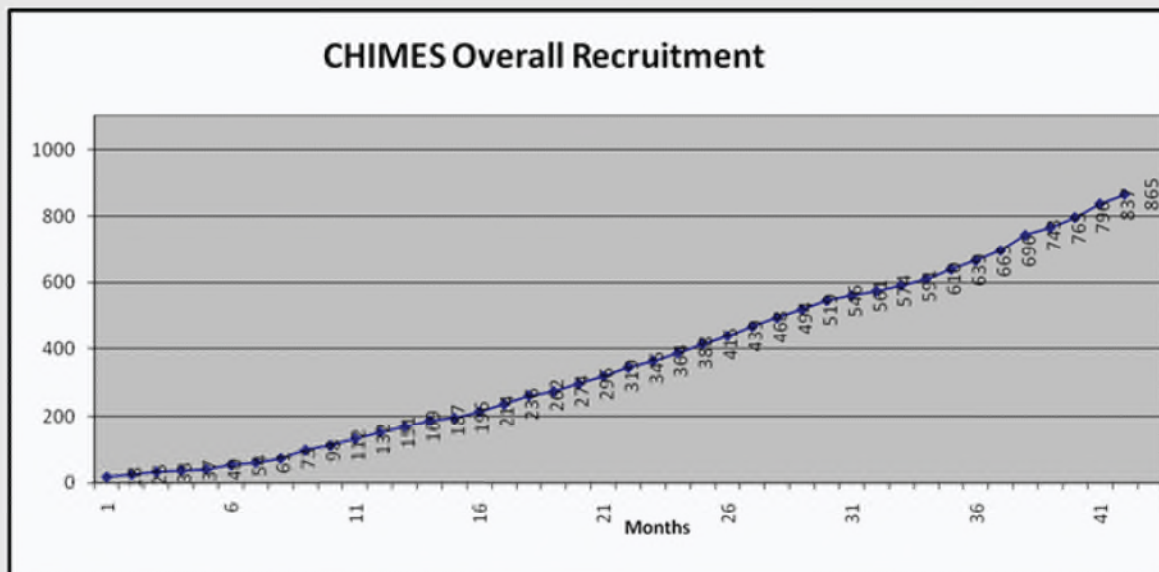
Stroke is a major cause of death and disability. Previous clinical studies performed in China have shown that NeuroAiDTM increases stroke patients' recovery in terms of neurological disability and functional outcome [Chen et al, 2009] and thus may be beneficial as part of a post-stroke rehabilitation programme. In the CHIMES study, we seek to test the hypothesis that NeuroAiDTM is superior to a Placebo in reducing neurological deficit and improving functional outcome after acute ischemic stroke in patients with cerebral infarction with intermediate range of severity ( $6 \leq \text{NIHSS} \leq 14$ ). More details of the study protocol have recently been published [Venketasubramanian et al, 2009]. CHIMES is currently the largest trial investigating the efficacy of a Traditional Chinese Medication on stroke recovery which is in compliance with international guidelines and using Western clinical trial standards. It involves centres in Philippines, Singapore, Thailand, Sri Lanka and Hong Kong and has the support of eminent clinicians and scientists from France, Australia and countries in South East Asia. Safety data for additional laboratory tests was conducted only in Singapore sites at the request of the Singapore regulators. These results were analysed with the investigators and steering committee remaining blinded to the treatment allocation [Young et al, 2010] and showed no safety concerns. The second CHIMES DSMB meeting took place on the 28th of March 2011 and reviewed safety and outcome on 659 patients. Safety data alone was also available for total of 743 patients. There were no safety concerns noted by the DSMB which recommended the investigators to continue recruitment to the full sample size of 1100 patients.

**Graphic/Table:**

## Current Progress (Recruitment)

As of 30<sup>th</sup> of April 2011, Chimes has **865** patients randomized, which is 78.5% of the target 1100. The enrolment of patients per country is:

Singapore: 412  
Philippines: 367  
Thailand: 64  
Sri Lanka: 17  
Hong Kong: 5



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## OAID53

### Subject area/topic: Ongoing Trial

#### SPACE-2: Stent-protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs. Endarterectomy. A three-arm Clinical Trial

Current recommendations for treatment of asymptomatic carotid stenosis are based on data from clinical trials performed in the 1990ies. There is good evidence of an improved of up-to-date best-medical treatment to prevent cerebro- and cardiovascular risk as compared to a decade ago. Considering a low risk rate with up-to-date pharmacotherapy, interventional therapies such as CEA and, in particular, CAS need their specific justification because they are associated with considerable periinterventional risks. SPACE-2 is conducted as a three-armed study with a randomized, controlled, open, multi-centre design comparing best medical treatment with CEA and CAS. All patients are treated in accordance with their individual risk factor profile and risk factors. Primary safety endpoint is assessed as the rate of any stroke and death from any cause within 30 days of treatment. The primary efficacy endpoint is the cumulative rate of any stroke or death from any cause within 30 days plus ipsilateral ischemic stroke within 5 years of follow up. Secondary endpoints also include myocardial infarction. 3,640 subjects are envisaged to be enrolled in the clinical trial. Randomization has started in Juli 2009. Currently, 34 centers in Germany, Austria and Switzerland are participating. The study is funded by the German Research Foundation (DFG) and the Federal Ministry of Education and Research (BMBF). The results of this trial are expected to be important for defining a proven standard for the best possible treatment of asymptomatic carotid artery stenosis and would have wide impact on managing this disease. Further centers are wellcome, probably the study will be extended to other European countries.

