Ongoing Clinical Trials Posters II
Thursday, February 13, 2014, 6:15 pm – 6:45 pm

International Stroke Conference 2014 abstracts and presentations are embargoed for release at the date and time of presentation or time of AHA/ASA news event. Ongoing Clinical Trials abstracts are embargoed for the date and time of the Ongoing Clinical Trials Poster Session start time. No information may be released before then.

Presentation Number: CT P1

Trial Abbreviation: SHINE Trial

Trial Contact Information: Karen C. Johnston, kj4v@virginia.edu, phone - 434 924-5323, Fax- 434 982-1726

Trial Email: kj4v@virginia.edu

Trial Name: Stroke Hyperglycemia Insulin Network Effort Trial

Trial Registry Number ID: NCT01369069

Trial Sponsor: NIH-NINDS

Trial Web Site: www.shinetrial.com

Publishing Title: Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial

Author Block: Karen C. Johnston, Amy C. Fansler, Univ of Virginia, Charlottesville, VA; Valerie L. Durkalski, Medical Univ of South Carolina, Charleston, SC; Askiel Bruno, Georgia Regents Univ, Augusta, GA; Christiana Hall, Univ of Texas, Southwestern, Dallas, TX; William G. Barsan, Univ of Michigan, Ann Arbor, MI

Abstract Body:

Background: Hyperglycemia is common in acute stroke patients. Ischemic stroke patients with hyperglycemia have worse outcomes than those with euglycemia. There is clinical equipoise regarding how hyperglycemia should be managed in acute ischemic stroke patients.

Objective: To assess the safety and efficacy of glucose control (80 - 130 mg/dL) using insulin infusion versus standard sliding scale insulin with target glucose <180 mg/dL.

Design: SHINE is a multicenter, randomized, controlled trial with 2 treatment arms. The randomization algorithm prevents serious imbalance in NIH Stroke Scale (NIHSS) score, IV thrombolysis and clinical center.

Population: Adult acute ischemic stroke patients with Type 2 diabetes mellitus and hyperglycemia at the time of enrollment (glucose >110 mg/dL) or admission glucose of ≥ 150mg/dL for patients without diabetes. Study participants must be enrolled within 12 hours of stroke symptom onset. Study participants will be recruited from approximately 60 sites.

Sample Size: Maximum of 1400 subjects

Intervention: Study participants are randomized to intervention (IV insulin drip with target glucose 80-130 mg/dL) or control treatment (subcutaneous sliding scale insulin with target glucose <180 mg/dL). The intervention group utilizes the GlucoStabilizer® computerized decision support tool to guide therapy. Treatment continues for up to 72 hours.
Outcome Measures: The primary efficacy outcome is a 90-day modified Rankin Scale with favorable outcome dependent on baseline stroke severity (sliding dichotomy). The primary safety outcome is severe hypoglycemia (<40 mg/dL).

Statistical Analysis: The efficacy analysis, using a two-sided alpha = 0.05, will have 80% power to demonstrate a clinically relevant treatment effect, defined as an absolute increase in favorable outcomes of 7% or higher. Safety will be declared if the absolute rate of severe hypoglycemia in the intervention group does not exceed that of the control group by more than 4%.

Trial Status: Enrollment is ongoing at 50 of the approximately 60 sites. Remaining sites will be activated in 2013 and 2014. As of November 1, 2013, 253 subjects have been enrolled.

Sponsor: NIH-NINDS U01NS069498, U01NS056975, U01NS059041

Author Disclosure Block:

K.C. Johnston: Research Grant; Significant; NIH-NINDS U01 NS069498. A.C. Fansler: Research Grant; Significant; U01-NS069498. V.L. Durkalski: Research Grant; Significant; U01-NS069498, U01-NS056975. A. Bruno: Research Grant; Significant; NIH-NINDS U01 NS069498. C. Hall: Research Grant; Significant; NIH-NINDS U01 NS069498. W.G. Barsan: Research Grant; Significant; U01-NS056975, U01-NS069498.
REVASCAT is a multi-center, randomized, controlled, open, blinded-endpoint trial. Subjects presenting with acute ischemic stroke within 8 hours from symptom onset and CTA or MRA proven arterial occlusion of the internal carotid or proximal MCA (M1) who are either ineligible for IV alteplase or have received IV alteplase therapy without recanalization are randomized following a 1:1 ratio to receive mechanical embolectomy with the CE MARK approved stentriever Solitaire FR device or medical management alone. The primary endpoint on the basis of intention-to-treat criteria is the distribution of the modified Rankin Scale scores at 90 days. Sample size is to be 690 patients for an estimated common odds ratio of 1.615 that corresponds to an absolute difference in treatment effect of 10%.

Randomization is done under a minimization process using age, baseline NIHSS, therapeutic window and vessel occlusion site. The study follows a sequential analysis (triangular model), with the first approach to test efficacy in 174 patients. If the study is continued at this point, further analyses will take place when data are available on 346, 518 and 690. Salvageable brain is evaluated by ASPECTS score on non-contrast CT or DWI-MRI. Secondary endpoints are infarct volume evaluated on CT at 24 hours by a central core-lab, dramatic early favorable response as determined by an NIHSS of 0-2 or NIHSS improvement ≥ 8 points at 24 hours, vessel recanalization evaluated by CTA or MRA at 24 hours in both treatment groups and successful recanalization in the Solitaire arm assessed by mTICI (modified Thrombolysis in Cerebral Infarction) 2b or 3 on the post-procedure angiogram adjudicated by a central core-lab. Safety variables will be mortality at 90 days, symptomatic ICH rates at 24 hours and procedural related complications adjudicated by an independent committee.

The trial started on November 24, 2012 and 85 patients have been randomized by mid October 2013.
Author Disclosure Block:

Abstract Body:

The Platelet-Oriented Inhibition in New TIA and minor ischemic stroke (POINT) Trial, is a prospective, randomized, double-blind, multicenter trial with the primary null hypothesis that, in patients with TIA or minor ischemic stroke treated with aspirin 50-325 mg/day, there is no difference in survival free of ischemic stroke, myocardial infarction, and ischemic vascular death at 90 days in those treated with clopidogrel (600 mg loading dose then 75 mg/day) compared to placebo when therapy is initiated within 12 hours of the time last known free of new ischemic symptoms.

Subjects are 18 years of age or older with high-risk TIA (defined as an ABCD2 score GE 4) or minor ischemic stroke (with an NIHSS 4) or minor ischemic stroke (with an NIHSS LE 3); each subject is followed for 90 days from randomization. A total of 5,841 patients will be recruited and the trial will be completed in 7 years. The first subject was enrolled on May 28, 2010. International sites will join the POINT trial in late 2013.

Principal Investigator: S. Claiborne Johnston, MD, PhD, University of California, San Francisco
Co-Principal Investigator: J. Donald Easton, MD, University of California, San Francisco
Contact: Mary Farrant, MBA, BSN, RN, University of California, San Francisco, POINT Trial Clinical Coordinating Center (CCC), San Francisco, California, United States, 94158; Phone 1-415-502-7304; Email: mary.farrant@ucsfmedctr.org.

Planned Number of Centers: 260; Present Number: 182
Planned Number of Subjects: 5,841; Present Number: 1,618
Sponsor: University of California, San Francisco (UCSF); National Institute of Neurological Disorders and Stroke (NINDS)
Collaborators: Neurological Emergencies Treatment Trials Network (NETT); Statistics and Data Management Center (SDMC) at Medical University of South Carolina (MUSC); POINT Clinical Research Collaboration (POINT CRC) at EMMES Corporation
Dates of Study: October 2009 - September 2016
ClinicalTrials.gov Identifier: NCT00991029;
http://clinicaltrials.gov/ct2/show/NCT00991029?term=POINT&rank=1
Author Disclosure Block:

C. Johnston: Other Research Support; Significant; NINDS. J. Easton: Other Research Support; Significant; NINDS. W. Barsan: Other Research Support; Modest; NINDS. R. Conwit: None. C. Dillon: Other Research Support; Modest; NINDS. J. Elm: Other Research Support; Modest; NINDS. A. Lindblad: Other Research Support; Significant; NINDS. L. Morgenstern: None. Y. Palesch: Other Research Support; Significant; NINDS. S. Poisson: None.
Rationale: The relationships between cryptogenic stroke and patent foramen ovale (PFO) are complex, and the role of percutaneous closure for prevention for recurrent stroke remains promising but uncertain. Objective: The REDUCE Study is designed to demonstrate that PFO closure with the GORE HELEX Septal Occluder or GORE Septal Occluder plus antiplatelet medical management is safe and effective and reduces the risk of recurrent stroke or imaging-confirmed transient ischemic attack (TIA) when compared to antiplatelet medical management alone in patients with a PFO and history of cryptogenic stroke or imaging-confirmed TIA. Design: Multicenter, multinational, randomized clinical trial.

Population:
- 664 men and Women, age 18 - 60 years
- Cryptogenic ischemic stroke or imaging-confirmed TIA
- Presence of Patent Foramen Ovale (PFO) confirmed by transesophageal echocardiography (TEE)
- No evidence of an alternative etiology for stroke

Intervention: Participants will be randomized 2:1 to PFO closure with the GORE HELEX Septal Occluder or GORE Septal Occluder plus antiplatelet medical management vs. antiplatelet medical management alone. Patients will be followed to at least 2 years for the primary endpoint, and up to 5 years for secondary endpoints.

Primary Outcome: Time to recurrent stroke or imaging-confirmed TIA, or death due to stroke through 24 months post-randomization. All events will be adjudicated by a blinded clinical events committee.

Secondary Outcomes: Proportion of participants with new ischemic lesions on MRI at 2 years compared to MRI obtained at baseline; systemic embolic events; PFO closure in device-arm subjects by transthoracic echocardiography (TTE); device- and procedure-related adverse events; time to recurrent stroke or imaging-confirmed TIA, or death due to stroke through 60 months post-randomization.

Statistical Analysis: Time to recurrent stroke or imaging-confirmed TIA will be compared using an unadjusted log-rank test and presented using Kaplan-Meier methods. The primary analysis will be by intention-to-treat.
Trial Status: Enrollment is ongoing at a maximum of 80 investigational sites in the United States, Denmark, Finland, Sweden, Norway, Canada, and the United Kingdom with no per-site subject limit.

Author Disclosure Block:

S.E. Kasner, WL Gore, Acorda, AstraZeneca, Biogen, Significant, Research Grant; Medtronic, Parexel, Novartis, GlaxoSmithKline, Boehringer Ingelheim, Abbvie, Pfizer, Significant, Consultant/Advisory Board.
Background and Objective-In studies comparing combined clopidogrel and aspirin with clopidogrel alone (MATCH) and aspirin alone (CHARISMA), clopidogrel plus aspirin did not show an additional risk reduction of vascular events, and did show an increase in hemorrhagic events. On the other hand, in 3 studies comparing combined cilostazol and aspirin with aspirin alone (TOSS, TOSS2, and CATHARSIS), cilostazol and aspirin showed no significant increase in serious hemorrhagic events compared with aspirin monotherapy, suggesting that dual antiplatelet therapy including cilostazol may be safer compared with conventional dual antiplatelet therapies. Thus we conduct a multicenter randomized trial (CSPS.com) to examine efficacy and safety of dual antiplatelet therapy including cilostazol in high risk patients with noncardioembolic stroke. Patients and Methods-A total of 4,000 patients with noncardioembolic ischemic stroke after 8-180 days of stroke onset, who have >50% intracranial or extracranial arterial stenosis, or 2 or more risk factors including age over 65 years, diabetes, hypertension, PAD, CKD, ischemic heart disease, and current smoking are randomized to either treatment with antiplatelet monotherapy (aspirin 81-100 mg daily or clopidogrel 50-75 mg daily), or dual antiplatelet therapy (combining cilostazol 200 mg daily with either aspirin or clopidogrel). Primary endpoint is recurrence of ischemic stroke; secondary endpoints are any stroke, hemorrhagic stroke, ischemic stroke plus transient ischemic attack, any death, and composite of stroke, MI, and any death. Safety endpoints are serious or life-threatening hemorrhage and other serious adverse events. The observation period is at least one year. The study period is from October 2013 to March 2017.
Presentation Number: CT P7

Trial Abbreviation: EXTEND-IA

Trial Contact Information: Dr Bruce Campbell, bruce.campbell@mh.org.au fax +61 3 9342 8427

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Trial Name: EXtending the time for Thombolysis in Emergency Neurological Deficits – Intra-Arterial

Trial Registry Number ID: ClinicalTrials.gov NCT01492725

Trial Sponsor: Neuroscience Trials Australia

Trial Web Site: http://clinicaltrials.gov/ct2/show/NCT01492725

Publishing Title: EXtending the Time for Thombolysis in Emergency Neurological Deficits - Intra-Arterial: The EXTEND-IA Trial

Author Block: Bruce C Campbell, Peter J Mitchell, Bernard Yan, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; Leonid Churilov, Henry Ma, Florey Inst of Neuroscience and Mental Health, Univ of Melbourne, Parkville, Australia; Mark W Parsons, John Hunter Hosp, Univ of Newcastle, Newcastle, Australia; Geoffrey A Donnan, Florey Inst of Neuroscience and Mental Health, Univ of Melbourne, Parkville, Australia; Stephen M Davis, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; for the EXTEND-IA Investigators

Abstract Body:

Background: The proven benefits of tPA within 4.5 hours of stroke onset are limited by modest reperfusion rates in patients with major vessel occlusion. Endovascular mechanical clot retrieval may increase reperfusion rates in these patients.

Objective: EXTEND-IA will test the hypothesis that dual target vessel occlusion and penumbral mismatch can select patients with favourable response to reperfusion using mechanical clot retrieval after standard IV tPA<4.5hrs from stroke onset. EXTEND-IA will provide much needed randomized evidence about the effectiveness of clot retrieval in a responder population defined by CT or MR mismatch.

Design: Investigator-initiated, prospective, randomised, open-label, blinded-endpoint (PROBE) phase 2 trial.

Population studied: Patients with ischemic stroke <4.5 hours from onset who are receiving tPA. Eligibility for the trial requires vessel occlusion of the ICA or MCA (M1/M2) and CT or MR “mismatch” using a perfusion threshold of Tmax>6sec and a perfusion:ischemic core lesion volume ratio of >1.2. Ischemic core volume, assessed using MR-DWI or CT-relative cerebral blood flow, must be <70mL. This is assessed using a fully automated software package (RAPID, Stanford University).

Intervention: Mechanical clot retrieval (Solitaire FR device, Covidien) after IV tPA vs tPA alone.

Outcome measures: The co-primary endpoint is reperfusion at 24hr and favourable clinical response (≥8 point reduction in National Institutes of Health Stroke Scale or reaching 0-1) at 3 days with secondary endpoints including recanalization, symptomatic hemorrhage and functional outcome (modified Rankin score at 90 days).

Analysis: Intention to treat.

Trial Status: Recruitment commenced August 2012 with 12 centres now open in Australia and New Zealand and a further 3 sites planned to open in 2014.

Author Disclosure Block:
Background: Occurrence of intracerebral hemorrhage (ICH) has been threatened the beneficial effect of antiplatelet or high dose statin therapy in ischemic stroke patients, especially in patients who are prone for hemorrhagic stroke. Cilostazol is known to accompany less bleeding complications. Therefore, we have compared the efficacy and safety of cilostazol versus aspirin and investigated the additional effect of Probucol in ischemic stroke patients with high risk of ICH.

Methods/design: Prevention of Cardiovascular events in iSchemic Stroke patients with high risk of cerebral hemorrhage (PICASSO) study was designed as a double-blinded randomized controlled multicenter trial with a 2 x 2 factorial design. Ischemic stroke patients with a history or imaging finding of pervious ICH, or with multiple microbleeds were enrolled, and then randomized into 4 groups (Group A: Cilostazol and Probucol; Group B: Aspirin and Probucol; Group C: Cilostazol; Group D: Aspirin). A co-primary endpoint including the safety (time to onset of ICH) and efficacy endpoint (time to onset of composite cardiovascular events) will be investigated. Log-rank test will be used to prove the superiority in safety, non-inferiority in efficacy of Cilostazol, and the superiority in the efficacy of Probucol. The study will be continued until the 1600 patients (400 patients for each group) are enrolled, and the last enrolled patient will be follow-up at least 12 months.

