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. Randomization is stratified by NIH Stroke Scale (NIHSS) score and IV thrombolysis.

**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 and are recommended to be enrolled within 3 hours of hospital arrival. Study participants will be recruited from approximately 60 sites (50 Neurological Emergency Treatment Trials (NETT) sites and 10 ancillary sites).

**Sample Size:** Maximum of 1400 subjects

**Intervention:** Study participants will be 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 will utilize the GlucoStabilizer® computerized decision support tool to guide therapy. Treatment will continue for up to 72 hours.

**Outcome Measures:** The primary efficacy outcome is 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 21 of the approximately 60 sites. Remaining sites will begin enrolling by early 2013. As of October 31, 2012, 43 subjects have been enrolled.

**Principal Investigator(s):**
Karen C. Johnston, MD, MSc (University of Virginia) - Administrative PI
Askiel Bruno, MD, MS (Georgia Health Sciences University) - Protocol PI
Christiana E. Hall, MD, MS (University of Texas Southwestern) - Recruitment PI

NETT Statistical and Data Management Center
Valerie Durkalski, PhD; Yuko Palesch, PhD (Medical University of South Carolina)

NETT Clinical Coordinating Center
William Barsan, MD; William Meurer, MD, MS (University of Michigan)

SHINE Project Director: Amy Fansler (University of Virginia)
Sponsor: NIH-NINDS U01NS069498, U01NS056975, U01NS059041

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Author Disclosure Block:  J.J. Wold: Research Grant; Significant; U01NS069498.  A. Bruno: Research Grant; Significant; NIH-NINDS069498.  V. Durkalski: Research Grant; Significant; NIH-NINDS U01NS069498, NIH-NINDS U01NS056975, NIH-NINDS U01NS059041.  K.C. Johnston: Research Grant; Significant; NIH-NINDS U01NS069498.
BACKGROUND: Magnesium is neuroprotective in preclinical models of stroke and has been safe and shown signals of potential efficacy when delivered early after onset of human cerebral ischemia. Delayed initiation of neuroprotective agents has hindered past phase 3 neuroprotective agent trials.

OBJECTIVE: To demonstrate that paramedic initiation of intravenous magnesium sulfate within 2 hours of symptom onset improves the longterm functional outcome of hyperacute stroke patients.

DESIGN: Multicenter, randomized, double-blind, placebo-controlled phase 3 trial.

POPULATION STUDIED: 1700 patients (850 in each arm) with acute stroke, including both cerebral infarction and intracerebral hemorrhage patients. Inclusion criteria: 1) likely stroke as identified by the Los Angeles Prehospital Stroke Screen (LAPSS), 2) age 40-95, 3) symptom onset within 2 hours of treatment initiation, 4) deficit present ≥ 15 minutes.

INTERVENTION: Paramedics administer a loading dose of magnesium sulfate (Mg) or matched placebo in the field, 4 grams over 15 minutes. In the ED, a maintenance infusion follows, 16 grams Mg or matched placebo over 24 hours.

OUTCOME MEASURE(S): The primary endpoint is the modified Rankin Scale measure of global disability, assessed using the Rankin Focused Assessment (RFA) 90 days after treatment. Secondary endpoints include NIHSS (neurologic deficit), Barthel Index (activities of daily living), and Stroke Impact Scale (quality of life).

ANALYSIS: The primary analysis will assess the difference in the distribution of mRS scores between treated and placebo groups, employing the Cochran-Mantel-Haenszel test statistic (shift analysis).

TRIAL SITES: Through 11/1/12, 308 ambulances, 42 EMS agencies, and 59 receiving hospitals throughout Los Angeles and Orange Counties are actively recruiting patients, and 2900 paramedics have been trained in study procedures. Site investigators include over 650 emergency physicians and over 150 neurologists, neurosurgeons, and hospitalists.

TRIAL STATUS: Through 11/1/12, 1672 patients had been enrolled. Median pretreatment stroke severity on the Los Angeles Motor Scale (LAMS) is 4. Adjudicated final diagnoses are acute cerebral ischemia in 72%, intracerebral hemorrhage in 24%, and stroke mimic in 4%. Treatment was initiated within 1 hour of onset in 73% and between 1-2 hours in 24%. Median interval from last known well to start of study agent is 46 minutes.
BACKGROUND: The management of acute ischemic stroke (AIS) is progressing. However, one of the remaining challenges is to develop a safer thrombolytic, solely targeted to the blood clot, devoid of non-fibrinolytic actions, and suitable for treatment beyond 3 hours after stroke onset. Desmoteplase is a novel, highly fibrin-specific thrombolytic agent in advanced development for AIS. Although desmoteplase and rt-PA share 70% structural homology, their proteolytic activities differ. Desmoteplase is 180-fold more fibrin selective than rt-PA in plasminogen activation. As a result, it mainly initiates local fibrinolysis without systemic activation and fibrinogen consumption, and thus potentially desmoteplase has a lower risk of hemorrhagic complications, including notably intracranial hemorrhage (ICH). In preclinical models desmoteplase, in contrast to rt-PA, is non-neurotoxic and does not increase blood-brain-barrier permeability. A preclinical review has recently been published by Medcalf RL, *Br J Pharmacol* 2012;165:75-89.