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Study	Title	Sponsor
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**OAID54**

**Subject area/topic: Ongoing Trial**

**The National Institute of Health Research Stroke Research Network Clinical Trials Portfolio**

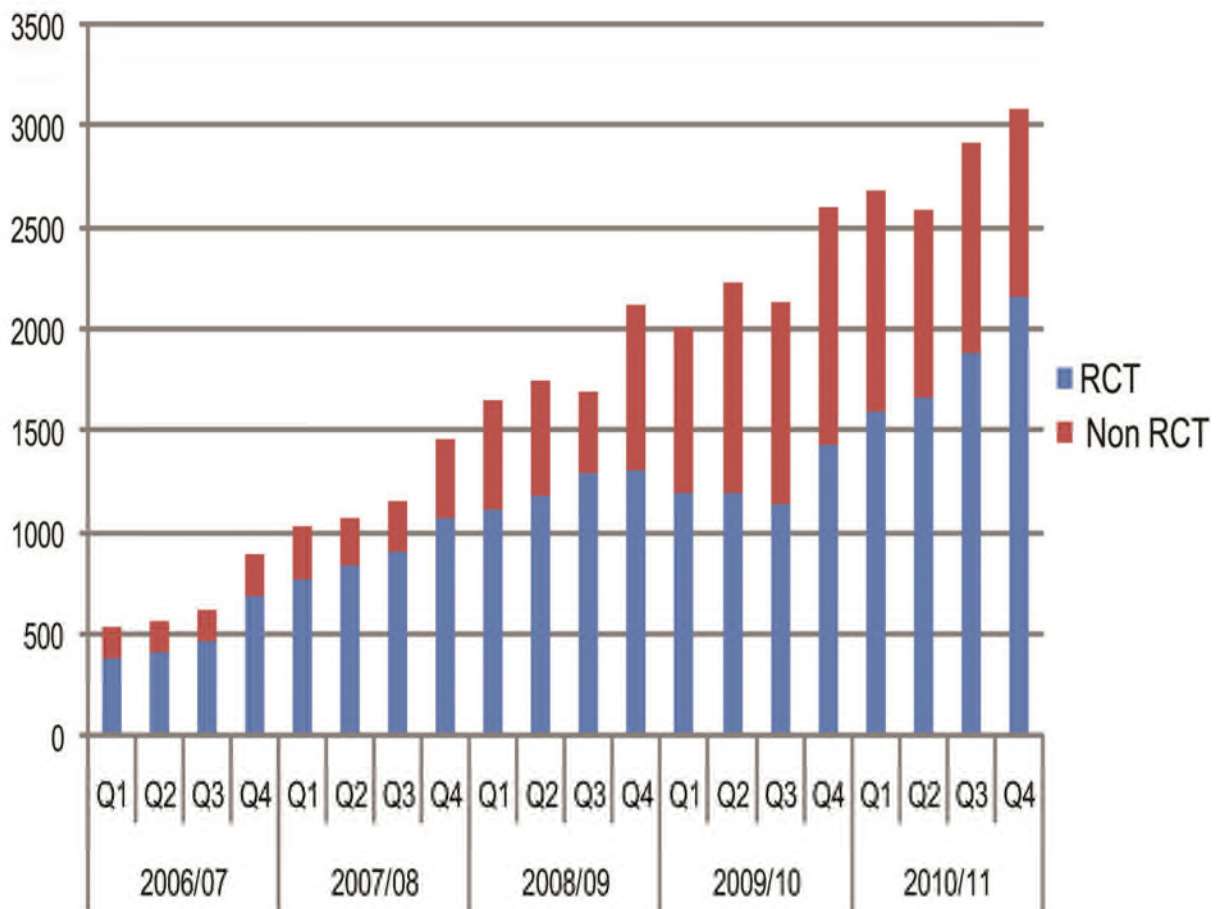
The National Institute for Health Research (NIHR) Stroke Research Network (SRN) was established in England in June 2005 to provide world-class health service infrastructure to support clinical stroke research and remove barriers to its conduct. NIHR SRN facilitates stroke research through investment in a national coordinating centre, 8 English local stroke research networks (\$7 million funding in 2008), and works closely with stroke research networks and structures in Scotland, Northern Ireland and Wales to enhance clinical stroke research infrastructure, clinical co-ordination, research nursing staff, imaging and pharmacy. In 2010 funding was provided to 8 Hyperacute Stroke Research Centres across England to support the delivery of hyperacute stroke studies (\$6 million funding over 3 years). Support is provided to academic studies funded through peer review and open national competition and commercial studies. International studies funded in open national competition are potentially eligible for NIHR SRN support. The UK wide study portfolio consisted of 96 open studies in April 2011 with a further 16 studies in set-up. Patients recruited into stroke studies increased from 2598 in 2006/07 to 11265 in 2010/11 with patient recruitment from 184 hospitals. Increased recruitment occurred in both academic and commercial funded studies and in all three areas of acute, rehabilitation and prevention research. Investment in stroke clinical research infrastructure has had a major impact on UK stroke research activity. Current activity suggests 6% of the incident UK stroke population participate in clinical stroke studies. The aim of NIHR SRN to increase the number of patients participating in stroke studies to 10000 each year (with 6500 participating in randomised controlled trials) by 2013 has been already achieved. NIHR SRN welcomes applications from academic chief investigators and commercial companies seeking support for UK patient recruitment to ongoing clinical trials.