Discussion: This study will deliver important information on the safety and efficacy of cilostazol comparing to aspirin, and the synergistic effect of adding Probucol in ischemic stroke patients with high risk of ICH.

Author Disclosure Block:

S. Kwon: Research Grant; Significant; Korea Ostuka pharmaceutical company support this study.
Presentation Number: CT P9

Trial Abbreviation: EXTEND

Trial Contact Information: ELISE COWLEY, ecowley@neurotrialsaustralia.com

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Trial Name: EXtending the time for Thombolysis in Emergency Neurological Deficits

Trial Registry Number ID: NCT00887328

Trial Sponsor: FLOREY NEUROSCIENCE INSTITUTES

Trial Web Site: http://www.start.csiro.au/about/extend

Publishing Title: Extending the Time for Thombolysis in Emergency Neurological Deficits - The Extend Trial

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Abstract Body:

Background: Current clinical application of thrombolysis in stroke is limited by the 4.5 hour time window and not applicable to patients with wake up stroke (WUS). Patient selection using advanced penumbral imaging criteria may allow extension of the therapeutic window.

Objective: To test the hypothesis that perfusion-diffusion mismatch can be used to select patients with favourable response to thrombolysis beyond conventional time windows.

Design: EXTEND is an investigator initiated, randomised, double-blind, placebo controlled phase 3 trial of intravenous alteplase vs placebo in patients with ischemic stroke 4.5-9 hours from stroke onset and WUS.

Methods: Patients with ischemic stroke within 4.5-9 hours from stroke onset and WUS patients, (WUS defined as the midpoint between time to sleep and awakening with the stroke symptoms <9 hours), are eligible for recruitment (n=200). Criteria for entry into the trial include perfusion-diffusion mismatch using a perfusion threshold of Tmax>6sec and a perfusion:diffusion lesion volume ratio of >1.2. Diffusion lesion volume must be <70mL. This will be assessed using a fully automated software package (RAPID, Stanford University). Reperfusion/recanalization will be assessed at 24 hours.

Outcome measures: The primary endpoint is mRS 0-1 at 90 days. Secondary endpoints will include mRS shift analysis, reperfusion, recanalization, quality of life and depression scales. Trial status: Recruitment commenced in June 2010 and there are 26 sites internationally and more sites to be initiated in 2014. A pooled analysis (n=400) will be performed with data from ECASS4 with identical protocol.

Author Disclosure Block:
Presentation Number: CT P10

Trial Abbreviation: TARDIS

Trial Contact Information: Mrs Sally Utton/Sally.utton@nottingham.ac.uk/Tel: +44 (0)115 82 30287/Fax: +44 (0)115 82 31771

Trial Email: tardis@nottingham.ac.uk

Trial Name: Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke

Trial Registry Number ID: ISRCTN47823388

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.tardis.org

Publishing Title: Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke (TARDIS). A Randomised Controlled Trial.

Author Block: Kailash Krishnan, Sally Utton, Hayley Foster, Tanya Payne, Margaret Adrian, Sarah Grant, Alice Durham, Katie Robson, Philip M Bath, Univ of Nottingham, Nottingham, United Kingdom

Abstract Body:

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 ischaemic heart disease, aspirin & dipyridamole (AD) for stroke, is superior to aspirin monotherapy. We hypothesise that triple antiplatelet therapy (ACD) will be superior to current guideline therapy (AD or C) 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 (3 years) phase, we assessed the safety, tolerability and feasibility of intensive antiplatelet therapy (ACD) versus guideline therapy given for 1 month in 902 patients with acute stroke/TIA. The main 5 year phase will assess the safety and efficacy of intensive or guideline therapy in up to 4,100 patients. The primary outcome is ordinal stroke severity (fatal/severe non-fatal/mild/TIA/none) at 90 days. Secondary outcomes include death, myocardial infarction (MI), vascular events, function, bleeding, serious adverse events; sub-studies will assess cerebral emboli and platelet function.

Trial status: The main phase of the trial commenced on 1st October, 2012, and will run for 5 years. As of 4th November, 2013, 1420 patients have been recruited from 80 centres (UK, Denmark, New Zealand).

Author Disclosure Block:

Presentation Number: CT P11

Trial Abbreviation: FAST-BP

Trial Contact Information: Nerses Sanossian

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Trial Name: The Field Administration of Stroke Therapy- Blood Pressure Pilot Trial

Trial Registry Number ID: NCT01811693

Trial Sponsor: NIH SPOTRIAS, UCLA Neurology, USC Neurology

Trial Web Site: http://clinicaltrials.gov/show/NCT01811693

Publishing Title: The Field Administration of Stroke Therapy- Blood Pressure (FAST-BP) Pilot Trial

Author Block: Nerses Sanossian, Univ of Southern California, Los Angeles, CA; Sidney Starkman, UCLA Stroke Ctr, Los Angeles, CA; Samuel Stratton, Univ of California Los Angeles, Los Angeles, CA; David S Liebeskind, UCLA Stroke Ctr, Los Angeles, CA; May A Kim-Tenser, Univ of Southern California, Los Angeles, CA; Neal Rao, UCLA Stroke Ctr, Los Angeles, CA; Lucas Restrepo, Univ of California Los Angeles, Los Angeles, CA; Latisha K Ali, Fiona Chatfield, Jeffrey L Saver, UCLA Stroke Ctr, Los Angeles, CA; FAST-BP Investigators and Coordinators

Abstract Body:

Background: Elevated blood pressure in the acute phase is associated with worse outcomes in both ischemic stroke and intracerebral hemorrhage. Prehospital lowering of BP may lead to earlier treatment with thrombolysis and reduce hemorrhage expansion.

Overview and Protocol Summary: The study design is an open-label dose escalation study with three dose tiers of prehospital-administered glyceryl trinitrate (GTN, Nitroglycerin) < 2 hours from symptom onset to 45 severely hypertensive stroke patients. Trained paramedics will identify subjects in the field and consent will be obtained by physician-investigators after cellular phone contact. Transdermal GTN patch will be applied in dose-tiers of 0.2mg/hour and 0.4mg/hour and combined sublingual GTN metered spray of 0.4 mg plus patch. Sites involved are the EMS system and 8 receiving Stroke Center hospitals in Orange County. The primary study endpoint is mean change in SBP from pre-treatment to ED arrival. The secondary study endpoints are: 1) mean change in SBP from pre-treatment to 30 minutes after ED arrival and 60 minutes after ED arrival; and 2) the proportion of patients with SBP < 180 mm Hg at ED arrival, 30, and 60 minutes after arrival. The control group will be matched from the placebo group in the Field Administration of Stroke Therapy Magnesium (FAST-MAG) clinical trial. It is anticipated that the trial will identify the most promising prehospital GTN regimen to advance to a pivotal, placebo-controlled, phase 3 trial.

Key Inclusion and Exclusion Criteria:

Inclusion Criteria
1) Suspected stroke identified with Los Angeles Prehospital Stroke Screen
2) Age 40-80, inclusive
3) Last known well time within 2 hours of treatment initiation
4) Deficit present for > 15 minutes
5) Systolic blood pressure ≥180

Exclusion Criteria
1) Coma
2) Rapidly improving neurologic deficit
3) Pre-existing disease that would confound outcome evaluations
4) Use of erectile dysfunction therapies in the previous 48 hours
5) Patient unable to give informed consent and no available legally authorized representative (LAR) to provide informed consent

Study progress to date: As of 11/4/2013 seven sites are active and four patients have been enrolled.

Author Disclosure Block:

BACKGROUND: Pioglitazone, a thiazolidinedione, increases insulin sensitivity by activating the nuclear transcription factor PPARγ. In addition to decreasing insulin resistance, pioglitazone improves dyslipidemia and endothelial function, reduces vascular inflammation, promotes fibrinolysis, and slows carotid atherosclerosis. In clinical trials among diabetic patients, it reduced the risk for stroke, MI, or death.

OBJECTIVE: To determine if pioglitazone, compared with placebo, is effective in lowering the risk for stroke or myocardial infarction among non-diabetic men and women with ischemic stroke or TIA.

DESIGN: Randomized, double-blind, placebo-controlled clinical trial.


POPULATION:
- Non-diabetic men & women
- Ischemic stroke or TIA within 6 months of enrollment
- At least 40 years of age
- Able to give informed consent
- Insulin resistant (by HOMA-IR index from fasting insulin and glucose values).

INTERVENTION: Participants are randomized to placebo or pioglitazone 15 mg tablets. The dose is increased each month to a final dose of three tablets daily. Thereafter, participants receive tablets containing placebo or 45 mg pioglitazone for once daily use.

PRIMARY OUTCOMES: Stroke and myocardial infarction.

STATISTICAL ANALYSIS: Time to first event by intention to treat.

STATUS: Recruitment was closed in January, 2013.

PROGRESS REPORT: A total of 3876 participants were randomized during 2005-2013. All participants will be followed for a maximum of five years or until June 2015.

Purpose:
Recanalization with standard IV rtPA therapy is least likely when clot length is ≥8mm. The goal of the THERAPY Trial is to assess safety and effectiveness of the Penumbra System® as adjunctive treatment to IV rtPA in stroke patients with large vessel occlusions and an extensive clot burden.

Methods:
The THERAPY Trial: The Randomized, Concurrent Controlled Trial to Assess the Penumbra System's Safety and Effectiveness in the Treatment of Acute Stroke is a prospective, multicenter study [N=692]. IV rtPA-eligible patients 18 to 85 years old presenting with acute ischemic stroke symptoms, NIHSS score ≥8 and with clot length ≥8mm in the anterior circulation are randomized 1:1 to combined treatment with the Penumbra System or IV rtPA therapy alone. The primary endpoints are 90-day functional outcome and incidence of serious adverse events. An independent Core Laboratory evaluates imaging, and a CEC/DSMB analyzes safety.

Results and Trial Updates:
There are 46 US centers with IRB approval and 59 randomized patients. Nine additional centers in Europe have committed to the trial, and Ethics Committee approval has been granted by the central investigational site in Dresden, Germany. Analysis of imaging screened failures in IV rtPA-eligible patients shows clots below 8mm in length are a small percentage of screened failures, in line with recent published data. Enrollment in EU centers is expected by the end of 2013.

Conclusions:
THERAPY may serve as the landmark study outlining the role of mechanical embolectomy in a stroke cohort unlikely to respond to IV rtPA. The clot length screening criteria serves to further reinforce selection of IV rtPA resistant patients, while not compromising the targeted population size.
P. Khatri: Other Research Support; Significant; Penumbra, Inc. J. Mocco: Other Research Support; Significant; Penumbra, Inc. O. Zaidat: Other Research Support; Significant; Penumbra, Inc. Speakers' Bureau; Modest; Penumbra, Inc. R. Gupta: Speakers' Bureau; Modest; Penumbra, Inc. R. von Kummer: Other Research Support; Significant; Penumbra, Inc.
BACKGROUND: A substantial proportion (30%-40%) of patients with ischemic stroke who arrive within 3 hours of symptom onset are not treated with intravenous (IV) recombinant tissue plasminogen activator primarily due to mild symptoms at the time of the treatment decision. However, approximately one-third of patients with untreated “mild strokes” are disabled at 90 days. The balance of risk versus benefit of thrombolysis for this group is uncertain based on available trials, and therefore presentation with “only minor or rapidly improving stroke symptoms” is currently considered a relative exclusion by clinical guidelines.

OBJECTIVE: To determine the efficacy of IV alteplase for treatment of acute ischemic stroke (AIS) in patients with mild stroke (“rapidly improving stroke symptoms” and “minor neurologic deficit”).

DESIGN: PRISMS is a double-blind, multicenter, randomized, phase 3b trial of patients with mild ischemic stroke within 3 hours of last known well time. Mild stroke is defined as a National Institutes of Health Stroke Scale (NIHSS) ≤5 and not clearly disabling. Patients meeting eligibility criteria are randomized 1:1 ratio to receive either (1) IV alteplase 0.9 mg/kg with oral aspirin placebo or (2) IV alteplase placebo with oral aspirin 325 mg.

SAMPLE SIZE: Approximately 948 patients will be enrolled across 75 sites in North America.

OUTCOME MEASURES: The primary outcome measure is the difference in the proportion of a favorable functional outcome between the 2 treatment groups, defined by a modified Rankin Scale (mRS) score of 0 or 1 at day 90 post-randomization.

STATISTICAL ANALYSIS: The primary efficacy analysis will test the hypothesis of superiority of IV alteplase therapy over standard medical care in AIS patients with mild symptoms. The primary efficacy outcome will be analyzed via a Cochran-Mantel-Haenszel test, stratified by pre-treatment NIHSS score (0-2 vs 3-5), age (<65 vs ≥65), and last known well time to treatment (0-2 hours vs 2-3 hours).
TRIAL STATUS: As of October 31, 2013, the trial is in the start-up phase, with screening to be initiated in 2014.

Author Disclosure Block:

P. Khatri: Other Research Support; Significant; Genentech (to UCMC Dept of Neurology), Penumbra (to UCMC Dept of Neurology). J.P. Broderick: Research Grant; Significant; Genentech. Other Research Support; Significant; EKOS Corporation, Schering-Plough. Honoraria; Significant; Genentech. E.C. Jauch: Research Grant; Modest; Genentech. S.R. Levine: Research Grant; Significant; NIH, Genentech, PCORI. J.G. Romano: Research Grant; Significant; University of Miami for MaRISS study. Consultant/Advisory Board; Modest; Genentech. J.L. Saver: Other; Significant; University of California Regents. S.D. Yeatts: Other Research Support; Significant; IMS III. Consultant/Advisory Board; Modest; Genentech. Y. Mu: Employment; Significant; Genentech, a member of the Roche group. Ownership Interest; Significant; Shareholder in Roche.
Presentation Number: CT P16

Trial Abbreviation: ICARE

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Trial Name: Interdisciplinary Comprehensive Arm Rehabilitation Evaluation: Stroke Initiative

Trial Registry Number ID: NCT00871715

Trial Sponsor: NIH NINDS (primary)/NICHD

Trial Web Site: www.icarestroketrial.org

Publishing Title: Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (ICARE): A Randomized Control Trial

Author Block: Steven L. Wolf, Emory Univ, Atlanta, GA; Alexander W. Dromerick, Natl Rehabilitation Hosp & Georgetown Univ, Washington, DC; Monica A. Nelsen, Christianne J. Lane, Christopher J. Hahn, Caron Park, Stanley P. Azen, Carolee J Winstein, Univ of Southern California, Los Angeles, CA

Abstract Body:

Background: Residual disability after stroke is substantial; 65% of patients at 6 months are unable to incorporate the paretic hand into daily activities. Given the constraints on treatment hours for upper extremity rehabilitation, comparison of a program derived from best practice and evidence-based interventions to current care is imperative. Task-oriented training programs have been rapidly adopted into clinical practice because they currently have the strongest evidence base. In the absence of any consensus on the essential elements or dose of training, a well-designed trial is needed to determine the effectiveness of a specific multidimensional task-based program governed by a comprehensive set of evidence-based principles. Objective: To determine if a structured training program, Accelerated Skill Acquisition Program (ASAP), is superior to usual and customary therapy of an equivalent dose (DEUCC) for arm and hand recovery one year after randomization. Secondary objectives are to compare ASAP to true (active monitoring only) usual and customary (UCC) therapy and to compare DEUCC and UCC. Design: ICARE is a parallel group, three-arm, single blind, phase III, superiority, randomized control trial of a theoretically-defensible, principle-based upper extremity therapy program that integrates 3 important components: skill, capacity, and motivation. Following baseline assessment at sites in Atlanta, Los Angeles and Washington, D.C., 361 adults were randomized, using a stratified block schema by site to balance group assignment by motor severity and time from stroke onset. Treatments were initiated in the out-patient setting between 14 and 106 days after stroke. To prevent unintended crossover, the ASAP protocol was embargoed and ASAP therapists did not provide UCC or DEUCC. Outcomes are measured 4 times: baseline, completion of treatment, and 6 months and 1-year after randomization. Analysis: The primary hypothesis is that the improvement in log-transformed WMFT time will be greater for the ASAP than the DEUCC group, tested at a 0.05 significance level. Trial Status: Collecting follow-up data; expected events: outcome data collection to end March 2014; database lock June 2014; primary analysis June-Aug 2014; unblinding Sept-Oct 2014.