DESIGN: Based on the preclinical profile of desmoteplase and the results of completed trials, two (N=880 in total) randomized, double-blind, placebo-controlled, phase III trials (DIAS-3 and DIAS-4) are currently ongoing. The objective of both trials is to evaluate the safety and efficacy of a single IV bolus injection of 90 μg/kg desmoteplase given 3-9 hours after onset of AIS. Post-hoc analyses of completed trials (Fiebach JB, et al. *Stroke* 2012;43:1561-6) showed that desmoteplase was superior to placebo in patients presenting with TIMI 0-1 (occlusion or high-grade stenosis (OR 4.1 [1.4-12.3]), in contrast to TIMI 2-3 (OR 1.1 [0.5-2.4]). Therefore, in DIAS-3 and DIAS-4, patients are included with TIMI 0-1 (and without extended ischemic edema) in proximal cerebral arteries as assessed by MR or CT angiography. These criteria are also the basis for the ongoing DIAS-J phase-II trial (NCT01104467), investigating a single IV bolus injection of 70 or 90 μg/kg desmoteplase in Japanese patients. The clinical trial protocols have been published by Von Kummer R, et al, *Int J Stroke* 2012;7:589-96.

OUTCOME MEASURES: Primary efficacy parameter is the proportion of patients achieving a modified Rankin Scale score 0-2 at day 90. Other outcomes include NIHSS score at Day 90, recanalization in patients with follow-up angiography, clinical outcome in patients with core-lesion <25 mL, and clinical outcome in patients with perfusion/diffusion mismatch. Safety outcomes comprise mortality, symptomatic ICH, symptomatic ischemic edema, and other major hemorrhagic events.

TRIAL STATUS: Mid-2012, total enrollment in DIAS-3 and DIAS-4 passed 500, while DMC review revealed no safety issues and supported further recruitment. DIAS-3 enrolls patients originating from sites in Europe, Asia and Australia; DIAS-4 from Europe, Latin America and North America.
Presentation Number: CT P4

Trial Abbreviation: STOP-IT Study

Trial Contact Information: Janice A. Carrozella, RN, BA, CCRA, carrozj@uc.edu  www.stopitstudy.org  513-475-8793

Trial Email: carrozj@uc.edu

Trial Name: The Spot Sign for Predicting and Treating ICH Growth (STOP-IT) Study

Trial Registry Number ID: NCT00810888

Trial Sponsor: NIH / NINDS

Trial Web Site: www.stopitstudy.org

Publishing Title: STOP-IT Study

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

Abstract Body:

Background:
Intracerebral hemorrhage is associated with a 50% case-fatality rate. Recombinant activated factor VII (rFVIIa) was proven to significantly reduce hematoma growth when administered within four hours of symptom onset in two placebo-controlled, blinded, randomized clinical trials. Because rFVIIa works to stop bleeding but should not otherwise affect the natural history of ICH, only patients destined to have hematoma growth will benefit from this therapy. CT angiography (CTA) is a widely available, fast, non-invasive tool that has shown promise for predicting hematoma growth. In multiple case series patients with contrast extravasation within their hematomas (the spot sign) had greater risk of subsequent hematoma growth and worse outcomes than patients without extravasation.
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.
• Determine the feasibility of using CTA to identify ICH patients at high risk of hematoma growth and to select patients for randomization to treatment with rFVIIa or placebo.
• Randomize ICH patients who present within five hours of symptom onset and have a spot sign to treatment with rFVIIa versus placebo, in order to (a) determine if rFVIIa is effective at reducing hematoma growth among patients with a spot sign and (b) provide preliminary efficacy data for this treatment paradigm.

Design:
STOP-IT will enroll patients with acute ICH less than five hours from symptom onset. Patients will be included in one of two study arms. 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, in order to determine the value of the spot sign for predicting hematoma growth and 2) patients who have a spot sign and are randomized to rFVIIa or placebo in order to determine the effect of study drug upon hematoma growth.

Population:
One hundred eighty-four subjects with intracerebral hemorrhage fulfilling inclusion and failing no exclusion criteria will be enrolled into one of two study arms at twelve 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 and their data will be compared to spot-positive patients treated with placebo to determine the sensitivity and specificity of the CTA spot sign for hematoma growth.