Graphic/Table:

**Table 1. Current portfolio of multicenter international trials open to recruitment**

<b>ACST-2</b>	Asymptomatic Carotid Surgery Trial-2 surgery versus stenting	BUPA Foundation, NIHR - Health Technology Assessment Programme (HTA)
<b>ARUBA</b>	A randomised trial of unruptured brain arteriovenous malformations	National Institutes of Health, US
<b>AVERT</b>	A Very Early Rehabilitation Trial - A Phase III, multi-centre, randomised controlled trial of very early rehabilitation after stroke	Chest, Heart and Stroke Scotland
<b>Clear III</b>	Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Haemorrhage phase III	National Institute of neurological disorders and stroke
<b>DIAS 4</b>	A double blind randomised study of desmoteplase 90micgram/kg vs placebo in patients with acute ischemic stroke	Lundbeck Ltd
<b>ENOS</b>	Efficacy of Nitric Oxide in Stroke trial	Medical Research Council
<b>EUPACT</b>	European Pharmacogenetics of Anticoagulant Therapy	Commission of the European Union through the EU FP7 Programme
<b>INTERACT2</b>	The second intensive blood pressure reduction in acute cerebral haemorrhage trial. An international randomised control trial to establish the effects of early intensive blood pressure lowering in patient with intracerebral haemorrhage	Australian MRC
<b>IRIS</b>	Insulin Resistance Intervention after Stroke	NIHR USA
<b>IST-3</b>	Third International Stroke Trial	Health Foundation, Medical Research Council, The Stroke Association
<b>MASH II</b>	Magnesium in aneurysmal subarachnoid haemorrhage	The Netherlands Heart Foundation
<b>MISTIE</b>	Minimally invasive surgery plus rt-PA for ICH evacuation (MISTIE)	NIHR USA
<b>PODCAST</b>	Prevention of Decline in Cognition After Stroke Trial	The Alzheimers Society, The Stroke Association
<b>PRET</b>	Patients Prone to Recurrence After Endovascular Therapy	MicroVention
<b>RENEURON</b>	A Phase 1 safety trial of CTX0E03 Drug Product delivered intracranially in the treatment of patients with stable ischaemic stroke	ReNeuron Group plc
<b>SISTERS</b>	SISTERS: Spasticity in Stroke – Randomized Study	NIHR, Medtronic Ltd
<b>STASH</b>	Simvastatin in Aneurysmal Subarachnoid Haemorrhage (STASH) - a multicentre randomised controlled study	British Heart Foundation
<b>STICH II</b>	Surgical Trial in Lobar Intracerebral Haemorrhage	Medical Research Council

**Chart 1: NIHR SRN Portfolio recruitment (2006-2011)**



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## OAID56

### Subject area/topic: Ongoing Trial

#### Preliminary results of the SURPRISE- study Stroke Prior to Diagnosis of Atrial Fibrillation Using Long-term Observation with Implantable Cardiac Monitoring Apparatus Reveal® (SURPRISE)

**Background** Atrial fibrillation is a recognized risk factor for stroke and death, and the SURPRISE study set out in 2010 to investigate the amount of paroxysmal atrial fibrillation among patients with a prior TIA or minor stroke using the latest heart monitoring system. By monitoring the patients with loop-recording we can discover AF in patients who would not be found under normal circumstances during a standard admission and follow-up. A database study of previously admitted stroke patients who later were diagnosed with AFIB suggests that a conservative estimate of 7 % is to be expected.

**Method** The study includes patients admitted to a Copenhagen stroke unit with an annual number of admissions 600 stroke patients. Patients are included after informed consent if complying with the following inclusion criteria: 1) <18 years of age and the ability to provide an informed consent, 2) CT or MRI showing lesions corresponding to the clinical cortical symptoms of a stroke, 3) EKG and telemetry without signs of arrhythmia; 4) No prior or known AFIB. The loop recorder is implanted subcutaneously and the patient transmits data from home for up to three years. The transmissions are monitored online in cooperation with a cardiologist.