Author Disclosure Block:
S.L. Wolf, None; A.W. Dromerick, None; M.A. Nelsen, None; C.J. Lane, None; C.J. Hahn, None; C. Park, None; S.P. Azen, None; C.J. Winstein, None.
**Presentation Number:** CT P17

**Trial Abbreviation:** STOP-IT Study

**Trial Contact Information:** Project Manager: Janice Carrozzella, MSN, CNP, CCRA; carrozj@uc.edu; PH: 513-475-8793

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**Trial Name:** The Spot Sign for Predicting and Treating ICH Growth Trial

**Trial Registry Number ID:** NCT00810888

**Trial Sponsor:** NIH / NINDS

**Trial Web Site:** www.STOPITSTUDY.org

**Publishing Title:** STOP-IT Study

**Author Block:** Matthew Flaherty, Univ of Cincinnati, Cincinnati, OH; on Behalf of STOP-IT Investigators

**Abstract Body:**

**Background:**
Early hematoma growth is common following intracerebral hemorrhage (ICH). Recombinant activated factor VII (rFVIIa) can reduce hematoma growth but will not help patient’s at low risk of expansion. CT angiography (CTA) is a widely available tool that has shown promise for predicting hematoma growth (via the “spot sign”). The next step in this treatment paradigm is to confirm the ability of CTA to predict hematoma growth and to explore the role CTA may play in the administration of hemostatic therapy.

**Objectives:**
- Determine the sensitivity and specificity of the CTA spot sign for hematoma growth.
- Randomize ICH patients who present within five hours of symptom onset and have a spot sign to treatment with rFVIIa versus placebo.

**Design:**
STOP-IT will enroll patients with acute ICH less than five hours from symptom onset. The treatment arm will include subjects with acute ICH and contrast extravasation (spot sign present) on CTA. The observational arm will include subjects with acute ICH without a spot sign. Comparisons will be made between 1) patients with a spot sign randomized to placebo and patients without a spot sign, and 2) patients who have a spot sign and are randomized to rFVIIa vs. placebo.

**Population:**
One hundred eighty-four subjects with intracerebral hemorrhage will be enrolled at eleven clinical sites across the United States and Canada.

**Interventions:**
Patients who have a spot sign present on CTA will be randomized 1:1 to treatment with either rFVIIa (80 mcg/kg) or placebo. Patients without a spot sign will be enrolled in a prospective observational arm.

**Outcome Measures:**
- Safety: Life-threatening thromboembolic complications.
• Hematoma growth among spot sign positive subjects, comparing subjects treated with rFVIIa to those treated with placebo.
• The sensitivity and specificity of the spot sign for predicting hematoma growth.

**Trial Status:**
Eleven clinical sites actively recruiting: 64 subjects enrolled as of 14-Oct-2013

**Trial Sponsor:**
NIH/NINDS

**Author Disclosure Block:**

**M. Flaherty:** Research Grant; Significant; NIH/NINDS Grant Support. Other Research Support; Significant; Novo Nordisk - Study Drug Support.
**Presentation Number:** CT P18

**Trial Abbreviation:** Find-AF randomised

**Trial Contact Information:** Rolf Wachter; wachter@med.uni-goettingen.de; Tel.: 0049551399258

**Trial Email:** -

**Trial Name:** Finding Atrial Fibrillation in Stroke

**Trial Registry Number ID:** NCT01855035

**Trial Sponsor:** University of Goettingen, Boehringer Ingelheim

**Trial Web Site:** -

**Publishing Title:** Finding Atrial Fibrillation in Stroke: Randomised Evaluation of Enhanced and Prolonged Holter Monitoring - Rationale and Design of Find-AF randomised

**Author Block:** Mark Weber-Krueger, Götz Gelbrich, Raoul Stahrenberg, Jan Liman, Univ of Goettingen, Germany, Goettingen, Germany; Pawel Kermer, Nordwestkrankenhaus Sanderbusch, Sande, Germany; Gerhard F. Hamann, Horst-Schmidt-Kliniken, Wiesbaden, Germany; Joachim Seegers, Anna Schulte, Falko Jürries, Univ of Goettingen, Germany, Goettingen, Germany; Find-AF randomised Study Group; Klaus Gröschel, Univ of Mainz, Germany, Mainz, Germany; Rolf Wachter, Univ of Goettingen, Germany, Goettingen, Germany

**Abstract Body:**

**Background**
Detection of paroxysmal atrial fibrillation (AF) after ischemic stroke is challenging. Episodes are often short, occur randomly and are frequently asymptomatic or accompanied by unspecific symptoms. While paroxysmal AF bears a similar risk of thromboembolism compared to sustained types, stroke recurrence can be prevented efficiently by oral anticoagulation, highlighting the clinical relevance of detecting the arrhythmia. However, the ideal mode and duration of ECG-monitoring after cerebral ischemia remain to be defined. It is well established that detection rates increase by prolonging the monitoring interval, but enhanced monitoring procedures are time-consuming and costly. So far, there has been no randomised clinical trial to evaluate repetitive prolonged continuous ECG-monitoring within a large and unspecific stroke population.

**Study Design**
Find-AF randomised (NCT01855035) is a randomised and controlled prospective multicentre trial to evaluate prolonged Holter-ECG-monitoring in patients with recent ischemic stroke. 400 patients with stroke related symptoms lasting ≤7 days and without previously diagnosed atrial fibrillation/flutter will be enrolled at 4 certified stroke centres in Germany. The patients will be randomised 1:1, receiving either “standard of care” diagnostic work-up (according to current stroke guidelines) or “enhanced and prolonged Holter-ECG-monitoring”. All patients will be followed up after 3, 6 and 12 months. Those within the monitoring arm will perform 10-day Holter-ECG-recordings at baseline and after 3 and 6 months. Newly diagnosed AF (in both arms) will be confirmed by an independent adjudication committee.

**Sample Size Estimation**
We decided to include 400 patients. Assuming a dropout rate of 15%, this would leave 340 patients. This would give our study a power of 83% to detect a difference presuming detection rates of 15% (intensified monitoring) vs. 5 % (usual care) and 98% power to detect a difference between 20% vs. 5%.

**Outcomes**
The primary endpoint will be the detection of atrial fibrillation/flutter within 6 months. We plan to complete the recruitment by summer 2014, first results can be expected by autumn 2015.

Author Disclosure Block:

**M. Weber-Krueger**: Research Grant; Significant; Study is supported by unrestricted grant from Boehringer Ingelheim. Other; Modest; Travel grant from Phizer Inc.  
**G. Gelbrich**: None.  
**R. Stahrenberg**: None.  
**J. Liman**: None.  
**P. Kermer**: None.  
**G.F. Hamann**: None.  
**J. Seegers**: None.  
**A. Schulte**: None.  
**F. Jürries**: None.  
**K. Gröschel**: Honoraria; Modest; Boehringer Ingelheim, Bristol-Myers Squibb. Other; Modest; Travel Grant from Boehringer Ingelheim.  
**R. Wachter**: Research Grant; Significant; Study is supported by unrestricted grant from Boehringer Ingelheim.
Abstract Body:

Background: Malignant infarction is characterized by the formation of rapidly accumulating cerebral edema, and decompressive craniectomy (DC) is the only proven therapy for this syndrome. An IV formulation of glyburide (RP-1127) was tested in GAMES Pilot, which suggested feasibility for a phase II study.

Objective: The primary objective is to assess the safety and efficacy of RP-1127 compared to placebo in severe anterior circulation ischemic stroke patients who are at high risk for developing malignant edema.

Design: This is a randomized, multi-center, double blind, two-stage, adaptive, phase II trial. Up to 240 patients total will be enrolled (~50 in stage 1 and up to 190 patients in stage 2).

Population studied: Eligible patients will have a baseline MRI DWI lesion between 82 cm³ and 210 cm³, age 18-75 years, and time from symptom onset to drug infusion of ≤ 10 hours. Patients who receive intra-arterial reperfusion therapy or are on sulfonylurea treatment at presentation are excluded.

Intervention: Enrolled patients are randomly assigned to either RP-1127 or placebo bolus and continuous infusion for 72 hours. Subjects undergo MRI at baseline and at 72-96 hours. Neurological assessments and safety parameters, including frequent glucose monitoring, are performed during the first 7 days. Modified Rankin Scale (mRS) assessment occurs at days 30 and 90.

Outcome measure: The primary outcome will be assessed by the incidence of mRS ≤4 without DC at 90 days. Safety will be assessed by the frequency/severity of adverse events, hypoglycemia (<55 mg/dL) and symptomatic hypoglycemia, and incidence of QTc interval prolongation > 500 ms.

Analysis Plan: An interim analysis will be conducted after stage 1 to re-estimate the sample size and assess futility. The primary analysis will be ITT and will combine patients enrolled in both stages using a weighted combination test (two-sided alpha= 0.05). As demonstrated by simulation, the design has 80% power under a 20-percentage-point effect size.

Trial Status: To date, 5 patients have been enrolled. There have been no episodes of hypoglycemia or symptomatic hypoglycemia. There have been no drug related significant adverse events.

Author Disclosure Block:
K.N. Sheth, Remedy Pharmaceuticals is the sponsor and provide drug at no cost, Modest, Other; J. Elm, None; S. Jacobson, Remedy Pharmaceuticals is the sponsor and provide drug at no cost, Modest, Other; W.T. Kimberly, Remedy Pharmaceuticals is the sponsor and provide drug at no cost, Modest, Other.
Background and Purpose: Accumulation of hemoglobin degradation products, in particular iron, in the brain plays a role in mediating secondary neuronal injury after intracerebral hemorrhage (ICH). The iron chelator, deferoxamine mesylate (DFO), exerts diverse anti-apoptotic, anti-inflammatory, and anti-phagocytic effects, and improves recovery in ICH animal models. We hypothesize that treatment with DFO could minimize neuronal injury and improve outcome in ICH patients. To test this hypothesis, we conducted a Phase I, open-label study to determine the safety and maximum-tolerated dose (MTD) of DFO in ICH patients. Daily infusions of DFO at doses up to 62 mg/kg/day (up to a maximum of 6000 mg/day) over a 3-day period were well tolerated with an acceptable safety profile. We recently initiated the HI-DEF Trial to determine if it is futile to move this MTD of DFO forward to Phase III efficacy evaluation, and to further assess its safety in a larger cohort of patients.

Methods: In this multi-center, double-blind, randomized, placebo-controlled phase II study, a total of 324 subjects with spontaneous ICH will be randomized (1:1) to DFO at 62 mg/kg/day (up to a maximum of 6000 mg/day) or placebo given by intravenous infusion over 5 days. Randomization will control for baseline ICH score (0-2 vs. ≥3) and ICH onset-to-treatment time (≤12h vs. >12-24h). Subjects will undergo repeated assessments up to 3 months. The proportion of subjects with a good clinical outcome (defined as modified Rankin Scale [mRS] score of 0-2) at 90 days will be compared using a futility analysis. Under the futility hypothesis, if the difference in good outcome proportion is <12% in favor of DFO, it would be futile to move DFO forward to Phase III.

Results/Study Status: The study was funded by the NIH/NINDS in September 2012 (U01- NS074425). Recruitment began in March 2013 and is currently underway in 28 US and Canadian sites. It is expected to continue through 2017.

Conclusions: The HI-DEF study will provide a crucial “go/no go” signal as to whether a Phase III trial to investigate the efficacy of DFO in ICH is warranted, and is expected to advance our understanding of the pathophysiology of secondary neuronal injury in ICH through multiple pre-planned exploratory analyses.
M. Selim: Research Grant; Significant; NIH/NINDS. Consultant/Advisory Board; Significant; Daiichi Sankyo, Inc. E. Siwila-Sackman: None.
Presentation Number: CT P21

Trial Abbreviation: HEAT

Trial Contact Information: Jennifer Ward; Email: jward@nmff.org; Phone: 312.503.3914

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Trial Name: New Generation Hydrogel Endovascular Aneurysm Treatment Trial

Trial Registry Number ID: NCT01407952

Trial Sponsor: Northwestern University


Publishing Title: The New-Generation Hydrogel Endovascular Aneurysms Treatment Trial

Author Block: Tarek El Ahmadieh, Najib El Tecle, Samer Zammar, Youssef Hamade, Bernard Bendok, Northwestern Univ, Chicago, IL

Abstract Body:

Background: Endovascular treatment of intracranial aneurysms has seen significant advances. One major limitation of the endovascular approach is the durability of treatment and aneurysm recanalization. To address this issue, one approach was the development of hydrogel coated coils. The hydrogel expands upon exposure to blood and thus enhances the coil packing density. Higher initial coil packing density may potentially result in lower rates of recurrence.

Hypothesis: Second Generation HydroCoil Embolic System allows for a higher packing density, higher initial occlusion, lower recanalization, and lower retreatment rates compared to bare platinum coils

Objective: To compare clinical and angiographic outcomes (initial complete occlusion, recanalization, retreatment, and adverse event rates) in patients receiving the 2nd generation Hydrocoil embolic system versus patients receiving bare platinum coils.

Methods: This is a randomized, controlled, multicenter, post-market clinical trial. Subjects between 18 and 75 years of age with ruptured or unruptured intracranial aneurysms (3-14 mm in size) who are amenable to endovascular treatment are randomly assigned 1:1 to either treatment arm: (1) the HydroCoil Embolic System (HES), or (2) the bare platinum coils. No bioactive coils, 1st generation Hydrocoils or liquid embolics are allowed in the study. In the HES arm, up to 10% of total coil length using bare platinum is allowed if deemed necessary by the investigator. Any type of bare platinum coil may be utilized in the bare platinum arm. Assist-devices can be used at the discretion of the investigator. The duration of the open enrollment phase will be 24 months or until the required number of subjects are enrolled (n = 600). Each subject will have a post procedure follow-up of at least 18 months. Subjects will be recruited from up to 50 national and international centers. Each Investigational Site will be expected to enroll at least 20 Subjects.

Results: A total of 177 patients have been enrolled so far in the study. The study is still ongoing.

Conclusions: A limitation of endovascular aneurysm treatment is recurrence. This trial aims to answer the question of whether the new generation hydrogel coil reduces recurrence rates when compared to bare platinum coils.

Author Disclosure Block:
T. El Ahmadieh: None. N. El Tecle: None. S. Zammar: None. Y. Hamade: None. B. Bendok: Research Grant; Significant; Microvention.
Presentation Number: CT P22

Trial Abbreviation: POSITIVE

Trial Contact Information: Aquilla S. Turk, DO turk@musc.edu

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Trial Name: POSITIVE: Perfusion Imaging Selection of Ischemic Stroke Patients for Endovascular Therapy

Trial Registry Number ID: In process

Trial Sponsor: Covidiene, Penumbra, Stryker, Toshiba

Trial Web Site: none

Publishing Title: Perfusion Imaging Selection of Ischemic Stroke Patients for Endovascular Therapy

Author Block: Edward C Jauch, Aquilla S Turk, Medical Univ of South Carolina, Charleston, SC; POSITIVE Trialists

Abstract Body:

Background: Intravenous (IV) tissue plasminogen activator (tPA) administration is safe and effective for treatment of acute ischemic stroke (AIS) within 4.5 hours of symptom onset. In clinical trials intraarterial thrombectomy (IAT) is safe up to 8 hours after symptom onset with newer devices resulting faster recanalization while maintaining a high degree of safety. Pilot data suggest patients selected with physiologic imaging benefit from IAT without time restrictions.