**Outcome Measures:**

**Primary Outcome: Clinical**
- Safety: Life-threatening thromboembolic complications defined as development of acute myocardial ischemia; acute cerebral ischemia; and acute pulmonary embolism through day 4 following completion of study drug administration.
- The rate of hematoma growth among spot sign positive subjects at 24 hours, comparing subjects treated with rFVIIa to those treated with placebo. Hematoma growth will be defined as a > 33% or > 6 cc increase in volume.

**Primary Outcome: Test Performance:**
- The sensitivity and specificity of the spot sign for predicting hematoma growth.

**Analysis (Imaging):**
De-identified baseline and 24-hour CTs will be provided to the University of Calgary. Hematoma volumes will be calculated by volumetric analysis. De-identified copies of the CTAs will be provided to Sunnybrook Health Sciences Centre for subsequent interpretation by a blinded neuroradiologist.

**Trial Status:**
Twelve clinical sites actively recruiting: 44 subjects enrolled as of 06-Nov-2012

**Principal Investigator:**
Matthew Flaherty, MD-University of Cincinnati

**Trial Sponsor:**
NIH/NINDS

**Author Disclosure Block:** **M. Flaherty on Behalf of STOP-IT Study Investigators:** Research Grant; Significant; NIH/NIND Funded. Other Research Support; Significant; Novo Nordisk, Inc. supplying study drug.
Introduction/Purpose:
It has been suggested that clots 8mm and longer may have a low likelihood of revascularization by IV rtPA therapy alone. Thin-sliced (2.5 mm or less) non-enhanced CT images may be used to determine clot lengths in large artery occlusions. The purpose of the THERAPY Trial is to assess safety and effectiveness of the Penumbra System® as adjuvant treatment to IV rtPA in a stroke cohort with large vessel occlusion and extensive clot burden in the anterior circulation.

Materials and Methods:
THERAPY is a prospective, multicenter, randomized, concurrent controlled study. Patients from 18 to 85 years old [n=582] presenting with acute ischemic stroke symptoms, an NIHSS score of at least 8 or aphasic, and eligible for IV rtPA with evidence of a clot length at least 8mm in the anterior circulation from reconstructed thin-sliced non-enhanced CT are randomly assigned 1:1 to IV rtPA therapy alone or combined IV rtPA therapy and adjunctive treatment with the Penumbra System. The primary endpoints are good 90-day functional outcome and incidence of serious adverse events. Secondary endpoints include good neurological and functional outcomes at discharge and 30 days, as well as the incidence of ICH. A Core Laboratory will assess imaging data, while a DSMB will monitor safety.

Results:
47 centers have committed to the THERAPY Trial, of which 32 have received IRB approval. To date, 26 centers have been initiated, and 13 patients are enrolled. We will present our initial enrollment experience to provide a detailed evaluation of our selection paradigm and to examine its value in application to a definitive acute stroke intra-arterial intervention trial.

Conclusion:
The randomized controlled THERAPY trial may serve as the landmark study to define the role of mechanical thrombectomy in a stroke cohort in whom IV rtPA is not efficacious and who may benefit from an IV-IA bridging approach. An examination of its unique selection criteria and that criteria’s effect on study enrollment will provide important information to the stroke community.

Author Disclosure Block:  J. Mocco: Other Research Support; Modest; Penumbra, Inc.. Honoraria; Modest; Penumbra, Inc.  P. Khatri: Other Research Support; Modest; Penumbra, Inc.  O. Zaidat: Other Research Support; Modest; Penumbra, Inc..
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 will be 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 efficacy; a Phase 3 efficacy study will follow if pre-specified milestones are achieved.

Methods: This is a prospective, randomized, single-blind, multi-center Phase 2/3 study. We aim to include 1600 ischemic stroke patients (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, age 22-80. Patients will be randomly assigned to either hypothermia permissively targeted to 33°C 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 phase 2 and includes frequency of target temperature reached within 6 hours from symptom, pneumonia rate, safety profile of iced saline infusion and study-wide average enrollment of at least 0.4 patients/site/month.

Status: The study team initiated 14 study sites in the US and 2 in Europe. Enrolment began January 2011. Currently, 46 subjects are enrolled. A safety review after the first 45 is underway by the FDA. Following this review, we expect to expand to 26 US sites and enroll 400 patients in Phase 2 of the ICTuS 2/3 trial. We are currently screening for additional study sites for this Phase 2 effort as well as expanding to 50 sites for Phase 3.

Sponsor: NINDS SPOTRIAS 3P50NS044227 and 5P50NS044148
Clinicaltrials.gov ID: NCT01123161

Cooling systems and catheters are provided by Philips/Innercool.
ARTSS-2

Trial Registry Number: NCT01464788

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 Argatroban, 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:
   a) Symptomatic intracranial hemorrhage
   b) Parenchymal hemorrhage 2
   c) 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

**Analysis:**
An interim analysis is planned after data is obtained from 75 enrolled patients. The primary outcome of the
interim analysis will be to compare the rates of 2-3 hour recanalization between Argatroban groups and
controls. Rates will be compared with those obtained from the ARTSS-1 trial. If Argatroban is associated with
greater rates of recanalization, particularly if other available data show a trend toward improved 90-day mRS
and minimal increase in sICH, then a grant proposal will be submitted for a pivotal efficacy trial.