**Results** 35 patients have been included and 29 implanted; 5 patients have shown AFIB (17,9 %) and have been anticoagulated. The mean CHADS2VAS score 4 among the patients who have been diagnosed with AF compared to 3,04 amongst the group without. In comparison to that the CHADS2 score was 3,8 vs. 2,25. Age in the AF group was 68 vs. 55,9 in the group without AF. 3 patients have been explanted (2 by patient request, 1 due to infection). The study continues enrolling until 100 patients have been included, which we expect to reach within 2011. Patients will be followed up for at least 18 months in order to document the frequency and the temporal evolution of AF after cryptogenic TIA or minor stroke.

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## **OAID57**

### **Subject area/topic: Ongoing Trial**

**Sleep Disordered Breathing in Transient Ischemic Attack (TIA)/Ischemic Stroke and Continuous Positive Airway Pressure (CPAP) Treatment Efficacy: An prospective multicentre trial - SAS CARE study.**

**Objective of the Study:** The study aims to observe the short term effect (3-month, SAS CARE 1) of sleep disordered breathing (SDB) on cardiovascular parameters, heart rate variability, endothelial function and surrogate markers of atherosclerosis after ischemic stroke or transient ischaemic attack (acute cerebrovascular ischemic events (AIE)). The long-term effect (SAS CARE 2) of Continuous Positive Airway Pressure (CPAP) on clinical vascular outcome, cardiovascular parameters, evolution of surrogate of atherosclerosis, heart rate variability and endothelial function after ACE will be observed over 12-24 months. The effect of CPAP therapy on cardio- and cerebrovascular events will be evaluated in patients with moderate-severe obstructive SDB (AHI>20) without sleepiness. **Outcomes:** The SAS CARE 1 study is planned to verify whether or not sleep disordered breathing has a detrimental 3 months effect on cardiovascular functions and markers after acute cerebrovascular events. The SAS CARE 2 study is designed to address whether or not the treatment of sleep disordered breathing with CPAP reduces the combined rate of mortality, stroke, cardiovascular events (myocardial infarction/revascularisation/instable angina/hospitalisation for heart insufficiency) over a 24 months period in patients after acute cerebrovascular events. **Preliminary Results:** Today 41 patients have been included in SAS CARE 1, 32 in SAS CARE 2. Seven patients have already been randomised to CPAP/non CPAP. Current recruitment status corresponds to expectations and let us anticipate by December 2011 the inclusion of n=100 in SAS CARE 1, n=100 in SAS CARE 2 (with n=30 randomized patients). **Potential impact of positive finding:** The SAS CARE study will contribute to our understanding of the clinical implications of SDB in patients with AIE and the feasibility/efficacy of CPAP treatment in selected patients with AIE and SDB. **ClinicalTrials.gov Identifier:** NCT01097967

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## OAID58

### Subject area/topic: Ongoing Trial

#### ARUBA - A Randomized Trial of Unruptured Brain AVMs

**RATIONALE:** Current invasive treatment for brain arteriovenous malformations (AVMs) is varied and includes endovascular procedures, neurosurgery, and radiotherapy alone and in combination, largely dependent on the decisions of the local clinical team. However, no controlled treatment data on invasive AVM therapy exist and recent data raise serious doubt about the treatment benefit for unruptured brain AVMs. **DESIGN:** ARUBA is an international, multicenter, randomized, controlled, open, prospective clinical trial. **SAMPLE SIZE:** 400 patients (1:1 random assignment). **POPULATION STUDIED:** Patients aged  $\geq 18$  years, diagnosed with an unruptured brain AVM considered treatable by the local investigators. **Outcome measures:** The primary outcome is the composite event of death from any cause or stroke (hemorrhage or infarction confirmed by imaging). Clinical outcome status will be measured by the Rankin Scale, NIHSS, SF-36, and EuroQol.

**INTERVENTIONS:** Patients will be randomly assigned to best possible invasive therapy (endovascular, surgical, and/or radiation therapy) versus medical management alone. Patients will be followed for a minimum of 5 years from randomization. **PRIMARY AIM:** To determine whether medical management is superior to invasive therapy for preventing the composite outcome of death from any cause or stroke (symptomatic hemorrhage or infarction confirmed by imaging) in the treatment of unruptured BAVMs. **ALTERNATE PRIMARY AIM:** To determine whether medical management is not inferior to invasive therapy for preventing the composite outcome of death from any cause or stroke (symptomatic hemorrhage or infarction confirmed by imaging) in the treatment of unruptured BAVMs. **SECONDARY AIM:** To determine whether treatment of unruptured BAVMs by medical management decreases the risk of death or clinical impairment (Rankin Score  $\geq 2$ ) at 5 years post-randomization compared to invasive therapy. **TRIAL STATUS:** N=150 patients have been enrolled worldwide. **SPONSOR:** NIH/NINDS **CONTACT:** [www.arubastudy.org](http://www.arubastudy.org)