Objective: To determine the safety and efficacy of IAT reperfusion in AIS patients ineligible for IV-tPA as selected by penumbral imaging criteria.

Design: POSITIVE is a prospective, randomized, multi-centered phase III trial with blinded primary outcome assessment of patients with AIS and salvageable penumbra on imaging randomized to treatment by endovascular mechanical thrombectomy or best medical therapy. Adult AIS patients, otherwise ineligible for IV-tPA, who present within 12 hrs from symptom onset, with a NIHSS>8 and who are determined to have significant viable penumbra are randomized to IAT vs. best medical management. Imaging must show large vessel proximal occlusion (distal ICA through MCA M1 bifurcation) and no evidence of hypodensity more than 1/3 of MCA or ASPECTS < 7. Patients randomized to IAT receive reperfusion per site investigator’s choice. All patients receive best medical management following AHA AIS Guidelines.

Population Studied: POSITIVE will enroll 750 patients at up to 20 North American centers.

Outcome Measure: The primary outcome measure is the 90-day global disability assessed by modified Rankin score (mRS), analyzed using simultaneous success criteria on the overall distribution of mRS and a minimum 5% difference in the proportion of subjects achieving functional independence (mRS 0-2).

Secondary outcome measures:
1) 90 day global disability in 0-8 hr and 8-12 hr cohorts assessed via mRS distribution
2) 30 and 90 day mortality
3) Symptomatic ICH within 24 hr
4) Procedure related SAE’s
5) Revascularization measured by TICI 2b or 3

Statistical Analysis: Statistical analysis of the primary endpoint will be conducted with a proportional odds model using raw mRS 0 to 6 (with 5 and 6 collapsed).

Trial Status: As of 11/1/13, 1 patient has been enrolled.
Author Disclosure Block:

**E.C. Jauch**: Research Grant; Significant; Covidiene, Stryker, Penumbra, Toshiba. **A.S. Turk**: Research Grant; Significant; Covidiene, Toshiba, Stryker, Penumbra, Siemens.
Abstract Body:

Introduction: The purpose of this study is to determine whether the combination of thrombolysis and hypothermia is superior to thrombolysis alone for the treatment of acute ischemic stroke. The study is being conducted in two stages: a Phase 2 study to assess the safety of various protocol changes, to demonstrate sufficient recruitment, and to allow an interim analysis for futility; and a Phase 3 efficacy study will follow if pre-specified milestones are achieved.

Methods: ICTuS 2/3 is a prospective, randomized, single-blind, multi-center Phase 2/3 study. We aim to include 400 in phase 2 (1200 in phase 3) treated within 3 hours of symptom onset with IV tPA (according to FDA or EMEA protocol), NIHSS ≥7 and ≤20 (right) and ≤20 (left hemisphere), age 22-82. Patients are randomly assigned to either hypothermia permissively targeted to 33ºC or normothermia. Favorable outcome is defined as a 90-day Modified Rankin score (mRS) of 0 or 1. Secondary outcome measures are: 90-day NIHSS, Barthel Index (BI), mortality, shift analysis of the mRS, global odds ratio of mRS, BI, NIHSS, incidence of symptomatic intracranial hemorrhage and 90-day Montreal Cognitive Assessment. An interim analysis for futility is planned after 400 patients and includes frequency of target temperature reached within 6 hours from symptom, pneumonia rate, safety profile of iced saline infusion and sufficient study-wide average enrollment of
at least 0.4 patients/site/month.
Status: The study includes 17 study sites in the US and Europe. Enrolment began January 2011. Currently, 85 subjects are enrolled. A safety review by the study DSMB and the FDA after the first 45 patients resulted in approval to expand the trial. Phase 2 of the ICTuS 2/3 trial will include 400 patients. We are currently seeking additional study sites.

Author Disclosure Block:

Presentation Number: CT P24

Trial Abbreviation: PODCAST

Trial Contact Information: Mrs Sally Utton/Sally.utton@nottingham.ac.uk/Tel: +44 (0)115 82 30287/Fax: +44 (0)115 82 31771

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Trial Name: Prevention of Decline in Cognition After Stroke Trial

Trial Registry Number ID: ISRCTN85562386

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.podcast-trial.org

Publishing Title: PODCAST: Prevention of Decline in Cognition After Stroke Trial: A Factorial Randomised Trial of Blood Pressure and Lipid Lowering

Author Block: Kailash Krishnan, Sally Utton, Sarah Grant, Katherine Whittamore, Polly Scutt, Philip M Bath, Univ of Nottingham, Nottingham, United Kingdom

Abstract Body:

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 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 trial aim 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 approximately 100 patients. The target Systolic Blood Pressure is <125 mmHg for the intensive BP lowering group and <140 mmHg for the guideline group. For the intensive lipid lowering group the target Low Density Lipoprotein-Cholesterol (LDL-C) is <1.4 mmol/L and <3 mmol/L for the guideline group. The primary outcome is Addenbrooke's Cognitive Examination. Secondary outcomes include vascular events, quality of life, functional outcome, depression and death.

Trial Status: The trial has UK Ethics and NHS RD approvals and has recruited 79 patients to date from 16 centres.

Author Disclosure Block:

K. Krishnan: None. S. Utton: None. S. Grant: None. K. Whittamore: None. P. Scutt: None. P.M.W. Bath: None.
Presentation Number: CT P25

Trial Abbreviation: AVERT

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Trial Email: avert@nsri.org.au

Trial Name: A Very Early Stroke Rehabilitation Trial

Trial Registry Number ID: ACTRN12606000185561

Trial Sponsor: NHMRC, NIH

Trial Web Site: http://www.florey.edu.au/research/avert

Publishing Title: Ongoing International Trial of Very Early Stroke Rehabilitation (AVERT): Progress

Author Block: Julie Bernhardt, The Florey Inst of Neuroscience and Mental Health, Heidelberg, Australia; AVERT Trialists’ Collaboration

Abstract Body:

Background: Early and frequent out of bed activity starting within 24 hours of stroke, may be an important component of effective stroke unit care. We hypothesize that early, frequent mobilizations out of bed will reduce death and disability and be cost effective, compared to standard care. We report on trial progress, participant demographics and data quality.

Methods: A Very Early Rehabilitation Trial (AVERT, ACTRN12606000185561) is a multi-centre, single blind randomized controlled trial. Randomization is concealed, with stratification by site and stroke severity. Included: Patients admitted to a stroke unit within 24 hours, rtPA patients with physician approval. Excluded: patients with severe pre-morbid disability, or who fail safety criteria. Early mobilization is delivered by nurses and physical therapists, commences within 24 hours and continues for 14 days. Patients in the control group receive standard care. Primary outcome: modified Rankin Scale (mRS) at 3 months. Sample size is 2104 patients (n=1052 per group) to detect 7% or greater reduction in death/disability. Analyses are intention to treat.

Trial status: At 4 November 2012, 36,856 patients have been screened, 6508 were eligible, with 1763 recruited from 55 hospitals in Australia, New Zealand, Malaysia, Singapore and the United Kingdom. Mean age: 70.4 (SD12.9) years; male: 62.2%; first stroke: 81.8%; rt-PA 22.6% (23.5% Australia, 18.4% New Zealand, 2.1% Malaysia, 5% Singapore, 31.9% UK). Stroke severity: 55.1%, mild, 30.7% moderate, 14.2% severe. Oxfordshire stroke classification: TACI 21.3%, PACI 31.4%, POCI, 9.7%, LACI, 25.1%, intracerebral hemorrhage 12.5%. 1644 patients have completed 3 month follow up, 11 drop outs (0.6%). Primary outcome (mRS) completion: 99.4%. Secondary outcome completion: 80.5-99.6%. The Data Monitoring Committee has met 10 times with no safety issues identified.

Discussion: Recruited patients are broadly representative of recruiting countries. Fewer patients with intracerebral hemorrhage are recruited from Asia. The trial is meeting data quality targets. We aim to complete recruitment by December 2014.

Author Disclosure Block:

J. Bernhardt: None.
Presentation Number: CT P26

Trial Abbreviation: SOCRATES

Trial Contact Information: Mary Farrant, MBA, BSN, RN, University of California, San Francisco (UCSF) Clinical Coordinating Center (CCC), San Francisco, CA, USA, 94158; Phone 1-415-502-7304 mary.farrant@ucsfmedctr.org

Trial Email: nardev.khurmi@astrazeneca.com

Trial Name: Acute Stroke Or Transient IsChemic Attack TReated with Aspirin or Ticagrelor and Patient OutcomES (SOCRATES) Trial

Trial Registry Number ID: D5134C00001

Trial Sponsor: AstraZeneca AB

Trial Web Site: http://www.astrazenecaclinicaltrials.com

Publishing Title: Acute Stroke or Transient IsChemic Attack TReated with Aspirin or Ticagrelor and Patient OutcomES (SOCRATES) Trial

Author Block: S. Claiborne Johnston, Univ of California San Francisco, San Francisco, CA; Pierre Amarenco, Stroke Ctr, Denis Diderot Univ and Medical Sch, Bichat Hosp, Paris, France; Gregory W. Albers, Stanford Univ Medical Ctr, Palo Alto, CA; J. Donald Easton, Univ of California San Francisco, San Francisco, CA; Nardev Khurmi, AstraZeneca, LP, Wilmington, DE; Kazuo Minematsu, Natl Cerebral and Cardivascular Ctr, Osaka, Japan; Carlos A. Molina, Vall d’Hebron Stroke Unit Hosp Univri Vall d’Hebron, Barcelona, Spain; KS Lawrence Wong, Chinese Univ of Hong Kong, Prince of Wales Hosp, Hong Kong, Hong Kong

Abstract Body:

The SOCRATES Trial is a randomized, double-blind, multicenter trial in patients with acute ischemic stroke or TIA evaluating ticagrelor (180 mg loading dose on the first day followed by 90 mg twice daily maintenance dose for the remainder of the study) as compared to aspirin (300 mg [three 100 mg tablets] on the first day followed by 100 mg once daily maintenance dose for the remainder of the study). Primary efficacy endpoint is composite of stroke, myocardial infarction, or death at 90 days. The primary safety analysis will be time from first dose of study medication to the first major bleeding event (PLATO trial definition). Subjects will be 40 years of age or older with an ischemic stroke (with a National Institutes of Health Stroke Scale score 5 or lower) or a high-risk TIA (defined as an ABCD2 score 4 or higher). Subjects will be randomized within 24 hours of the time last known free of new ischemic symptoms and study drug will be initiated immediately thereafter. A total of 9,600 subjects will be enrolled from about 1,000 sites worldwide. The study is expected to start in Q4 2013 and to end by Q1 2016.

Author Disclosure Block:

S. Johnston: Consultant/Advisory Board; Significant; Significant. P. Amarenco: Consultant/Advisory Board; Significant; Significant. G.W. Albers: Consultant/Advisory Board; Significant; Significant. J. Easton: Consultant/Advisory Board; Significant; Significant. N. Khurmi: Consultant/Advisory Board; Significant; Significant. K. Minematsu: Consultant/Advisory Board; Significant; Significant. C.A. Molina: Consultant/Advisory Board; Significant; Significant. K. Wong: Consultant/Advisory Board; Significant; Significant.
BACKGROUND AND PURPOSE: The outcome of patients with stroke might be improved by blocking inhibitory signals that reduce axonal outgrowth after stroke, such as myelin associated glycoprotein (MAG). After experimental stroke, a systemically administered anti-MAG monoclonal antibody (GSK249320) crosses the blood brain barrier, increases neurite outgrowth, and improves behavioral outcome, with treatment time window measured in days. In 47 healthy humans, a single IV GSK249320 infusion was well tolerated with no reported serious adverse events (AE), and all AE were mild or moderate. A placebo-controlled study in 42 stroke patients found that 2 IV infusions of GSK249320, initiated 24-72 hr post-stroke and given 9 days apart, were well tolerated with overall AE profile consistent with the population studied. The current study aims to expand these results in a Phase II Proof of Concept (PoC) study. METHODS: MAG104615 is a placebo-controlled, double-blind, multicenter, randomized, repeat dose study. Primary endpoint for assessing PoC is a clinically meaningful improvement in lower limb motor recovery, specifically, change in gait velocity from baseline to Day 90. Secondary endpoints include gait velocity at Day 180, other measures of motor recovery, changes in disability, safety, pharmacokinetics, and GSK249320 immunogenicity profile. Entry criteria include stroke onset 24-72 hr prior to first infusion of investigational product; ischemic supratentorial stroke with either >15mm or volume >4cc; NIHSS score 3-21; age 18-90; and stroke-related leg motor deficit. Exclusion criteria include able to walk >0.8m/s; previous symptomatic stroke <3 mo prior; pre-stroke mRS>2; unresponsiveness; significant aphasia, pre-existing gait deficit, or active pre-existing neurologic or psychiatric disease; contraindication to MRI; pregnancy; or lactation. Subjects will be randomized (1:1) to receive two IV infusions of either 15mg/kg GSK249320 or placebo, stratified by baseline gait velocity. Bayesian methods will be used to conduct a futility analysis when ~70 subjects complete Day 90, as well as for the primary analysis at the conclusion of the study. CONCLUSIONS: Study enrollment has begun across 35 sites. Enrollment is anticipated to be completed 3Q2014.
S.C. Cramer, GlaxoSmithKline, Modest, Consultant/Advisory Board; MicroTransponder, Modest, Consultant/Advisory Board; L. Enney, GlaxoSmithKline, Significant, Employment; T. Thompson, GlaxoSmithKline, Significant, Employment; C. Twomey, GlaxoSmithKline, Significant, Employment.
Presentation Number: CT P28

Trial Abbreviation: THAWS Trial

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Trial Name: THrombolysis for Acute Wake-up and unclear-onset Stroke trial

Trial Registry Number ID: UMIN000011630

Trial Sponsor: None

Trial Web Site: None

Publishing Title: Thrombolysis With Alteplase 0.6mg/kg Body Weight for Acute Wake-up and Unclear-onset Stroke Trial (THAWS)

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Abstract Body:

Rationale: About one fourth of acute ischemic stroke patients suffer with unclear-onset time, e.g., during sleep. A large group of these patients are reported to have a potential to recover with intravenous thrombolysis. Magnetic resonance imaging (MRI) findings with positive diffusion-weighted imaging and negative fluid-attenuated inversion recovery (negative FLAIR pattern) can identify acute ischemic stroke patients within 4.5 h from symptom onset.

Aims and hypothesis: This trial aims to test the efficacy and safety of intravenous thrombolysis with alteplase of 0.6mg/kg body weight (officially approved dosage in Japan) using MRI-based selection in ischemic stroke patients with unclear time of symptom onset. We hypothesize that stroke patients with unclear-onset time and a negative FLAIR pattern will improve with intravenous thrombolysis more frequently than those without.

Design: The THAWS is an investigator initiated, multicenter (33 hospitals in Japan), prospective, randomized, open label, blinded-endpoint assessment clinical trial. Patients with unclear-onset time of stroke symptom beyond 4.5 h and within 12 h after symptom recognition will be evaluated with a multimodal MRI. Three hundred patients with a negative FLAIR pattern will be randomized 1:1 to either intravenous thrombolysis with alteplase of 0.6mg/kg body weight (n=150) or standard treatment (n=150). We generally follow the trial design of the WAKE-UP (ClinicalTrials.gov Identifier NCT01525290) except the blinded label treatment. Intracranial hemorrhage will be assessed on follow-up MRI after 22-36 h. Final clinical outcome will be assessed 90 days after stroke. Patient enrollment period is planned between early 2014 (after the approval from Ministry of Health, Labour and Welfare, Japan) and March 2017.

Study outcomes: The primary efficacy endpoint is favorable outcome defined by modified Rankin Scale 0-1 at 90 days. The safety outcome measures are symptomatic intracranial hemorrhage at 24 h, serious bleeding during study period and mortality at 90 days.