**Trial Status:**
Ongoing: 19 out of 105 patients enrolled.

**PI / Coordinator Name(s):**
Andrew D. Barreto, MD & James C. Grotta, MD/Loren Shen, RN, BSN & Pej Hemati

**PI / Coordinator Affiliation:**
The University of Texas Health Science Center, Houston

**Trial Sponsor(s):**
NIH; The University of Texas Health Science Center, Houston

**Trial Website:** [www.houstonstroke.com](http://www.houstonstroke.com)

REVASCAT (clinicalTrials.gov, NCT01692379) is a multi-center, randomized, controlled, open, blinded-endpoint trial. The study is funded by Fundació ICTUS Malaltia Vascular by means of an unrestricted grant from Covidien Inc.

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 will be randomized following a 1:1 ratio to receive mechanical embolectomy with the CE MARK approved stentriever Solitaire FR device or medical management alone. No other endovascular treatment methods including ia lytics are allowed per protocol. The primary endpoint on the basis of intention-to-treat criteria will be the distribution of the modified Rankin Scale scores at 90 days. Randomization will be 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 for 346, 518 and 690 patients respectively.

Key inclusion criteria include: proof of vascular occlusion by CTA or MRA, clinical severity of stroke at presentation (NIHSS ≥ 6) and a small infarct core size as evaluated by ASPECTS score on plain CT within 4.5 hours on presentation (ASPECTS ≥ 7) and on CT perfusion, CT angiography source images (ASPECTS ≥ 6) in the 4.5 to 8 hour time window. Secondary endpoints are infarct volume evaluated on CT at 24 hours by an independent core lab., dramatic early favorable response as determined by an NIHSS of 0-2 or NIHSS improvement ≥ 8 points at 24 hours, proportion of patients achieving favorable outcome (mRS ≤ 2) between the two arms, vessel recanalization evaluated by CTA or MRA at 24 hours in both treatment groups and successful recanalization in the Solitaire arm assessed by TICI (Thrombolysis in Cerebral Infarction) 2b or 3 on the post-procedure angiogram adjudicated by a central corre-lab. Safety endpoints will be mortality at 90 days, symptomatic ICH rates at 24 hours and procedural related complications: arterial perforation, arterial dissection, and embolization in a previously uninvolved vascular territory adjudicated by an independent adverse events committee.
Sample size is projected to be 690 patients for an estimated common odds ratio of 1.615 that corresponds to an absolute difference in treatment effect of 10%. The study will take place in Catalonia, Spain (population approximately 8 million) where endovascular treatment for acute stroke is performed at 4 regional stroke centers. All 4 treating hospitals have committed to treating all eligible patients. There are approximately 300 acute endovascular stroke procedures performed annually in Catalonia. Enrollment is expected to start in November 2012.

Author Disclosure Block: T.G. Jovin: Ownership Interest; Modest; Silk Road. Consultant/Advisory Board; Modest; Silk Road. E. Cobo: None. Á. Chamorro: None. M. de Miquel,: None. C. Molina: None. A. Rovira: None. L. San Román: None. J. Serena: None. A. Davalos: Consultant/Advisory Board; Modest; Covidien.
BACKGROUND: The SOLITAIRE™ FR Revascularization Device is a retrievable stent designed to restore blood flow in patients experiencing ischemic stroke due to large intracranial vessel occlusion and has demonstrated high rates of recanalization and good clinical outcome in open series and an active comparator controlled trial.

OBJECTIVE: To determine if subjects experiencing an acute ischemic stroke due to large vessel occlusion, treated with combined IV t-PA and Solitaire™ FR within 6 hours of symptom onset have less stroke-related disability (mRS) than those subjects treated with IV t-PA alone.

DESIGN: Global, multicenter, two-arm, prospective, randomized, open, blinded endpoint (PROBE) IDE study comparing functional outcomes (defined by mRS) in acute ischemic stroke patients with established penumbral mismatch who are treated with either IV t-PA alone or IV t-PA in combination with Solitaire™ FR mechanical thrombectomy intervention.

POPULATION STUDIED: The sample size is up to 833 patients. Key inclusion criteria are: age 18-85, prestroke functional independence, NIHSS 8-29, start of IV t-PA within 4.5 hours of onset, M1 MCA or intracranial ICA occlusion on CTA or MRA, and target mismatch penumbral profile on multimodal CT or MR imaging.