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## **OAID59**

### **Subject area/topic: Ongoing Trial**

**THE URICO-ICTUS STUDY. A phase 3 study of Combined Treatment With Uric Acid and rtPA Administered Intravenously in Acute Ischemic Stroke Patients Within the First 4.5 Hours of Symptoms Onset.**

**Background:** Oxidative stress is a major contributor to brain damage in patients with ischemic stroke. Uric acid (UA) is a potent endogenous antioxidant molecule. In experimental ischemia in rats, the exogenous administration of UA is neuroprotective and enhances the effect of rt-PA. Moreover, in acute stroke patients receiving rtPA within 3 hours of stroke onset the intravenous administration of UA is safe, prevents an early fall in UA levels and reduces an early increase in oxidative stress markers and in matrix degrading enzymes (MMP9) levels. **Purpose of the study:** To determine whether the combined treatment with UA and rtPA is superior to rtPA alone in terms of clinical efficacy in acute ischemic stroke patients treated within the first 4.5 hours of symptoms onset. **Study design:** Multicenter, interventional, randomized, double blind, vehicle controlled, efficacy study with parallel assignment (1:1). **Estimated enrollment:** 420 patients over 3 years, starting in June 2011. **Treatment arms:** Included patients will receive a single intravenous infusion of 1000 mg of UA dissolved in a vehicle (500 ml of 0.1% Lithium Carbonate and 5% Mannitol) (n=210), or vehicle alone (n=210). **Inclusion and exclusion criteria:** The study will include patients older than 18 years old, treated with iv rtPA within the first 4.5 hours of clinical onset with a baseline NIHSS  $\geq 6$  and  $< 25$  and a mRS score  $\leq 2$  prior to the ischemic event. Patients with renal insufficiency, gout or asymptomatic hiperuricemia treated with allopurinol will be excluded. **Outcome measures:** The primary outcome measure is the proportion of patients achieving a mRS of 0 to 1 at 3 months after treatment, or 2 in those patients with a prior qualifying mRS of 2. **Secondary outcome measures** include final infarction volume measured at 72 hours and the proportion of patients with symptomatic intracranial hemorrhage ( $\geq 4$  points increase in NIHSS score).

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## **OAID60**

### **Subject area/topic: Ongoing Trial**

#### **Chinese Assessment for Vinpocetine In Neurology (CAVIN)**

**Title: The treatment of Vinpocetine (Cavinton) in patients with cerebral infarction, an open, randomized, multi-center control study Objective: Evaluate the efficacy and safety of Vinpocetine (Cavinton) for treatment of cerebral infarction. Method: this is an open, randomized, multi-center control study in 9 hospitals in China nationwide. The cerebral infarction patients in test group are given intravenous infusion drip of Vinpocetine 30 mg/day and Citicoline 0.4g once daily. The patients in control group are given intravenous infusion drip of Citicoline 0.4g once daily without vinpocetine. Oral aspirin 75-100mg or clopidogrel sulfate tablets 75mg once a day for both groups. At baseline, 1st, 2nd and 12th week, Modified Rankin Scale and Mini-Mental State Examination (MMSE) will be evaluated as primary endpoints, Barthel index, NIHSS score, Transcranial Doppler (TCD) and adverse events also are examined as second endpoints. Study status: The study started on May 20, 2010. It was approved by Ethic Committee of The Military General Hospital of Beijing. As of May 1, 2011, 68 patients were enrolled and 52 finished the observation period. No adverse events were reported during the trial up to now**

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## OAID62

**Subject area/topic: Ongoing Trial**

### **POST-STROKE SPASTICITY PATIENTS IN THE BOTOX® ECONOMIC SPASTICITY TRIAL (BEST): CHARACTERISATION OF FUNCTIONAL IMPAIRMENT AND PRIORITIES FOR IMPROVEMENT**

**Background:** Patients with post-stroke spasticity (PSS) generally exhibit multiple functional deficits. A key issue is therefore which impairments to prioritise for intervention. **Methods:** Adults with focal PSS were randomised to BOTOX® (BoNT-A) + standard care (SC) or placebo + SC for up to 2 treatment cycles, followed by an open-label phase up to 52 weeks. Eligible patients were BoNT-A-naïve and demonstrated some preserved function in the limb to be treated. Those with fixed contractures and causes of spasticity other than stroke were excluded. Outcome variables were chiefly the attainment of individualised functional goals, mutually agreed between patient and investigator, using goal attainment scaling. **Results:** In the study population (n=273), time since last stroke was: <6 months (9.5%), 6-12 months (19.8%) or >12 months (69.2%). Injection sites for administration of study medication were in the lower limb only (26%), upper limb only (29%) or both upper and lower limbs (45%). Study medication was injected in the right, left and both sides of the body in 37.4%, 62.3% and 0.4% of patients, respectively. Around two-thirds of patients had multifocal spasticity and in 95% of patients spasticity was moderate or severe. Availability of physiotherapy ranged from 0-25 sessions/week (median=2) and the median number of occupational therapy sessions/week was 2 (range: 0-14). Potential benefits from spasticity treatment for the patients were indicated by the types of functional goals set including improvements in active functioning of the upper or lower limb (ambulation= 178 goals; feeding = 39; dressing= 27) and passive function (relief of pain=46 goals; improved posture= 29 goals). **Conclusion:** The priority for many patients with PSS within this study was to address impaired mobility followed by the need to perform activities of daily living. Interventions may be dependent upon the time since stroke and the availability of physiotherapy and/or occupational therapy.