Discussion: The results of this trial will provide data on therapeutic effects of low-dose intravenous thrombolysis for ischemic stroke patients with unclear-onset time using MRI-based selection.
Author Disclosure Block:

Presentation Number: CT P29

Trial Abbreviation: TO-ACT trial

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Trial Email: j.coutinho@amc.nl

Trial Name: Thrombolysis Or Anticoagulation for Cerebral venous Thrombosis

Trial Registry Number ID: NCT01204333

Trial Sponsor: Academic Medical Centre

Trial Web Site: http://www.to-act-trial.org/

Publishing Title: Thrombolysis or Anticoagulation for Cerebral Venous Thrombosis (TO-ACT trial)

Author Block: Jonathan M. Coutinho, Academic Medical Ctr, Amsterdam, Netherlands; José M Ferro, Hosp Santa Maria, Lisbon, Portugal; Susanna M. Zuurbier, Academic Medical Ctr, Amsterdam, Netherlands; Patrícia Canhão, Hosp Santa Maria, Lisbon, Portugal; Isabelle Crassard, Hôpital Lariboisière, Paris, France; Charles B. Majoie, Jim A Reekers, Academic Medical Ctr, Amsterdam, Netherlands; Emmanuel Houdart, Hôpital Lariboisière, Paris, France; Rob J. de Haan, Academic Medical Ctr, Amsterdam, Netherlands; Marie-Germaine Bousser, Hôpital Lariboisière, Paris, France; Jan Stam, Academic Medical Ctr, Amsterdam, Netherlands

Abstract Body:

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 ≥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
The trial started in April 2011. Currently, 23 patients have been included. Investigators who are interested in participation can contact us at j.coutinho@amc.nl

Author Disclosure Block:

Presentation Number: CT P30

Trial Abbreviation: DECOMPRESS – 2

Trial Contact Information: jmferro@fm.ul.pt

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Trial Name: DECOMPRESS – 2

Trial Registry Number ID: None

Trial Sponsor: Hospital Santa Maria

Trial Web Site: none

Publishing Title: Prospective Registry of Decompressive Surgery for Patients With Cerebral Venous Thrombosis (decompress-2)

Author Block: Jose M. Ferro, Patrícia Canhão, Hosp Santa Maria, Lisbon, Portugal; Jonathan M. Coutinho, Jan Stam, Academic Medical Ctr, Amsterdam, Netherlands; Marie-Germaine Bousser, Hôpital Lariboisière, Paris, France

Abstract Body:

Background: a retrospective registry and a systematic review of published cases showed that decompressive surgery is lifesaving in patients with acute severe cerebral venous thrombosis (CVT) and parenchymal lesions with impeding herniation. However, retrospective design and publication bias may overestimate the effect of the intervention. Objective: to describe in a prospective registry the vital and functional outcome of CVT patients treated by decompressive surgery, and to identify subgroups of CVT patients who benefit most from this surgery. Inclusion criteria: consecutive cases of CVT with parenchymal lesions treated by decompressive craniectomy or hematoma evacuation. Outcome at discharge and follow up: outcome will be measured at 6 and 12 months by an investigator not directly involved in the surgical intervention. The opinion of the patient and main caregiver concerning the results of surgery will be registered. Evaluation of cognition, mood, anxiety, Quality of life, caregiver burden and professional life: this evaluation will be performed at 6 and 12 months follow up using MMSE, HADS, EuroQol, Expanded Caregiver Strain Index and Post Stroke working Activity Questionnaireres. Sample size: we aim to collect 100 patients with the contribution of 80 recruiting centres. Primary outcome and prognostic variables: the primary outcome is the modified Rankin Scale dichotomised between favourable (0-4) and unfavourable outcome (5 or death) at last available follow up. Prognostic variables will be age, delay to surgery, Glasgow Coma Scale score, fixed pupils, lesion characteristics, and type of surgery. Statistical analysis: for the analysis of the outcomes at last follow up, Cox regression analysis will be used and Hazard ratios with 95% CI calculated. Current status: inclusion started in January 2012, 56 centres are currently participating in the study and 15 patients from 9 centres are already included.

Author Disclosure Block:

**Presentation Number:** CT P31

**Trial Abbreviation:** MR WITNESS

**Trial Contact Information:** Stacey Brown, sbrown25@partners.org, 617-724-1538 (phone), 617-643-3939 (fax)

**Trial Email:** mrwitness@partners.org

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

**Trial Registry Number ID:** NCT01282242

**Trial Sponsor:** Massachusetts General Hospital; NIH P50NS051343; Genentech provided alteplase and modest per patient supplementary support

**Trial Web Site:** http://www.mrwitness.org

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

**Author Block:** Ona Wu, Massachusetts General Hosp, Boston, MA; Lawrence L. Latour, NIH/NINDS Intramural Stroke Program, Bethesda, MD; Shlee S. Song, Cedar Sinai Medical Ctr, Los Angeles, CA; Karen L. Furie, Brown Univ, Providence, RI; Steven Warach, Seton/UT Southwestern Clinical Resesarch Inst of Austin, Austin, TX; Lee H. Schwamm, Massachusetts General Hosp, Boston, MA; MR WITNESS Investigators

**Abstract Body:**

**Background:** Many patients are discovered with acute stroke symptoms whose onset is unwitnessed. Current FDA guidelines 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 (LKW). We propose to use advanced MRI as the surrogate “witness” when no human witness is available.

**Objectives:** (1) Determine the safety of IV rt-PA therapy for subjects with unwitnessed stroke onset but MRI evidence of early stroke - FLAIR negative for acute stroke or SIR<1.15, for which SIR is the signal intensity (SI) ratio (SIR) of FLAIR SI in the lesion to SI in normal contralateral tissue. (2) Validate novel MRI profiles to improve sensitivity while maintaining high specificity for detecting subjects with acute stroke. (3) Explore imaging surrogates of clinical efficacy in subjects with unwitnessed stroke onset who are treated with rt-PA.

**Design:** Multi-center, open-label, single-arm, Phase IIa safety study

**Population:** 80 adult subjects 18-85 years of age with acute ischemic stroke who arrive between 4.5 h and 24 h since LKW and within 3 h of symptom discovery AND have MRI evidence of early stroke. Subjects must be eligible to receive rt-PA using ECASS 3 criteria, excluding LKW criterion and previous combined history of stroke and diabetes.

**Intervention:** Enrolled subjects will receive standard dose IV alteplase (0.9 mg/kg with maximum dose <=90 mg) according to AHA guidelines.

**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.

**Analyses:** Only subjects who receive rt-PA will be included in the safety analysis. Lesion size and reperfusion rates will be compared between enrolled subjects and non-thrombolyzed historical controls.

**Trial Status:** 34/80 (42.5%) subjects have been enrolled to date. Recruiting centers are Massachusetts
General Hospital, NIH/NINDS Washington Hospital Center & Suburban Hospital, Washington University in St. Louis, Cedar Sinai Medical Center, UCLA Medical Center, and Seton/UT Southwestern. 5 additional sites are anticipated.

Author Disclosure Block:

O. Wu: Research Grant; Significant; P50NS051343, R01NS059775, R01NS063925, Genentech. Consultant/Advisory Board; Modest; Penumbra. L.L. Latour: None. S.S. Song: None. K.L. Furie: None. S. Warach: None. L.H. Schwamm: Research Grant; Significant; Genentech, P50NS051343. Other; Modest; International Steering Committee DIAS trial, Lundbeck.
Abstract Body:

**Background:** Symptomatic VBD carries a high risk of stroke, averaging 10-15% per year. Advances in endovascular angioplasty and stenting have created new treatment options, but these interventions carry significant risks. Selection criteria for appropriate candidates remain uncertain. Determining predictors of stroke in this population is an important step toward identifying those high risk patients most suitable for intervention. Preliminary studies suggest that the risk of stroke in VBD is strongly related to intracranial blood flow compromise.

**Objective:** To test the hypothesis that patients with symptomatic VBD, those with distal blood flow compromise, determined by magnetic resonance (MR) blood flow imaging, are at higher risk of subsequent posterior circulation stroke than those with normal flow.

**Design:** 6 year multicenter, prospective, observational cohort study, with a recruitment goal of 80 patients.

**Population Studied:** Patients with symptomatic VBD. Inclusion criteria: stroke or TIA in the vertebrobasilar territory; ≥ 50% stenosis or occlusion of extracranial or intracranial vertebral or basilar arteries; symptoms within 60 days of enrollment; ≥ 18 years of age and ability to provide informed consent. Exclusion criteria: major disabling stroke prohibiting follow-up; limited life expectancy; known cardiac disease associated with cardioembolic risk; blood dyscrasias; non-atherosclerotic vertebrobasilar disease; unilateral vertebral stenosis or occlusion; inability to undergo MRI or cerebral angiography.

**Study Procedures:** Blinded hemodynamic assessment with MR based imaging, consisting of quantitative MR angiography and MR perfusion, at enrollment and at 6 month intervals for at least one year. Clinical assessments at routine intervals up to two years maximum.

**Outcome Measures:** The primary endpoint is fatal and nonfatal ischemic stroke in the vertebrobasilar territory.

**Analysis:** Analysis will consist of time-to-event comparison using the log-rank test between patients
designated as 'low flow' versus 'normal flow' based upon enrollment MR imaging.

**Trial status:** Enrollment was closed at all sites, as of July 30, 2013; a total of 82 subjects were enrolled, and the final year of follow-up is in progress.

**Author Disclosure Block:**

- **S. Amin-Hanjani:** Research Grant; Significant; NIH/NINDS. Other Research Support; Modest; GE Healthcare. **D. Pandey:** Research Grant; Modest; NIH/NINDS. **K. Thulborn:** Ownership Interest; Significant; Thulborn Associates, Inc. (owner). **D. Richardson:** None. **M. Elkind:** None. **G. Zipfel:** Research Grant; Modest; American Heart Association, Hope Center for Neurological Disorders, Pfizer, Barnes Jewish Hospital Foundation. Research Grant; Significant; NIH. **D. Liebeskind:** None. **F. Silver:** Other Research Support; Significant; Boehringer Ingelheim Canada. Speakers' Bureau; Modest; Servier Canada. Speakers' Bureau; Significant; Boehringer Ingelheim Canada. Consultant/Advisory Board; Modest; Bristol-Myers Squibb Canada, Bayer Canada. Consultant/Advisory Board; Significant; Boehringer Ingelheim Canada. **S. Kasner:** None. **C. Derdeyn:** Research Grant; Significant; NIH/NINDS, MicroVention Inc. Ownership Interest; Modest; Pulse Therapeutics, nFocus Inc., Consultant/Advisory Board; Modest; Pulse Therapeutics. Consultant/Advisory Board; Significant; W.L. Gore and Associates. **P. Gorelick:** Research Grant; Significant; Lundbeck Inc. **F. Charbel:** Ownership Interest; Significant; VasSol Inc.
Presentation Number: CT P33

Trial Abbreviation: ESCAPE

Trial Contact Information: 1-855-483-6761

Trial Email: esctrial@ucalgary.ca

Trial Name: Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times

Trial Registry Number ID: NCT01778335

Trial Sponsor: University of Calgary

Trial Web Site: http://www.ucalgary.ca/stroketrials

Publishing Title: Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times

Author Block: Philip M Choi, Andrew M Demchuk, Mayank Goyal, Karla J Ryckborst, Bijoy Menon, Eesa Muneer, Mohammed Almekhlafi, Univ of Calgary, Calgary, AB, Canada; Ashfaq Shuaib, Univ of Alberta, Edmonton, AB, Canada; Frank L Silver, Toronto Western Res Inst, Toronto, ON, Canada; Daniel Roy, Ctr hospitalier de l'Univ de Montréal - Notre-Dame, Montreal, QC, Canada; Donald F Frei Jr, Colorado Neurological Inst, Denver, CO; Tudor G Jovin, Univ of Pittsburgh Medical Ctr, Pittsburgh, PA; Walter Montanera, Univ of Toronto, Toronto, ON, Canada; Michael D Hill, Univ of Calgary, Calgary, AB, Canada

Abstract Body:

Background: There is no convincing, randomized trial evidence that modern endovascular therapy is better than routine care, including routine intravenous thrombolysis, for acute ischemic stroke.

Objective: To show that rapid endovascular revascularization amongst radiologically selected (small core/proximal anterior circulation occlusion) patients with ischemic stroke results in improved outcome compared to patients treated in clinical routine. The secondary objectives are to demonstrate the safety and feasibility of achieving rapid endovascular revascularization in this population of patients.

Design: A Phase 3, randomized, open-label study with blinded outcome evaluation.

Main Inclusion criteria:
1. Last seen well to randomization time <12 hours.
2. CTA reveals a large artery proximal intracranial occlusion of the ICA (T or L occlusion), M1-MCA or horizontal segment of MCA or M1-MCA equivalent (both or all three M2-MCAs occluded; the occluded vessels are judged to be the dominant arterial supply to the hemisphere).
3. Endovascular treatment intended/can to be initiated within 60 minutes of CT/CTA with target CTA to first recanalization of 90 minutes.
4. Informed consent.

Main Exclusion criteria:
1. Baseline NCCT reveals moderate to large core of early ischemic changes in the territory of the symptomatic intracranial occlusion (ASPECTS<6).
2. Baseline venous weighted CTA reveals insufficient collaterals in the symptomatic MCA territory as determined by a collateral certified physician interpretation using MIP images and compared to the contralateral side, OR CT perfusion CBF or CBV ASPECTS < 6.
3. Chronic intracranial occlusion.
4. Pre-stroke functional dependence for ADLs or major co-morbid illness.

**Intervention & Outcome Measures:** All patients will receive routine guideline-based best medical care (including IV-tPA). Control arm subjects will receive best medical care. Intervention arm subjects will additionally receive endovascular intervention. Primary outcome is the mRS at 90 days.

**Analysis:** Intention to treat analysis using ordinal logistic regression to assess the shift along the mRS score.

**Trial Status:** Active, Recruiting. Estimated final total site number: 20 in Canada, US, Europe, Asia.

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**Author Disclosure Block:**

- **P.M.C. Choi:** None.  
- **A.M. Demchuk:** None.  
- **M. Goyal:** Consultant/Advisory Board; Modest; Covidien.  
- **K.J. Ryckborst:** None.  
- **B. Menon:** None.  
- **E. Muneer:** None.  
- **M. Almekhlafi:** None.  
- **A. Shuaib:** None.  
- **F.L. Silver:** Speakers' Bureau; Modest; Boehringer Ingelheim Canada, Bristol-Myers Squibb Canada, Servier. Consultant/Advisory Board; Modest; Boehringer Ingelheim Canada, Bayer Inc Canada, Bristol-Myers Squibb / Pfizer Canada.  
- **D. Roy:** None.  
- **D.F. Frei:** None.  
- **T.G. Jovin:** Ownership Interest; Modest; Stock in Silk Road Medical.  
- **W. Montanera:** None.  
- **M.D. Hill:** None.
International Stroke Conference 2014 abstracts and presentations are embargoed for release at the date and time of presentation or time of AHA/ASA news event. Ongoing Clinical Trials abstracts are embargoed for the date and time of the Ongoing Clinical Trials Poster Session start time. No information may be released before then.

Presentation Number: CT P34

Trial Abbreviation: TICH-2

Trial Contact Information: Mrs Sally Utton/Sally.utton@nottingham.ac.uk/Tel: +44 (0)115 82 30287/Fax: +44 (0)115 82 31771

Trial Email: University of Nottingham, United Kingdom

Trial Name: Tranexamic acid for IntraCerebral Haemorrhage 2

Trial Registry Number ID: ISRCTN93732214

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: tich-2.org

Publishing Title: Tich-2 Trial - Tranexamic Acid for Intracerebral Haemorrhage 2

Author Block: Philip M Bath, Kailash Krishnan, Sally Utton, Hayley Foster, Tanya Payne, Margaret Adrian, Sarah Grant, Alice Durham, Katie Robson, Nikola Sprigg, Univ of Nottingham, Nottingham, United Kingdom

Abstract Body:

Rationale: To assess in a pragmatic phase III prospective double blind randomised placebo-controlled trial whether tranexamic acid is safe and reduces death or dependency after primary intracerebral haemorrhage (PICH). The results will determine whether tranexamic acid should be used to treat PICH, which currently has no proven therapy.