INTERVENTION: Patients in both treatment groups receive IV t-PA at 0.9 mg per kg. Patients allocated to the device arm will undergo mechanical thrombectomy with up to 3 passes of the SOLITAIRE™ FR stent retriever. Rapid procedure start is emphasized, within 90 minutes after penumbral imaging.

OUTCOME MEASURE(S): The primary endpoint is degree of global disability at 90 days, assessed via the modified Rankin Scale performed by certified raters blinded to treatment assignment. Secondary clinical endpoints are all-cause mortality, functional independence (mRS 0-2) at 90 days, early neurologic deficit improvement (NIHSS change at 24h); secondary technical efficacy endpoints include revascularization/reperfusion at 24h, and infarct volume at 24h.

ANALYSIS: The primary analysis will assess the difference in the distribution of modified Rankin Scale scores between treated and placebo groups (shift analysis).

TRIAL SITES: 60 centers in the United States (40) and internationally.

TRIAL STATUS: First patient enrollment is expected in Q4 2012.

Author Disclosure Block:  J.L. Saver: Research Grant; Modest; Covidien. Consultant/Advisory Board; Significant; Covidien. E. Levy: Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest;
Covidien. **H. Diener:** Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest; Covidien. **V. Pereira:** Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest; Covidien. **M. Goyal:** Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest; Covidien. **R. Jahan:** Research Grant; Modest; Covidien. Consultant/Advisory Board; Modest; Covidien.
Presentation Number: CT P10

Trial Abbreviation: ESCAPE

Trial Contact Information: Phone: 1-403-944-8065 FAX: 1-403-270-2283 Co-coordinator: Karla J.Ryckborst
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Trial Name: Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times

Trial Registry Number ID: Pending

Trial Sponsor: Covidien

Trial Web Site: unavailable

Publishing Title: Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing Ct to Recanalization Times (E S C A P E)

Author Block: Jamsheed A Desai, Sachin Mishra, Mohammed A Almekhlafi, Karla J Ryckborst, Muneer Eesa, Bijoy Menon, Andrew Demchuk, Mayank Goyal, 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. There is nevertheless, strong evidence that endovascular therapy can result in faster, more complete recanalization and that this should result in better stroke outcomes. Patients with a small core of infarct but a significant clinical deficit do benefit from reperfusion even at late time windows.

Objective: The primary objectives are 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 of this study are to demonstrate the safety and feasibility of achieving rapid endovascular revascularization in this population of patients (<90 min CT-recanalization; <120 min ESCAPE-center door to recanalization).

Design: A Phase3, randomized, open-label with blinded outcome evaluation, controlled design.

Population Studied: The study will test the hypothesis that patients undergoing endovascular revascularization will show a 20% absolute risk benefit (RR = 1.5 relative benefit) over patients receiving clinical routine care. The assumed rate of good outcome in the control arm is 40% and 60% in the treatment arm. With 85% power and no interim analyses for efficacy, the sample size consists of 242 evaluable patients (141 in each group). Sample size is inflated to 250 for crossovers, loss to follow-up etc.

Inclusion criteria:
1. Acute ischemic stroke,
2. Age >18,
3. Last seen well to randomization time <12hours,
4. NIHSS>5,
5. Pre-enrollment Barthel index(BI)>90,
6. 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; and
7. Endovascular treatment intended to be initiated (groin puncture) within 60 minutes of CT/CTA with target CTA to first recanalization of 90 minutes.
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. Chronic intracranial occlusions,
3. Baseline venous weighted CTA reveals insufficient collaterals in the symptomatic MCA territory using MIP images and compared to the contralateral side,
4. Inadequate endovascular access
5. Suspected intracranial dissection causing stroke,
6. Pregnancy,
7. Severe or fatal comorbid illness, and
8. Subject cannot complete follow

Intervention: All patients will receive routine guideline-based best medical care (including IV-tPA as appropriate in a 4.5h window). Control arm subjects will receive best medical care. Intervention/experimental arm subjects will additionally receive endovascular thrombectomy or thrombolysis.

Outcome measures: Primary efficacy outcomes are NIHSS score 0-2 OR mRS 0-2 at 90 days. Secondary outcomes include: mRS shift analysis, mortality at 90 days, EuroQOL, Trails A&B, BI ≥ 90, BI shift analysis, Economic (cost-effectiveness) analysis and Qualitative evaluation of the waiver/deferral of consent process

Analysis: The primary analysis will be an intention to treat analysis and will use a generalized linear mixed model comparing the proportions of patients in each treatment group that achieve the primary outcome while adjusting for the variables used in the minimum sufficient balance algorithm

Abstract Body:

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. It is desirable to develop strategies to enhance the effectiveness of rehabilitative therapy on motor recovery particularly in the early phase after stroke, as the speed of recovery is fastest at this early stage.