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## OAID63

**Subject area/topic: Ongoing Trial**

### **USING A GOAL ATTAINMENT SCALE (GAS) IN POST-STROKE SPASTICITY (PSS) PATIENTS**

**Background:** When undergoing rehabilitation, conventional outcome measures in patients with PSS often record reduced spasticity rather than increased function. GAS is a way of individualising measurements of functional improvement, although there is an educational element that needs to be fulfilled for its successful application. **Methods:** Adults with focal PSS were randomised to BOTOX® (BoNT-A)+standard care (SC) or placebo+SC for up to 2 treatment cycles, followed by an open-label phase up to 52 weeks. Eligible patients were BoNT-A-naïve and demonstrated some preserved function in the limb to be treated. Those with fixed contractures and causes of spasticity other than stroke were excluded. The primary outcome measure was the percentage of patients achieving their principal active functional goal. **Results:** Goal-setting and scaling are skills that must be learned by healthcare professionals, as establishing agreed goals and predicting outcomes may not be part of routine practice. It is a mutual process between patient and physician, and while goals must be meaningful and relevant to the patient's everyday life and their priorities, they must also be realistic in terms of the feasibility of achievement within their rehabilitation regimen. Multiple factors may influence this aspect of goal-setting: other stroke-related impairments, spasticity severity and the presence of co-morbidities. Scaling the achievement of goals must be consistent between patients, with unambiguous and easily defined levels that are aligned with clinical observations. While in clinical practice, 5-point Likert scales have generally been used for this purpose, in clinical trials, a 6-point scale (including a level for deterioration from baseline) may be more useful for quantifying the degree of treatment response. **Conclusion:** GAS is a method for assessing functional improvement in PSS patients, but it requires training and experience to ensure appropriate outcomes are defined and quantifiable.

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**OAID64**

**Subject area/topic: Ongoing Trial**

### **The Second European Carotid Surgery Trial (ECST-2)**

**Background:** Randomized trials some years ago established the benefit of carotid endarterectomy (CEA) in patients with symptomatic or asymptomatic carotid stenosis. A risk model derived from the European Carotid Surgery Trial showed that only patients with a high risk of stroke on medical therapy benefit from CEA. For many patients there is neither clear benefit nor harm from CEA. Medical therapy to prevent stroke in patients with carotid disease has improved considerably since these original trials were concluded, with more widespread use of statins, more active lowering of blood pressure and more effective antiplatelet agents. Therefore optimized medical therapy (OMT) using up-to-date regimes may obviate the need for CEA or stenting in many patients with carotid disease. We therefore designed ECST-2 to address the question: is OMT alone equally efficient in the long-term prevention of stroke compared with revascularisation and OMT combined in patients at low and intermediate risk for stroke? **Methods:** ECST-2 is an international, multicentre, randomised, controlled, open, prospective clinical trial. Patients with asymptomatic or symptomatic carotid stenosis ( $\geq 50\%$  by NASCET criteria) suitable for CEA or stenting with a low or intermediate Carotid Artery Risk (CAR) score will be randomized between OMT alone or revascularisation and OMT combined. OMT will include adjustment to achieve target blood pressure and cholesterol levels. The CAR score will estimate the 5 year ipsilateral stroke risk of patients based on their demographic characteristics. The trial has the primary outcome of long term survival free of any stroke, MI or procedural death. Secondary outcome measures include cerebral infarction and haemorrhage on MRI, disability, cognitive decline, and economic measures. **Progress:** We are currently recruiting centres and will commence randomization in 2011. **Funding:** The trial is funded by a grant from the UK National Institute for Health Research.