Design: Patients will be randomised (1:1) to receive either tranexamic acid or placebo (0.9 % saline) within 8 hours of acute primary intracerebral haemorrhagic stroke. Randomisation will be computerised and minimised on key prognostics age; sex; time since onset; systolic blood pressure; stroke severity (NIHSS); presence of intraventricular haemorrhage and known history of antiplatelet treatment. Patients randomised to placebo will receive intravenous normal saline. Patients, investigators and outcome assessors will be blind to treatment allocation. The primary outcome is death or dependency (modified Rankin Scale, mRS) and telephone follow-up is at day 90.

Trial status: The start-up phase of the trial commenced on 1 March 2013 and will run for 4 years. The recruitment target is 300 participants in the start up phase and 2,000 in the main phase. As at 4th November, 2013, 181 patients have been recruited from 36 centres. The objective is to have 80 UK centres and 40 international centres.

Author Disclosure Block:

Presentation Number: CT P35

Trial Abbreviation: STOP-AUST

Trial Contact Information: atte.meretoja@unimelb.edu.au

Trial Email: atte.meretoja@unimelb.edu.au

Trial Name: The Spot sign and Tranexamic acid On Preventing ICH growth –AUstralasia Trial

Trial Registry Number ID: ClinicalTrials.gov NCT01702636

Trial Sponsor: National Stroke Research Institute, Parkville, VIC, Australia

Trial Web Site: http://clinicaltrials.gov/show/NCT01702636

Publishing Title: The Spot Sign and Tranexamic Acid on Preventing Intracerebral Hemorrhage Growth - AUStralasia Trial

Author Block: Nawaf Yassi, Atte Meretoja, Melbourne Brain Ctr @ The Royal Melbourne Hosp, The Univ of Melbourne, Parkville, Australia; Leonid Churilov, Florey Inst of Neuroscience and Mental Health, The Univ of Melbourne, Parkville, Australia; Bruce C Campbell, Melbourne Brain Ctr @ The Royal Melbourne Hosp, The Univ of Melbourne, Parkville, Australia; Christen Barras, Peter Mitchell, Dept of Radiology, The Royal Melbourne Hosp, The Univ of Melbourne, Parkville, Australia; Bernard Yan, Melbourne Brain Ctr @ The Royal Melbourne Hosp, The Univ of Melbourne, Parkville, Australia; Geoffrey A Donnan, Florey Inst of Neuroscience and Mental Health, The Univ of Melbourne, Parkville, Australia; Stephen M Davis, Melbourne Brain Ctr @ The Royal Melbourne Hosp, The Univ of Melbourne, Parkville, Australia; STOP-AUST Investigators

Abstract Body:

Background: Early hematoma expansion after intracerebral hemorrhage (ICH) is associated with poor clinical outcome. Contrast extravasation ‘spot-sign’ on computed tomography angiography (CTA) is a marker of ongoing bleeding and is associated with hematoma expansion. Tranexamic acid is an anti-fibrinolytic agent which may attenuate hematoma growth and improve outcome after ICH in patients with a CTA spot-sign. Objective: STOP-AUST aims to test the hypothesis that ICH patients selected with CTA ‘spot-sign’ will have lower rates of hematoma growth when treated with intravenous tranexamic acid within 4.5 hours of stroke onset compared with placebo.

Design: Multicenter, prospective, randomised, double-blind, placebo-controlled, investigator-led phase II trial.

Population Studied: Patients ≥18 years of age with ICH who present within 4.5 hours of onset and demonstrate the CTA spot sign. Patients with ICH volume >70ml, oral anticoagulant use, Glasgow coma scale <8, or brainstem ICH will be excluded, as will patients with ICH known or suspected to be caused by trauma, vascular malformation, venous sinus thrombosis, tumor, infection or thrombolytic therapy.

Intervention: Patient will receive 1g intravenous tranexamic acid or placebo bolus (over 10min), followed by 1g intravenous tranexamic acid or placebo infusion over 8 hours.

Outcome Measures: The primary outcome measure is ICH growth defined as either >33% or >6ml increase from baseline volume measured on a computed tomography (CT) scan at 24±3 hours after treatment. Secondary outcomes include ICH growth as a continuous variable, thromboembolic events and 3 month modified Rankin Scale score.

Analysis: The primary efficacy analysis will be performed on an intention to treat basis. The primary outcome will be compared between treatment and control arms adjusted for baseline volume using binary logistic regression.
Trial Status: Recruitment has commenced at 4 Australian sites with a plan for approximately 12 further sites to open in 2014.

Author Disclosure Block:

A New Method for Rehabilitating Stroke-induced Dysphagia: A Randomised Controlled Trial of Swallowing Treatment Using Electrical Pharyngeal Stimulation (STEPS)

Introduction: Dysphagia is common after stroke and independently associated with poor functional outcome, pneumonia and malnutrition. Although the optimal treatment of dysphagia remains undefined, a novel method, electrical pharyngeal stimulation (EPS), has shown promise in pilot studies.

Method: The STEPS prospective international randomised controlled trial is assessing the safety and efficacy of EPS versus sham in 140 patients with recent onset stroke and dysphagia, assessed by videofluoroscopy. Treatment is delivered via a proprietary catheter that houses both nasogastric tube capability with integrated stimulation electrodes driven by the Phagenyx™ generator (Phagenesis Ltd). Treatment is given on three consecutive days comprising a stimulation paradigm developed in pilot studies (5 Hz, 75% of maximum tolerated intensity for 10 minutes); patients receiving sham receive all trial procedures but without EPS. The primary outcome is the mean of the worst swallows on videofluoroscopy at 2 weeks post treatment. Key secondary outcomes at 2 and 12 weeks include clinical measures of swallowing (Toronto Bedside Swallowing Screening Test, Dysphagia Severity Rating Scale), feeding status, weight, pneumonia, impairment (NIHSS), disability (Barthel Index), dependency (modified Rankin Scale), quality of life, and adverse events.

Results: The trial is running across 13 sites in five countries (Denmark, France, Germany, Spain, UK) and has passed its interim analysis phase. To date 74 patients have been randomised and treated. The results will be presented in 2014.

Conclusion: Electrical Pharyngeal Stimulation is a promising treatment for stroke-induced dysphagia and the STEPS trial will provide the first large scale evidence on its potential efficacy.

Author Disclosure Block:

J. Love: Employment; Significant; Employee of Phagenesis Limited. S. Hamdy: Ownership Interest; Modest; Phagenesis Limited. P.M.W. Bath: Honoraria; Modest; Phagenesis Limited.
Abstract Body:

BACKGROUND: NINDS extended CREST follow-up through 2016, and so mean follow-up (F/U) will be 7.5 years compared to 2.5 as originally reported.

OBJECTIVE: To evaluate the long-term clinical and anatomic durability of carotid stenting (CAS) vs. surgery (CEA) as assessed by ipsilateral stroke and restenosis.

DESIGN: CREST (ClinicalTrials.gov NCT00004732) is a multicenter, randomized trial with blinded endpoint adjudication. F/U of CAS and CEA subjects includes annual visits and midpoint telephone visits up to 10 years.

POPULATION: Symptomatic and asymptomatic CREST subjects.

OUTCOMES: The primary aim is to assess CAS vs CEA in the prevention of ipsilateral stroke. Secondary aims assess 1) effect modifiers of age, sex, stenosis, symptomatic status; 2) temporal change or patterns in relative efficacy; 3) restenosis or revascularization; 4) patient outcomes and utilization of healthcare services by linking CREST subjects with inpatient and outpatient CMS data files.

ANALYSIS: Statistical analysis (time-to-event modeling with adjustment for major baseline covariates) will assess post procedural treatment differences from Day 31 up to ten years, providing 90% power to detect a hazard ratio of 1.67.

TRIAL STATUS: At 106 US and Canadian sites, 1458 (71%) of surviving subjects are active; 8 have completed 10 years of F/U, and 949 have consented to CMS database linkage. One of the most innovative aspects of the long-term F/U, the linkage of CREST subjects with CMS and other national database files can establish a resource that will enhance current follow-up strategies and provide alternative methods to ascertain patient outcomes for future clinical studies.

Trial devices have been approved by the FDA and Health Canada. Published in the New England Journal of Medicine, Lancet Neurology, Circulation, Stroke, Clinical Trials and the Journal of Vascular Surgery, CREST analyses have contributed to carotid disease treatment guidelines. CREST will assess the durability of CAS...
and CEA in symptomatic and asymptomatic subjects for one of the longest periods in carotid trials. Further research (CREST-2) is planned for CREST’s consortia of sites and core centers.

Author Disclosure Block:

ARTSS-2: A Pilot, Phase IIb, Randomized, Multi-center Trial Of Argatroban In Combination With Recombinant Tissue Plasminogen Activator For Acute Stroke

Author Block: Andrew D Barreto, Univ of Texas Houston Health Science Ctr, Houston, TX; Andrei V Alexandrov, Univ of Alabama, Birmingham, AL; Navdeep Sangha, Zahra Ajani, Kaiser Permanente, Los Angeles, CA; Steven R Levine, Clotilde Balucani, SUNY Downstate, Brooklyn, NY; James Frey, Barrow Neurological Inst, Phoenix, AZ; Loren Shen, Waldo Guerrero, Amber Jacobs, Hari Indurpuri, Rigo Delgado, Univ of Texas Houston Health Science Ctr, Houston, TX; April Sisson, Lynn Merritt, Univ of Alabama, Birmingham, AL; Claudia Pedroza, Mohammad H Rahbar, James C Grotta, Univ of Texas Houston Health Science Ctr, Houston, TX; Gary Ford, Anand Dixit, Claire Oyston, Newcastle Hosp, Newcastle, United Kingdom; Usman Khan, St. Georges Healthcare, London, United Kingdom; Martin James, Royal Devon and Exeter, Devon, United Kingdom; Christine Roffe, Univ Hosp of North Staffordshire, Staffordshire, United Kingdom; Bart Piechowski, Kings Coll Hosp, London, United Kingdom; Jesse Dawson, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom; Rob Simister, Univ Coll London Hosp, London, United Kingdom

Abstract Body:

Background:
Recombinant tissue plasminogen activator (rt-PA), fails to reperfuse brain in most patients with large thrombi. In our Phase IIa low-dose safety study (n=65), the two drugs appear safe when delivered concomitantly and recanalization rates were greater than with historical controls. This study will provide evidence-based hypotheses and data needed to design a larger definitive trial.

Objective:
Primary: Estimate overall treatment benefit (improvement in disability) among stroke patients treated with rt-PA who are randomized to also receive either low-dose or high-dose Argatroban, or neither.
Secondary:
1) Verify the safety of low-dose combination Argatroban and rt-PA and test the safety of high-dose combination treatment.
2) Assess rates of early recanalization.

Design:
Multicenter phase IIb prospective randomized trial.

Study Population:
105 total ischemic stroke patients all treated with IV-rt-PA; age ≥18 years; proximal (intracranial) artery occlusion as imaged by either TCD or CTA, or clinically suspected occlusion with NIHSS ≥10.
Intervention(s):
Patients are randomized to 1 of 3 arms (n=35 each):
1) Low-dose Argatroban* 1.0μg/kg/min continuous infusion of Argatroban, preceded by a 100 μg/kg bolus.
Infusion titrated to achieve an aPTT of 1.75 times baseline + IV-rt-PA;
2) High-dose Argatroban* 3.0μg/kg/min continuous infusion of Argatroban, preceded by a 100 μg/kg bolus.
Infusion titrated to achieve an aPTT of 2.25 times baseline + IV-rt-PA;
3) Intravenous-rt-PA alone.
Argatroban will continue for a maximum of 48 hours.
Outcome Measure(s):
Primary: Excellent functional outcome (% 0 or 1 on the mRS) at Day 90 as assessed by blinded personnel.
Secondary:
1) Safety as measured by the incidence of:
Symptomatic intracranial hemorrhage, Parenchymal hemorrhage 2, Major systemic hemorrhage
2) Rates and completeness of arterial recanalization assessed at baseline and 2-3 hours by TCD or CTA
3) Neurological deficits improvement from baseline to 2 hours, 24 hours, end of Argatroban infusion, Day 7 discharge and day 90 as measured by NIHSS
4) Quality of Life - obtained by standard gamble, time-trade-off method, and visual analogue scale
5) Cost utility analysis
Trial Status:
Ongoing: 48 out of 105 patients enrolled.

Author Disclosure Block:

Abstract Body:

Background: In the US, blacks have a higher prevalence of hypertension (HTN) and a higher incidence of ischemic stroke compared to whites. In Kaiser Permanente Northern California (KPNC), a setting where all members have similar access to healthcare and a very high overall rate of HTN control, blacks still had poorer blood pressure (BP) control than whites. It has been suggested that greater difficulty in controlling BP and lifestyle differences may account for this difference. The “Shake, Rattle and Roll” trial is named for: 1) “shake” the salt habit; 2) “rattle” the intensity of current BP management; and 3) adapt and “roll” out the interventions to other communities.

Objective: To determine whether a primary prevention intervention of either lifestyle coaching or an intensive pharmacotherapy protocol is more effective than usual care in improving rates of BP control in blacks and thereby reducing disparities between black and white.

Design: A pragmatic clustered randomized controlled trial

Population studied (including sample size): All primary care providers (PCPs) at Kaiser Oakland and their panels of black patients are randomized to one of 3 arms, stratified by panel size. There are approximately 12,000 blacks in the HTN registry at Oakland. We have 80% power to detect an overall treatment effect of 4% with 180 people in each study arm.

Interventions: 1) usual care; or 2) enhanced monitoring of current KPNC BP management protocol; or 3) culturally tailored diet and lifestyle coaching focused on the DASH eating plan.

Outcomes: Proportion of patients with sustained BP control at 1 year post-study enrollment.

Analysis: No analysis yet because trial is in early phases.

Trial Status: We cluster randomized 107 PCPs and their panels to one of 3 arms. We have identified 389 black patients with uncontrolled BP for the usual care arm, 414 for enhanced monitoring, and 381 for lifestyle arm. We have enrolled 389 in usual care, 193 in enhanced arm, and 108 in lifestyle arm.

Author Disclosure Block:

Background:
There is no accepted strategy to enhance the effects of motor training on functional recovery after stroke, the most common cause of adult long-term disability. There is emerging evidence that suggests that novel noninvasive intervention, tDCS enhances aspects of cortical plasticity and motor behavior in healthy volunteers and chronic stroke patients.

Objectives:
1. To determine whether tDCS application will improve motor recovery of the upper extremity subacutely after stroke beyond what is achievable with standard rehabilitative treatment (SRT) alone.
2. To collect preliminary data on the neural substrates underlying recovery of motor function after SRT alone (sham condition) and with additional brain stimulation. (tDCS condition)

Design:
We are enrolling patients from University of Texas Southwestern Medical Center (UTSW) who had a single ischemic stroke resulting in moderate to severe hand weakness within 5-15 days of the stroke onset. We added a second subgroup of patients who can't move their hand. Eligible patients are randomized in one of the two study arms: SRT + tDCS or in SRT + sham stimulation. Patients receive 20 minutes of tDCS or sham of the affected motor cortex simultaneously with SRT Monday-Friday for a total of ten sessions. Outcome measures are collected at discharge, 3 months and at 12 months. We perform functional MRI in volunteers and in a subgroup of patients before and after the stimulation and follow-up and TMS studies.

Population Studied:
We will consent up to 160 eligible subjects aged 18-85 years old.