Objectives:
1. To determine whether tDCS application will improve motor recovery of the upper extremity 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 and have moderate to severe hand weakness but are able to activate their wrist flexors are included within 5-15 days of the stroke onset. We added a separate subgroup of patients with no hand movement. 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 18-80 years old.

Intervention:
TDCS is a noninvasive form of cortical stimulation that uses a battery-powered device. Weak current (1mA) is 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 (WMFT), Jebsen-Taylor Test (JTT), Motor Activity log (Uswatte, Taub et al. 2005), Medical Research Council Scale (MRC), Modified Ashworth-Spasticity scale (ASS), Abilhand scale (AHS), Barthel Index (BI), NIH stroke scale (NIHSS).

Analysis:
Two way analysis of variance (ANOVA) involving two factors: treatment group (tDCS or Sham) and stratum (uFM over or less than 30).

Trial Status: Total 52 subjects have been enrolled so far. (37 acute stroke patients and 15 volunteers for the imaging component of the study)

Author Disclosure Block:  **T.M. Hodics**: Research Grant; Significant; NIH/NICHD K23 grant. **A.W. Dromerick**: None. **B. Xu**: None. **J. Pezzullo**: Consultant/Advisory Board; Modest; Consultant for NIH grant. **B. Upreti**: Employment; Significant; NIH/NICHD grant. **J. Hidler**: None. **J. Hart**: None. **K. Kowalske**: None. **L.G. Cohen**: None.
Background and Objective:
The ATACH-I pilot trial effectively showed that an early reduction of the systolic blood pressure (SBP) is not only feasible but also safe in patients with ICH. We now have initiated a multi-center, randomized Phase III trial, the ATACH II Trial, to definitively determine the efficacy of early and intensive reduction of the SBP using intravenous (IV) Nicardipine initiated within 4.5 hours of symptoms onset in subjects with spontaneous supratentorial ICH.

Design:
The ATACH II trial is a multi-center, randomized, concurrently-controlled, parallel-arm, Phase III trial, where eligible subjects are randomized to intense SBP reduction (SBP ≤ 140 mm Hg) and standard SBP (SBP ≤ 180 mm Hg) treatment in a 1:1 ratio. The study is currently being conducted at more than 50 sites in the United States, China, Japan, Taiwan and South Korea. To be included in the study, subjects must present with a primary supratentorial ICH and receive treatment with IV Nicardipine within 4.5 hours from the onset of symptoms. In order to be considered, the initial SBP value for subjects who have not received any IV antihypertensive agent must be greater than 180 mmHg at the time of presentation. For subjects who received an IV antihypertensive agent at the time of presentation, BP must remained > 140 mmHg before randomization. The goal for the standard BP reduction group is to reduce and maintain SBP < 180 mm Hg until 24 h from randomization. The goal for the intensive BP reduction group is to reduce and maintain SBP < 140 mm Hg for 24 h from randomization. The primary BP reduction agent for this trial is Nicardipine hydrochloride. Post-discharge follow-up is conducted at 30 days (±7 days) by telephone to assess the mRS. The second follow-up consists in an in-person visit at 90 days (±14 days) to assess the mRS and quality of life using Euro-QOL.

Population and trial status: actively enrolling since January 2011; as of November 7, 2012, 101 subjects of the target 1,280 have been enrolled.

Outcome Measure: Death or disability (defined by mRS of 4 to 6) at 90 days from randomization. The primary hypothesis is that intensive SBP reduction reduces the likelihood of death or disability at Day 90 by absolute 10% (or relative 17%) or greater compared with standard SBP reduction.

Analysis: The primary efficacy outcome is analyzed using the generalized linear model with log link function adjusting for age, baseline GCS, and presence/absence of IVH. It is tested at the two-sided alpha level of 0.05.

PI Affiliations: University of Minnesota; Medical University of South Carolina

Trial Sponsor: National Institute of Neurological Disorders and Stroke (NINDS)
Author Disclosure Block:  A.I. Qureshi: Employment; Modest; University of Minnesota. Research Grant; Significant; NIH (ATACH)-II. 1R01NS062091-01A2. Y.Y. Palesch: None. A. Investigators: None.
Presentation Number: CT P13

Trial Abbreviation: EXTEND-IA

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

Trial Registry Number ID: NCT01492725

Trial Sponsor: National Stroke Research Institute Australia


Publishing Title: EXTEND-IA: A Randomised Controlled Trial of Intra-Arterial Reperfusion Therapy After IV t-PA Within 4.5hr of Stroke Onset Utilizing Dual Target Imaging Selection

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

Abstract Body:

Background: The proven benefits of tPA within 4.5 hours of ischemic 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.

Aim: EXTEND-IA will test the hypothesis that dual target vessel occlusion and penumbral mismatch can be used to select patients with favourable response to reperfusion using mechanical clot retrieval after standard IV tPA &lt4.5hrs from stroke onset.