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## OAID65

### Subject area/topic: Ongoing Trial

#### Characterisation of Post-Stroke Spasticity (PSS) Patients: The Botox® Economic Spasticity Trial (BEST)

**Background:** PSS has a profound impact on individuals and caregivers, but there are few detailed descriptions of the PSS patient population. **Methods:** Adults with focal PSS were randomised to BOTOX® (BoNT-A) + standard care (SC) or placebo + SC for up to 2 treatment cycles, followed by an open-label phase up to 52 weeks. Eligible patients were BoNT-A-naïve, demonstrated preserved function in the limb to be treated. Those with fixed contractures and causes of spasticity other than stroke were excluded. Baseline patient, disease and resource utilisation characteristics are presented here. **Results:** The intent-to-treat population comprised 273 patients (59% male, 97% Caucasian). Median age was 62.6 years (range: 22.6–82.4) and 56% of patients were <65 years. Ischaemic and haemorrhagic stroke had been experienced by 203 and 57 patients, respectively. In the majority of patients, stroke severity was defined as moderate (72%) or severe (23%). Median time since the last stroke was 22.8 months (range: 2.9–402.6) and in 69% of the patients this occurred >1 year prior to study entry. The mean (+/- standard deviation [SD]) total Resistance to Passive Movement Scale (REPAS) score was 21.3 +/- 9.14. Around two-thirds of patients had multifocal spasticity and in 95% of patients spasticity was moderate or severe. Co-morbidities included hypertension (61%), depression (40%) and hypercholesterolaemia (27%). Prior to baseline, the patients received a median of 2 physiotherapy and 2 occupational therapy sessions per week. Caregiver support was received by 67% of the patients, for a mean +/- SD of 3.8 +/- 4.5 hours/day. Mean +/- SD baseline EQ-5D score was 0.54 +/- 0.27; SF-12 mental and physical component summary scores were 50.4 +/- 9.50 and 47.7 +/- 10.06, respectively. **Conclusion:** For many patients spasticity remains a problem >1 year after stroke and is associated with substantial caregiver burden, significant resource use and diminished quality of life.

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## OAID66

### Subject area/topic: Ongoing Trial

#### Intravenous Autologous Bone Marrow Derived Stem Cell Therapy For Patients With Subacute Ischemic Stroke (InVeST): A Multi-Centric Randomized Controlled Trial

**Back ground and objective:** We are conducting a randomized controlled clinical trial (CTRI- PROVCTRI/2008/091/00046) to evaluate the safety and efficacy of administrating bone marrow derived stem cell intravenously to patients with subacute ischemic stroke. Our aim includes determination of dose response gradient on effects using several parameters: the National Institute of Health Stroke Scale (NIHSS) score modified Barthel Index (BI), Modified Ranking Scale (mRS) and reduction in infarct volume. **Method:** In this multi-centric randomized controlled clinical study five centers are participating. We have recruited 120 consecutive, eligible and consenting patients, aged 18-75 years with ischemic stroke involving MCA or ACA territory infarct between 7 to less than 30 days of onset of stroke with moderate severity in stable condition. Patients are randomly allocated by central telephone/fax/email. For stem cell arm, bone marrow has been aspirated from iliac crest and the harvested mononuclear cells infused into antecubital vein. Outcome measures for safety are immediate reactions after cell infusion and evidence of tumor formation at one year in whole body FDG-PET scan. Efficacy measurement time points are 7 (+2 days), 90(-7 to +14 days), 180 (-7 to +28 days) and 365 (-7 to +28 days) to determine clinical progress using NIHSS, BI, mRS, MRI, PET scan and EEG. BI and mRS are measured by blinded assessors centrally on telephone. Primary outcome is modified Barthel Index score at six months post-randomisation. **Results:** 120 patients have been recruited, 60 in each arm, from 31 January 2009 to 16 June 2010. Stem cell arm has been administered bone marrow mononuclear cells (mean 280.73 million with CD 34+ mean 2.85 million). Central telephonic follow up has been completed in 119 patients. One patient's remaining follow-up is due on 15th June 2011. **Conclusion:** Our multicentric trial has achieved the planned recruitment and near complete follow- up within the expected time frame. Central randomization and blinded telephonic assessment provide strengths to the validity of collected data. Randomisation has achieved adequate baseline similarity of prognostic factors.

**Topic:** "Intravenous Autologous Bone Marrow Derived Stem Cell Therapy For Patients With Subacute Ischemic Stroke (InVeST): A Multi-Centric Randomized Controlled Trial"

**Table: 1**

<b>Baseline Characteristics</b>	<b>Stem Cell (n=60 )</b>	<b>Control (n=60 )</b>
<b>Age in years</b>	<b>50.68 ± 11.59</b>	<b>52.55 ± 12.12</b>
<b>Sex (Male)</b>	<b>41 (68.33 %)</b>	<b>36 (60.00 %)</b>
<b>History of stroke</b>	<b>8 (13.33 %)</b>	<b>3 (5.00 %)</b>
<b>Hypertension</b>	<b>19 (31.67 %)</b>	<b>27 (45.00 %)</b>
<b>Diabetes</b>	<b>9 (15.00 %)</b>	<b>11 (18.33 %)</b>
<b>Dyslipidemia</b>	<b>1 (1.67 %)</b>	<b>0 (0 %)</b>
<b>Heart Disease</b>	<b>6 (10.00 %)</b>	<b>12 (20.00 %)</b>
<b>Atrial Fibrillation</b>	<b>3 (5.00 %)</b>	<b>4 (6.67 %)</b>
<b>Positive family history of stroke in first degree relative</b>	<b>2 (3.33 %)</b>	<b>1 (1.67 %)</b>
<b>Smoker</b>	<b>22 (36.67 %)</b>	<b>23 (38.33 %)</b>
<b>Alcoholic</b>	<b>23 (38.98 %)</b>	<b>20 (33.33 %)</b>
<b>Mean Infarct Volume in cc ± SD (Range) (n=92; Stem cell=47, Control=45)</b>	<b>65.193 ± 63.799 (0.6-255.9)</b>	<b>75.894 ± 58.963 (1.0 – 258.7)</b>
<b>Supported by Department of Biotechnology, Ministry of Science &amp; Technology, New Delhi, India</b>		