Intervention:
TDCS is a noninvasive form of cortical stimulation that uses weak current (1mA) delivered for 20 minutes through surface electrodes which are positioned above the motor cortical representational field of the affected hand (anodal stimulation) and over the contralesional forehead.
Outcome Measures:
The upper extremity component of Fugl-Meyer test (uFM), the Wolf Motor Function Test, Motor Activity log , Medical Research Council Scale, Modified Ashworth-Spasticity scale, Abilhand scale, Barthel Index, NIH stroke scale.
Analysis:
Two way analysis of variance involving two factors: treatment group (tDCS or Sham) and stratum (uFM over or less than 30).
Trial Status: Total of 60 subjects have been enrolled.

Author Disclosure Block:

Collateral status varies widely in patients with acute ischemic stroke. Individuals with poor collateral status suffer larger infarct volumes, poor response to thrombolytics, and increased risk for hemorrhagic transformation, poor outcome and death. The mechanisms responsible for this variation are unknown.

Recently, it has been shown that mice with naturally occurring differences in genetic background have approximately 45-fold variation in pial collateral number and diameter. This results in a wide variation in collateral-dependent blood flow and infarct volume after experimental middle cerebral artery occlusion. A single polymorphic locus (Dce1) has been linked to 80 percent of this variation. The same genetic variant, or a closely related one, may contribute to the wide variation in collateral status in humans. Objective: GENEDCSS is a prospective observational study to determine if variation in collateral score, stroke severity and functional outcome are linked to a polymorphism(s) at human Dce1, and/or at related candidate loci, in patients with acute M1 stroke. Design: Based on power analysis, the Pilot phase of the study will compare a minimum of 100 each of patients with the highest and lowest collateral scores. Collateral score will be obtained from image files cross-scored at the University of North Carolina (UNC), UCLA and the University of Calgary. Genetic analysis will be conducted at UNC. If successful, a rapid diagnostic marker could be developed to help distinguish individuals with poor versus good collaterals. Eventual identification of the causal gene(s) would also provide therapeutic targets for future development aimed at the collateral circulation. GENEDCSS is a large ongoing multicenter registry that began September, 2013. Additional sites are welcomed. Trial sponsor: investigator initiated; formal funding under review. Trial contact information: James Faber (PI, University of North Carolina) jefaber@med.unc.edu, 919-966-0327 (ph), 919-966-6927 (fax), Anne Beckwith (coordinator) beckwitha@neurology.unc.edu, 919-843-8797 (ph).
Presentation Number: CT P42

Trial Abbreviation: STARTING-2

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Trial Email: nmboy@unitel.co.kr

Trial Name: The STem Cell Application Researches and Trials In NeuroloGy-2 Study

Trial Registry Number ID: NCT01716481

Trial Sponsor: Samsung Medical Center

Trial Web Site: none

Publishing Title: Intravenous Transplantation of Mesenchymal Stem Cells Preconditioned With Early Phase Stroke Serum

Author Block: Suk Jae Kim, Samsung Medical Ctr, Seoul, Korea, Republic of; Gyeong Joon Moon, Samsung Biomedical Res Inst, Seoul, Korea, Republic of; Won Hyuk Chang, Yun-Hee Kim, Gyeong-Moon Kim, Chin-Sang Chung, Kwang Ho Lee, Jun Ho Jang, Samsung Medical Ctr, Seoul, Korea, Republic of; Yoon Mi Kang, Yong Man Kim, Hyun Soo Kim, Pharmicell Corp, Seongnam, Korea, Republic of; Cindy W Yoon, Inha Univ, Incheon, Korea, Republic of; Ji Won Kim, Natl Medical Ctr, Seoul, Korea, Republic of; Soo Kyoung Kim, Gyeongsang Natl Univ Hosp, Chinju, Korea, Republic of; Yeon Soo Ha, Wonkwang Univ, Iksan, Korea, Republic of; Oh Young Bang, Samsung Medical Ctr, Seoul, Korea, Republic of

Abstract Body:

Background
Several recent clinical trials have investigated mesenchymal stem cell (MSC) therapy for patients with ischemic stroke. We previously reported the results of a controlled trial on the application of autologous MSCs in patients with ischemic stroke with a long-term follow-up of up to 5 years (the ‘STem cell Application Researches and Trials In NeuroloGy’ (STARTING) study). The results from this pilot trial are challenging, but also raise important issues. In addition, there have been recent efforts to improve the safety and efficacy of MSC therapy for stroke.

Objective
The study tests the hypothesis that patients with ischemic stroke with moderate to severe persistent neurologic deficits will have better outcomes with intravenous transplantation of autologous MSCs expanded with autologous serum obtained during the acute phase of stroke than patients receiving standard treatment.

Design
The trial is a prospective, randomized, open-label, blinded-endpoint (PROBE) clinical trial.

Population studied and intervention
Both acute and chronic stroke patients will be selected based on clinical and radiological features. The subjects will be randomized into one of two groups: (A) a MSC group (n = 40) or (B) a control group (n = 20). Autologous MSCs will be intravenously administered after ex vivo culture expansion with autologous ischemic serum obtained as early as possible, to enhance the therapeutic efficacy (ischemic preconditioning).

Outcome measures and Analysis
For the primary outcome analysis, the categorical shift in mRS at 90 days after treatment will be determined as 0 to 5 mRS levels. Deaths (a mRS score of 6) will be included in the category of worst outcome (a mRS score of 5). Additional objective outcome measurements will be performed using multimodal MRI and detailed
functional assessments by blinded observers.

**Trial status**
Start date: November 2012.
Expected end date: February 2016.
Expected publication date: May 2016.
Status at time of submission of this article: recruitment ongoing

**Author Disclosure Block:**

Presentation Number: CT P43

Trial Abbreviation: SETIN-HYPERTENSION

Trial Contact Information: nmboy@unitel.co.kr

Trial Email: nmboy@unitel.co.kr

Trial Name: Safety and Efficacy of Therapeutic INduced HYPERTENSION in Acute Non-cardioembolic Ischemic Stroke

Trial Registry Number ID: NCT01600235

Trial Sponsor: Samsung Medical Center

Trial Web Site: none

Publishing Title: Safety and Efficacy of Therapeutic INduced HYPERTENSION in Acute Non-cardioembolic Ischemic Stroke

Author Block: Suk Jae Kim, Sookyung Ryoo, Sung-Ji Park, Gyeong-Moon Kim, Chin-Sang Chung, Kwang Ho Lee, Samsung Medical Ctr, Seoul, Korea, Republic of; Soo Kyoung Kim, Gyeongsang Natl Univ Hosp, Chinju, Korea, Republic of; Moon Ku Han, Seoul Natl Univ Bundang Hosp, Seongnam, Korea, Republic of; Sung-II Sohn, Keimyung Univ, Daegu, Korea, Republic of; Jun Lee, Yeungnam Univ, Daegu, Korea, Republic of; Oeung-Kyu Kim, Inje Univ, Pusan, Korea, Republic of; Pil Wook Chung, Kangbuk Samsung Medical Ctr, Seoul, Korea, Republic of; Sang Min Sung, Pusan Natl Univ, Pusan, Korea, Republic of; Oh Young Bang, Samsung Medical Ctr, Seoul, Korea, Republic of

Abstract Body:

Objective and Hypothesis
The purpose of this study is to evaluate the safety and efficacy of the induced hypertension using phenylephrine in patients with noncardioembolic ischemic stroke. The investigators hypothesized that phenylephrine-induced hypertension can result in good clinical response without serious complications in patients with noncardioembolic ischemic stroke.

Design
The trial is a multicenter, prospective, randomized, open-label, blinded-endpoint (PROBE) clinical trial.

Population studied
Patients with acute ischemic stroke confirmed by diffusion-weighted imaging (DWI) performed within 24 hours of symptom onset or symptom worsening (defined by a 2-point or more increase in NIH stroke scale (NIHSS) score including one or more increase in the motor score of affected upper and lower limbs in NIHSS during hospitalization or clear history of symptom worsening judged by investigator before hospitalization) confirmed by DWI performed within 24 hours of aggravation will be selected.

Intervention
The subjects will be randomized into one of two groups: (A) a phenylephrine-induced hypertension group (n = 85) or (B) a conventional treatment group (n = 85).

Outcome measures
The primary outcome measure is the change of NIHSS between days 0 and 7. Additional clinical and radiological outcome measures will also be assessed by blinded observers.

Analysis
The proportion of patients with two points or more improvements in NIHSS between day 0 and day 7 will be
compared between two groups. The percentage of patients meeting a modified Rankin Scale score of 0, 1 or 2 at day 90 will also be compared.

**Trial status**
Start date: June 2012.
Expected end date: September 2014.
Expected publication date: January 2015.
Status at time of submission of this article: recruitment ongoing

**Author Disclosure Block:**

- **S. Kim:** None.  
- **S. Ryoo:** None.  
- **S. Park:** None.  
- **G. Kim:** None.  
- **C. Chung:** None.  
- **K. Lee:** None.  
- **S. Kim:** None.  
- **M. Han:** None.  
- **S. Sohn:** None.  
- **J. Lee:** None.  
- **O. Kim:** None.  
- **P. Chung:** None.  
- **S. Sung:** None.  
- **O. Bang:** None.
**Presentation Number:** CT P44

**Trial Abbreviation:** IMNSR

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**Trial Name:** International Maternal Newborn Stroke Registry

**Trial Registry Number ID:** not applicable

**Trial Sponsor:** World Federation of Neurology

**Trial Web Site:** to be determined

**Publishing Title:** International Maternal Newborn Stroke Registry

**Author Block:** Mariana Ciobanu, Wake Forest Sch of Med, Winston Salem, NC; Adam Kirton, Alberta Children's Hosp, Calgary, AB, Canada; Gabrielle deVeber, Hosp for Sick Children, Toronto, ON, Canada; Cheryl Bushnell, Wake Forest Sch of Med, Winston Salem, NC

**Abstract Body:**

**BACKGROUND:** Pregnancy and delivery confer a high risk for both maternal and perinatal strokes with a combined incidence of 1 stroke per 1,000 maternal infant pair. There are likely to be as yet undiscovered interactions among maternal and infant characteristics in the pathogenesis of both stroke subtypes. A combined registry of maternal and newborn strokes is novel, feasible and will inform efforts to improve maternal and child brain health worldwide.

**DESIGN:** multicenter, international registry of cases and controls

**STUDY POPULATION:** anticipated 288 maternal/newborn stroke dyads with 1:1 controls for each age group.

**Study Aims:**
- Develop an international registry of mother-newborn dyads experiencing stroke and matched controls across multiple race-ethnicities and geographic regions to enable study of common pathogenetic mechanisms for stroke
- Collect clinical and laboratory data and research samples of placenta, plasma and DNA from maternal and newborn stroke patients, their respective pairs, and controls for future analysis of genotypes and biomarkers.

**OUTCOME MEASURE(S):** This registry will collect identifiable etiologies of maternal/newborn strokes based on clinical and imaging data, and risk factors. Outcomes collected at 3 months and 1 year post stroke include the Pediatric Stroke Outcome Measure for the newborn stroke group and modified Rankin Score and measures of the ability to care for the infant in the maternal stroke group.

**ANALYSIS:** Statistical analysis will include comparison of the risk factor, pregnancy, and delivery characteristics between cases and controls.

**REGISTRY SITES:** two North American (North Carolina, US and Alberta, Canada) and 2 international sites (Chile, Philippines)

**REGISTRY STATUS:** We developed the protocol and data collection form for web-based data entry, and obtained IRB approval. Enrollment is ongoing at 3 of the 4 sites: 2 subjects have been enrolled. We have secured funding from World Federation of Neurology to expand our established pilot network to an additional 8 global sites.

**Author Disclosure Block:**
M. Ciobanu: None. A. Kirton: None. G. deVeber: None. C. Bushnell: Research Grant; Significant; World Federation of Neurology, World Stroke Organization.
Background: Minor stroke and TIA are associated with a high risk of early neurological deterioration and disability. This is especially true when an intracranial occlusion is present, which can be seen in up to 10% of these patients. TNK-tPA (TNKase) compared to alteplase is easier to administer, has a longer half-life, higher fibrin specificity and possibly a lower rate of intracranial hemorrhage. Therefore, it may be an ideal thrombolytic agent in this population.

Methods: TEMPO is a multi-centre, prospective cohort, TNK-tPA dose-escalation, safety and feasibility trial. Patients with TIA or minor stroke with an NIHSS < 6 within a 12h treatment window will be enrolled. Patients must have an intracranial arterial occlusion on CTA and not show signs of well-evolved infarction on NCCT. 50 patients will be enrolled. The first 25 patients have been treated at a dose of 0.1 mg/kg, after which safety was established. A second cohort of 25 patients will be treated at a dose of 0.25 mg/kg. Primary outcomes will be the rate of symptomatic intracranial and extracranial hemorrhage and the feasibility of enrolment and treatment. Secondary outcomes include complete neurological (NIHSS 0-1) and functional (MRS 0-1) recovery at 90 days, recanalization at 4-8 h and minor bleeding.

Results: 25 patients (mean age 67.2, 48% males) have been enrolled since July 2012 with a median baseline NIHSS of 3.0. Site of intracranial occlusions were: M1 (6), M2 (10), M3 (5), P2 (1) branches, vertebral artery/PICA (2) and undetermined (1). Arterial recanalization between 4-8 h was complete in 21.7 %, partial in 26.1% and no recanalization was seen in 52.2%. Median ASPECTS at 24 hours was 8. 23 patients have concluded the 90 days assessment, of which 18/23 (78.3%) reached neurological recovery and 12/23 (52.2%) functional recovery. There were no drug related complications.

Conclusion: Assuming safety of this approach in both dose tiers, we will pick the higher of the two doses and proceed with a randomized trial in this population. An international trial would be required with 500 patients to show a 10% treatment effect size.
**Presentation Number:** CT P46

**Trial Abbreviation:** J-STARS

**Trial Contact Information:** Masayasu Matsumoto, MD, PhD, e-mail; jstars-office@umin.ac.jp, web; http://jstars.umin.ne.jp, fax; +81-82-505-0490, tel; +81-82-257-5201

**Trial Email:** jstars-office@umin.ac.jp

**Trial Name:** Japan Statin Treatment Against Recurrent Stroke

**Trial Registry Number ID:** NCT00221104

**Trial Sponsor:** Translational Research Informatics Center, Kobe, Hyogo, Japan; The Japanese Ministry of Health, Labour and Welfare

**Trial Web Site:** http://jstars.umin.ne.jp

**Publishing Title:** Present Status of J-STARS and Substudies

**Author Block:** Masayasu Matsumoto, Naohisa Hosomi, Shiro Aoki, Dept of Clinical Neuroscience and Therapeutics, Hiroshima Univ Graduate Sch of Biomedical and Health Sciences, Hiroshima, Japan; Masanori Fukushima, Yoji Nagai, Translational Res Informatics Ctr, Kobe, Japan; Kazuo Minematsu, Chiaki Yokota, Natl Cerebral and Cardiovascular Ctr, Osaka, Japan; Hideki Origasa, Div of Biostatistics and Clinical Epidemiology, Univ of Toyama Graduate Sch of Med and Pharmaceutical Sciences, Toyama, Japan; Shinichiro Uchiyama, Dept of Neurology, Tokyo Women's Medical Univ Sch of Med, Tokyo, Japan; Setsuro Ibayashi, Seiai Rehabilitation Hosp, Fukuoka, Japan; for the J-STARS collaborators

**Abstract Body:**

**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 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase could decrease the incidence of coronary heart disease and first occurrence of stroke in Japanese patients with hypercholesterolaemia (MEGA study). The neuroprotective mechanism beyond cholesterol-lowering effects could be expected to attenuate cerebrovascular inflammation and atherosclerosis.

**Objective:** This study hypothesizes if the treatment with a low-dose pravastatin (10mg/ day) prevents recurrent stroke in Japanese patients with ischemic stroke with safety.

**Design:** J-STARS is a multicenter, prospective, randomized, open label, blinded-endpoint, active controlled, parallel group trial.