Methods: EXTEND-IA is a prospective randomized open-label, blinded-endpoint (PROBE) phase 2 trial of mechanical clot retrieval (Solitaire FR device) after standard 0.9mg/kg IV tPA vs tPA alone in patients with ischemic stroke &lt4.5 hours from onset. Criteria for entry into the trial include vessel occlusion of the internal carotid artery (ICA) or or middle cerebral artery (MCA M1 or M2 segment) and CT or MR “mismatch” using a perfusion threshold of Tmax&gt 6sec, a perfusion:infarct core lesion volume ratio of &gt1.2 and an absolute mismatch volume &gt10mL. Infarct core volume, assessed using MR-DWI or CT-relative cerebral blood flow, must be &lt70mL. This will be assessed using a fully automated software package (RAPID, Stanford University) installed at each center. An interim analysis after 60 patients will determine the final sample size which will be between 100-150 patients. The co-primary endpoint is reperfusion at 24 hours 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).

Progress: Recruitment has commenced at 7 centers in Australia and New Zealand with a further 8 sites planned.

Conclusions: EXTEND-IA will provide much needed randomized evidence about the effectiveness of clot retrieval in a responder population defined by CT or MR mismatch.

**Presentation Number:** CT P14

**Trial Abbreviation:** EVREST Multicenter

**Trial Contact Information:** Avon Saldanha, saldanhaA@smh.ca 416-864-6060 x 7879

**Trial Email:** saldanhaA@smh.ca

**Trial Name:** Efficacy of Virtual Reality using Wii Gaming Technology in Stroke rehabilitation: a Multicentre randomized clinical trial (EVREST MULTICENTRE)

**Trial Registry Number ID:** NCT01406912

**Trial Sponsor:** Heart and Stroke Foundation of Canada, Ontario Stroke Network and Ontario Ministry of Health

**Trial Web Site:** [http://clinicaltrials.gov/ct2/show/NCT01406912](http://clinicaltrials.gov/ct2/show/NCT01406912)

**Publishing Title:** Efficacy of Virtual Reality Using Wii Gaming Technology in Stroke Rehabilitation: A Multicentre Randomized Clinical Trial (EVREST Multicentre)

**Author Block:** Gustavo Saposnik, St Michael's Hosp, Dept of Health Policy, Management and Evaluation, Univ of Toronto, Toronto, ON, Canada; Robert Teasell, Univ of Western Ontario, London, ON, Canada; Muhammad Mamdani, Avon Saldanha, Applied Health Res Ctr, Li Ka Shing Knowledge Inst, Toronto, ON, Canada; James Salhas, McMaster Univ, Hamilton, ON, Canada; Kevin Thorpe, Dalla Lana Sch of Public Health, Toronto, ON, Canada; Andreas Laupacis, St Michael's Hosp, Dept of Health Policy, Management and Evaluation, Univ of Toronto, Toronto, ON, Canada; William McIlroy, Univ of Waterloo, Waterloo, ON, Canada; Mindy Levin, McGill Univ, Montreal, QC, Canada; Leonardo Cohen, NINDS, Natl Inst of Health (NIH), Bethesda, WA; Mark Bayley, Toronto Rehabilitation, Toronto, ON, Canada; on behalf of EVREST Multicenter Investigators; for the Stroke Outcomes Research Canada (SORCan) Working Group

**Abstract Body:**

**Background:** Traditional stroke rehabilitation has several limitations. Novel interventions are needed. Virtual reality (VR) applies relevant concepts in rehabilitation showing benefits in motor function improvement after stroke.

**Design:** EVREST is a randomized multi-centre clinical trial with an active control and blinded outcome assessment.

**Hypothesis:** VR provides an effective strategy to intensify treatment and promote motor recovery after stroke.
relative to traditional rehabilitation.

**Objective:** To examine the efficacy of VR technology using the Nintendo Wii© gaming system (VRWii), as compared to recreational activity (RA), in the promotion of functional recovery of the upper extremity post stroke.

**Research Question:** 1) Does VR added to traditional rehabilitation therapy; improve motor function in patients with a recent ischemic stroke (i.e. within 3 months), relative to RA? Secondary Research Questions: 2) Does VR Wii gaming technology help improve quality of life relative to RA?; 4) How does the motor improvement pattern compare between the VRWii and RA groups?

**Eligibility criteria:** age 18-85 years, mild to moderate ischemic stroke (as determined by the Chedoke-McMaster scale ≥3) within 90 days.

**Intervention:** Participants will be randomized to receive an intensive program consisting of 10 sessions of either Wii gaming technology, or recreational activities (matching cards, dominoes, and playing 'jenga'), 60 minutes each, over a 2-week (14±3 days) period. All patients will also receive usual care (e.g. physiotherapy, occupational therapy).