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**OAID67**

**Subject area/topic: Ongoing Trial**

**PARACETAMOL (ACETAMINOPHEN) IN STROKE 2 (PAIS 2): A RANDOMIZED, PLACEBO-CONTROLLED CLINICAL TRIAL OF HIGH-DOSE PARACETAMOL IN PATIENTS WITH ACUTE STROKE AND A BODY TEMPERATURE OF 37.0°C OR ABOVE**

**Background:** Subfebrile temperatures and fever are common in the first hours after stroke and are related to poor functional outcome. Whether treatment aimed at lowering body temperature improves functional outcome remains unclear. In the Paracetamol (Acetaminophen) in Stroke (PAIS 1) trial, a double-blind, placebo-controlled randomized clinical trial of 1400 patients with acute stroke, treatment with paracetamol (6 g daily, 3 days) was associated with more improvement on the modified Rankin scale (mRS) at 3 months if the baseline body temperature was 37°C or above (odds ratio 1.43; 95% confidence interval (CI): 1.02-1.97). As these results are based on a post-hoc subgroup analysis, further study is needed. **Objective:** To assess the effect of high-dose paracetamol on functional outcome in patients with acute stroke and a body temperature of 37.0 °C or above. **Methods:** PAIS 2 is a multicenter, randomized, double-blind placebo-controlled clinical trial. Fifteen-hundred patients with acute ischemic stroke or intracerebral hemorrhage will be included within 12 hours of symptom onset. Patients will be treated with paracetamol in a daily dose of 6 g or matching placebo for three consecutive days. The primary outcome is improvement on the full mRS at 3 months, estimated with multiple ordinal logistic regression. **Discussion:** PAIS 2 is a much needed trial, because observational studies have suggested that the use of paracetamol as recommended in guidelines (low dose, late start of treatment in selected patients) is not likely to be effective. Yet, when, high dose prophylactic antipyretic treatment will be proven effective, a simple, safe and extremely cheap therapy will be available for many patients with acute stroke.

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## OAID68

### Subject area/topic: Ongoing Trial

#### MR WITNESS: A Phase IIa Safety Study of Intravenous Thrombolysis with Alteplase in MRI-Selected Patients

**Rationale:** Many patients are discovered with acute stroke symptoms whose onset is unwitnessed. Current FDA indications exclude them from intravenous (IV) alteplase or rt-PA therapy because it has been more than 3 h since the patient was last known to be well. We propose to use advanced MR imaging as the “witness” to testify when the stroke actually started in patients who do not have a human witness. **Objectives:** (1) Determine the safety of IV rt-PA in subjects with unwitnessed stroke onset but MRI evidence of early stroke. (2) Validate novel MRI profiles to improve the sensitivity while maintaining high specificity for detecting subjects with acute stroke. (3) Explore the clinical efficacy of using imaging surrogates in subjects with unwitnessed stroke onset who are treated with rt-PA. **Subjects:** 80 adult male and female subjects 18-80 years old with acute ischemic stroke who arrive between 4.5 h and 24 h since last known well and within 3 h of symptom discovery. Subjects must be eligible to receive rt-PA using ECASS 3 criteria, excluding last seen well criterion. **Design:** Multi-center, open-label, single-arm, Phase IIa safety study. **Treatment:** Standard dose IV rt-PA. **Procedures:** Non-research baseline MRI and 24h post-treatment CT. Research MRI will be obtained post-drug infusion and at 30 days. NIH Stroke Scale (NIHSS) scores will be recorded at baseline, post-drug, and prior to 24 h CT. At five-day or discharge and at 30 day, NIH SS, Barthel Index (BI), and modified Rankin Scale (mRS) scores will be obtained. At 90 day, mRS and BI will be obtained. **Outcome Measures:** The primary outcome for this study is rt-PA safety as evidenced by no significant increase in symptomatic ICH rates using ECASS 2 definition observed in the ECASS 3 trial (5.3%). Secondary safety outcome will be no significant increases in rate of symptomatic edema. Lesion size and reperfusion rates will be compared in thrombolysed and non-thrombolysed subjects to determine benefit.

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