**Population studied:** Eligibility includes, 1) ischemic stroke from 1 month to 3 years after the onset, except for cardiogenic embolism, 2) 45-80 years old, and 3) total cholesterol level of 180-240mg/dl without the prescription of statin. Exclusion criteria includes, 1) ischemic stroke of other determined cause according to the TOAST classification, 2) ischemic heart disease necessary to require statin, and 3) hemorrhagic disorders.

**Interventions:** Patients were randomized into the group receiving pravastatin 10mg/day or that having no statin.

**Outcome Measures:** The primary outcome for this study is cerebrovascular events. The secondary outcomes include the events of ischemic or hemorrhagic stroke, cardiovascular events, death of all causes, hospital admission, dementia, and cognitive impairment.

**Statistical Analysis:** 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 2009, and have been in the process of follow-up (mean 4.7 years at October, 2013). Mean age 66.2 years; 25.4% atherothrombotic infarction, 64.2%
lacunar infarction. The protocol paper including baseline data has been published (Nagai Y et al., Int J Stroke, 2013). The latest status including substudies (e.g. J-STARS Echo, hsCRP and Genomics) will be presented at the conference.

Author Disclosure Block:

Presentation Number: CT P47

Trial Abbreviation: pending

Trial Contact Information: Laura R. Saurebeck, RN, BSN, MS (855)472-0072

Trial Email: pending

Trial Name: NIH Stroke Trials Network

Trial Registry Number ID: pending

Trial Sponsor: NIH/NINDS

Trial Web Site: pending

Publishing Title: NIH Stroke Trials Network

Author Block: Laura Sauerbeck, Joseph P Broderick, Univ of Cincinnati Medical Ctr, Cincinnati, OH

Abstract Body:

**Background:** The 2012 Stroke Progress Review Group and National Institute of Neurological Disorders and Stroke (NINDS) identified a critical need for a network infrastructure for the development of new approaches in prevention, treatment, and recovery to decrease the global burden of stroke. In 2013 the National Institutes of Health (NIH) issued funding opportunity announcements for the elements of a Stroke Trial Network including: Regional Coordinating Stroke Centers (RCCs), National Coordinating Center (NCC) and Data Management Center (DMC).

**Objective:** The goal of this network is to maximize efficiencies in conducting multi-site trials, including the use of master trial agreements (MTAs), a central IRB (CIRB), common data elements (CDEs) and standard operating procedures (SOPs). The network will collaborate with existing networks, such as the Neurological Emergencies Treatment Trials Network and international consortia, to conduct larger trials.

**Design:** The network will utilize 25 regional coordinating centers with strong relationships among all areas of care to maximize recruitment. Each RCC will be responsible for the governance of their identified performance sites and adding new sites. The RCCs will contribute to trial applications for peer review and the execution of NIH-funded trials originating outside of the Stroke Network. Third party entities can be involved in protocols by negotiating with NINDS for the clinical co-development of an agent or device. The NCC and the CIRB have been awarded to the University of Cincinnati, and the DMC is expected to be awarded in early 2014.

**Educational and mentoring programs for stroke management and execution of research projects will be implemented in collaboration with the other networks.**

**Performance Measures:** Metrics evaluated include timing of the execution of MTAs, RAs, the development of RCC SOPs, recruitment, retention and data quality.

**Discussion:** This infrastructure will foster the development and execution of NIH-funded trials from the bench to clinical practice. The network expertise will allow for the development of an experienced stroke workforce, while enhancing research training.

Author Disclosure Block:

**L. Sauerbeck:** Research Grant; Significant; NS 086872.
**J.P. Broderick:** Research Grant; Significant; NS086872.
**Presentation Number:** CT P48

**Trial Abbreviation:** DIAS-J

**Trial Contact Information:** Birgit Bjørnlund, Tel +45 36434244, fax +45 36438216, email: RBJ@lundbeck.com

**Trial Email:** BRBJ@lundbeck.com

**Trial Name:** Randomised, double-blind, placebo-controlled, dose-escalating study of desmoteplase in Japanese patients with acute ischemic stroke

**Trial Registry Number ID:** NCT01104467

**Trial Sponsor:** Lundbeck Japan K.K

**Trial Web Site:** none

**Publishing Title:** Safety and Tolerability of Two Doses of Desmoteplase in Japanese Patients With Acute Ischemic Stroke (DIAS-J): A Randomized, Double-blind, Placebo-controlled Study

**Author Block:** Etsuro Mori, Tohoku Univ Graduate Sch of Med, Sendai, Japan; Kazuo Minematsu, Natl Cerebral and Cardiovascular Ctr, Osaka, Japan; Jyoji Nakagawara, Integrative Stroke Imaging Ctr, Dept. of Neurosurgery, Natl Cerebral and Cardiovascular Ctr, Osaka, Japan; Takenori Yamaguchi, Natl Cerebral and Cardiovascular Ctr, Osaka, Japan; DIAS-J Trial Investigators

**Abstract Body:**

The management of acute ischemic stroke (AIS) would benefit from the development of safe thrombolytics, which are highly fibrin-specific and fibrin-selective, devoid of non-fibrinolytic actions, and suitable for treatment beyond 3 hours after stroke symptoms onset. Desmoteplase is the most fibrin-specific thrombolytic agent in advanced clinical development for AIS. The aim of this prospective, randomized, double-blind, multi-centre, dose-escalation, phase II clinical trial (DIAS-J; NCT01104467; 90 days study duration per patient) was to investigate the safety and tolerability of desmoteplase in Japanese patients with AIS within 3-9 h after stroke symptoms onset. Two doses, 70 µg/kg and 90 µg/kg, were sequentially investigated. Each dose cohort included 24 patients, randomised 2:1 so that in each cohort, 16 patients received desmoteplase and 8 patients received placebo. The patients included were aged 20 to 85 years, had a clinical diagnosis of AIS (4 to 24 points on the National Institutes of Health Stroke Scale), and had an occlusion or high-grade stenosis of the Middle Cerebral Artery (segment M1 or M2) detectable using magnetic resonance angiography (MRA) at baseline. Desmoteplase or placebo was administered as a single intravenous bolus injection over 1-2 minutes. Safety and tolerability were assessed by the incidence of symptomatic intracranial hemorrhage (sICH) within 72 h of treatment (primary outcome), asymptomatic ICH (aICH), symptomatic cerebral oedema, and adverse events. The last patient has been recruited and the trial is approaching completion.

Sponsor: Lundbeck Japan K.K.; Chairman of Coordinating Investigators: T. Yamaguchi, National Cerebral and Cardiovascular Centre, Osaka; Trial Contact: Birgit Bjørnlund, +45 36434244, BRBJ@lundbeck.com

**Author Disclosure Block:**
E. Mori: Consultant/Advisory Board; Modest; Lundbeck. K. Minematsu: Consultant/Advisory Board; Modest; Lundbeck. J. Nakagawara: Consultant/Advisory Board; Modest; Lundbeck. T. Yamaguchi: Consultant/Advisory Board; Modest; Lundbeck.
Abstract Body:

**Background:** Recurrent stroke risk drops profoundly with BP control and a healthy lifestyle. Yet these factors are suboptimal in most stroke survivors and worse among indigent, minority populations.

**Objective:** To test the impact and conduct a cost analysis of a Chronic Care Model/community-based intervention on control of systolic blood pressure (SBP) in socioeconomically disadvantaged individuals with recent stroke/TIA.

**Design:** Randomized-controlled trial.

**Population Studied:** 500 adults (>40 years) with ischemic/hemorrhagic stroke or TIA <90 days prior, recruited from the 4 Los Angeles County-Department of Health Services (LAC-DHS) hospitals. LAC-DHS, the 2nd largest US municipal health system, serves 800,000 individuals each year (>90% minority and 2/3 uninsured).

Exclusion criteria: SBP <120 mm Hg, unable to speak English, Spanish, Korean, Mandarin, or Cantonese, or unable to comprehend study due to communication/cognitive impairments.

**Intervention:** Intervention subjects are assigned a care manager (CM)-community health worker (CHW) team. CMs (physician assistants or nurse practitioners) develop care plans with physician guidance, adjust medications at clinic visits (following evidence-based algorithms) and communicate regularly with CHWs. CHWs lead community Chronic Disease Self-Management classes and conduct home visits to: reinforce self-management skills for home BP monitoring, healthy lifestyle, and medication adherence; act as a liaison with the healthcare system, and assess for social isolation and depression. CHWs and CMs use tablets with
software providing decision support. Control subjects receive usual care.


Analysis: Intention-to-treat analysis to compare outcomes between usual care and intervention arm participants at 12 months. Cost analysis and sustainability plan will be developed.


Author Disclosure Block:

Background: Adherence to 5 healthy lifestyle practices - eating a healthy diet, exercising regularly, maintaining a normal body mass index (BMI), not smoking, and limiting alcohol - lowers risk of cardiac and cerebrovascular events and reduces post-stroke cardiovascular and all-cause mortality. Yet few stroke survivors adhere to all 5 practices and socioeconomically disadvantaged race/ethnic minorities face formidable barriers.

Objective: To conduct a pilot test of an outpatient care intervention, HEALS, to: estimate and compare effect sizes for short-term changes in BMI, diet, exercise, and smoking cessation; conduct a formative evaluation to assess adherence to intervention and improve implementation feasibility, and develop tools for measuring program costs, in preparation for a subsequent large-scale, definitive randomized-controlled trial (RCT).

Design: RCT

Population: 100 adults (>40 years) with ischemic stroke/TIA >90 days prior, recruited from one Los Angeles County-Department of Health Services safety net hospital. Exclusion criteria: SBP <120 mm Hg, unable to speak English/Spanish or unable to comprehend study due to communication/cognitive impairments.

Intervention: Participants in the intervention arm attend a series of six 120-minute group clinics over 2 months, led by occupational therapists (OTs). OTs promote self-management skills, educate regarding diet, exercise, and smoking, and guide participants to improve lifestyle and set short term realistic goals, while addressing individual barriers. Control group receives usual care.

Outcomes Measurements/Analyses: Outcomes measured at 6-month follow-up by interview and examination include achieving: 5% BMI reduction (or normal BMI), 5 servings of fruits/vegetables/day, 150 minutes moderate activity/week, complete smoking cessation. Intention-to-treat analyses will be conducted to estimate effect sizes for each of these outcomes. The formative evaluation will assess session attendance and participant use of educational materials and goal-
setting strategies.

**Trial Status:** Enrolled 41 of 100 study participants.

**Author Disclosure Block:**

A. Towfighi, None; E.M. Cheng, None; N. Valle, None; M. Ayala-Rivera, None; K. Martinez, None; B. Martinez, None; C. Ayala, None; H. Dombish, None; A. Charlton, None; D. Wang, None; D. Ochoa, None; B.G. Vickrey, None.
Presentation Number: CT P51

Trial Abbreviation: VICCTA

Trial Contact Information: Email and Website

Trial Email: viccta@glasgow.ac.uk

Trial Name: The Virtual International Cardiovascular and Cognitive Trials Archive

Trial Registry Number ID: VICCTA

Trial Sponsor: VICCTA Collaboration & University of Glasgow

Trial Web Site: www.viccta.org

Publishing Title: Advancing Knowledge by Optimising use of Existing Data: VICCTA Collaboration

Author Block: Azmil H Abdul-Rahim, Myzoon Ali, Rachael L Fulton, Univ of Glasgow, Glasgow, United Kingdom; David A Fitzmaurice, Gregory Y Lip, Univ of Birmingham, Birmingham, United Kingdom; Jonathan Mant, Univ of Cambridge, Cambridge, United Kingdom; Barry R Davis, Univ of Texas Sch of Public Health, Houston, TX; Albert L Waldo, Case Western Reserve Univ, Cleveland, OH; Colin Berry, John J McMurray, John R Petrie, Naveed Sattar, Gordon D Lowe, Univ of Glasgow, Glasgow, United Kingdom; Matthias Herz, F. Hoffman-La Roche, Basel, Switzerland; Kennedy R Lees, Univ of Glasgow, Glasgow, United Kingdom; * for VICCTA Steering Committee, VICCTA Collaboration, Glasgow, United Kingdom

Abstract Body:

Background and Purpose: Long after the original research question has been answered, archived clinical trial data represent a valuable resource for secondary analyses that can generate hypotheses, assist in understanding the natural history of disease and inform future trial design. The Virtual International Stroke Trial Archive (VISTA) has shown for stroke medicine how much can be achieved. We now report establishment and progress with the Virtual International Cardiovascular and Cognitive Archive (VICCTA), that extends data access to wider cardiovascular and cognition fields.

Methods: Using the successful model of VISTA, we developed specific eligibility criteria for entry of trial or registry data into six subsections of the new archive and are already populating the archive with trial datasets. We invite trialists to lodge data on heart failure, ischaemic heart disease, atrial fibrillation, diabetes & metabolic, thrombo-embolism and cognition. Each subsection is led by a committee comprising the contributing trialists and founders. These committees manage their respective sub-archives, review proposed uses of data and provide scientific feedback on analyses and manuscripts. Detailed information on data contribution and access is publicly available on the VICCTA website.

Results: VICCTA so far holds international trial datasets with approximately 198,108 patients’ data. Assimilation of new trials to all subsections of the archive is ongoing but with extensive data already available, the archive is open to analysis proposals. The first projects are expected to present results in 2014.

Conclusions- VICCTA is a living archive of completed cardiovascular clinical trials and registries. It offers a broad package for cardiovascular and cognition researchers, facilitating access to networks of investigators and to a wealth of data for use in epidemiology, proof-of-concept, endpoint optimisation and exploratory studies. VICCTA has the potential to deliver valuable research output, bringing added value to the original work, and offers young researchers unparalleled access to clinical experts for collaboration. We welcome the contribution of further data to VICCTA and invite researchers to collaborate as contributors or users.
Author Disclosure Block:

Presentation Number: CT P52

Trial Abbreviation: ENOS

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Trial Name: Efficacy of Nitric Oxide in Stroke

Trial Registry Number ID: ISRCTN99414122

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.enos.ac.uk

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

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Abstract Body:

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, given as glyceryl trinitrate (GTN), is safe and effective in improving outcome after acute stroke. Approximately 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 14th October, 2013, 4011 patients had been recruited from 173 centres (Australia, Canada, China, Denmark, Egypt, Georgia, Greece, Hong Kong, India, Italy, Malaysia, New Zealand, Norway, Philippines, Poland, Republic of Ireland, Romania, Singapore, Spain, Sri Lanka, Sweden, Turkey and UK).

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Presentation Number: CT P53

Trial Abbreviation: EuroHY-P-1

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Trial Name: A European, multicentre, phase III, clinical trial of hypothermia for acute ischaemic stroke

Trial Registry Number ID: -

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.eurohyp1.eu

Publishing Title: A European, Multicentre, Phase III, Clinical Trial of Hypothermia for Acute Ischaemic Stroke: EuroHYP-1

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Abstract Body:

Background: Systematic review of animal studies modeling ischaemic stroke suggests that cooling is the most promising neuroprotective intervention identified to date. In these animal studies, cooling to 35°C reduced infarct size by about one third. Cooling awake patients with ischaemic stroke to 35°C has been shown feasible and safe, but whether this is safe and effective has not been tested in a large clinical trial.

Aims: To determine whether systemic cooling to 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: Open, randomised, phase III, multicentre, international clinical trial with masked outcome assessment testing the safety and efficacy of therapeutic cooling in 1500 awake adult patients with acute ischaemic stroke. 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 either surface or endovascular cooling to 34 to 35°C, maintained for 24 hours. Shivering and discomfort will be prevented and treated with anti-shivering drugs. All patients will receive best medical treatment, including alteplase, if indicated. The primary outcome is centrally adjudicated modified Rankin Scale (mRS) at 90 days (shift analysis). A trial with 750 patients per arm has 90% power to detect a 7% absolute improvement in the mRS at the 5% significance level.

Conclusion: Trial set up is on-going in the UK, with recruitment expected to start late 2013.

Author Disclosure Block:

P.M.W. Bath: None. K. Lees: None. M. Macleod: None. N. Sprigg: None.