**Sample size:** 140 patients (70 allocated to each arm) recruited from 7 rehabilitation facilities.

**Primary outcome:** Difference in motor function performance as measured by the time taken to complete a number of relevant tasks, as per the widely used Wolf Motor Function Test.

**Secondary efficacy outcomes** include a 4-point improvement on the box & block test, and quality of life as measured by the Stroke Impact Scale, at the end of intervention and 4 weeks post-intervention.

**ClinicalTrials.gov Identifier:** NCT01406912

**Author Disclosure Block:** G. Saposnik: Research Grant; Significant; This study is funded by Heart and Stroke Foundation of Canada (HSFC), the Ontario Stroke Network and the Ontario Ministry of Health. R. Teasell: None. M. Mamdani: None. A. Saldanha: None. J. Salhas: None. K. Thorpe: None. A. Laupacis: None. W. McIlroy: None. M. Levin: None. L. Cohen: None. M. Bayley: 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 plus antiplatelet medical management vs. antiplatelet medical management alone. Patients will be followed for 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 at least 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, Canada, Denmark, Finland, Sweden, Norway, and the United Kingdom with no per-site subject limit.

Author Disclosure Block: S.E. Kasner: Research Grant; Significant; WL Gore Assoc (PI for REDUCE trial).
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 aim to achieve high data quality with ≥90% data completion targets for primary outcomes, and most secondary outcomes ≥90% with cognitive and mood tests ≥80%.

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: Medically stable patients within 24 hours of stroke. Excluded: patients with severe pre-morbid disability and co-morbidities. Early rehabilitation is delivered by nurses and physical therapists, commences within 24 hours and continues for a maximum of 14 days. Control group patients receive standard care. Primary outcome: modified Rankin Scale at 3 months. Secondary outcomes: Barthel, Rivermead, Days to Walking (DTW), Irritability, Depression and Anxiety (IDA), Assessment of Quality of Life (AQoL), Montreal Cognitive Assessment (MoCA) and costs. Sample size is 2104 patients (n=1052 per group). Analyses will be intention to treat.

Trial status: 53 hospitals are participating in Australia, New Zealand, Malaysia, Singapore and the United Kingdom. At 31 October 2012, 26,558 patients have been screened, 4153 were eligible, with 1430 patients recruited. Recruited patients: mean age: 72.5 (SD14.0) years; male: 62.5%; first stroke: 81.7%; rtPA: 21.6%. Stroke severity: 54.4%, mild, 30.9% moderate, 14.7% severe. Oxfordshire stroke classification: TACI 21.9%, PACI 30.6%, POCI, 10.1%, LACI, 25.0%, hemorrhagic 12.4%. Past medical history: Hypertension 67.1%; smoking 53.2%; high cholesterol 40.7%, diabetes 22.2%; atrial fibrillation 21.2%, angina 81.1%, peripheral vascular disease 4.1%. 1334 patients have completed 3 month follow up with 5 drop outs (0.4%). Secondary outcome completion rates are 99.6% mRS, 99.3% Barthel, 98.8% Rivermead, 99.9% DTW, IDA, 98.5%, 92.0% AQoL, 84.9% MoCA (n=1018) and 99.5% costs.

Discussion: Recruited patients are broadly representative of stroke demographics of recruiting countries. We are not recruiting hemorrhagic stroke patients in Asia. The trial data quality is high and is exceeding data completion targets for all outcomes. The Data Monitoring Committee has met 9 times and no safety issues have been identified. We aim to complete recruitment in December 2014.


Trial Sponsors: National Health & Medical Research Council (Australia) Project Grant, Singapore Health, Northern Ireland Chest Heart Stroke, Chest Heart Stroke Scotland, The Stroke Association UK.

Author Disclosure Block: J. Bernhardt: None. T. Cumming: None.
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 the total number of treatment hours for upper extremity rehabilitation, determining whether a program based on best practice and evidence-based interventions is superior to current care is imperative. Task-oriented training programs are rapidly being 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 task-specific 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 there is a difference in arm and hand recovery one year after randomization between those who participate in a structured training program termed Accelerated Skill Acquisition Program (ASAP), and those who participate in usual and customary therapy of an equivalent dose (DEUCC), as measured by the Wolf Motor Function Test (WMFT) time score. Two secondary objectives are to compare ASAP to a true (active monitoring only) usual and customary (UCC) therapy group and to compare DEUCC and UCC.

Design: ICARE is a parallel group, three arm, single blind, Phase III, superiority, randomized, controlled trial of ASAP, a theoretically-defensible, principle-based upper extremity training program that integrates three essential elements: skill, capacity, and motivation. Study related treatments are provided in the out-patient setting initiated between 14 days and 106 days after stroke. 360 adults are being randomized at sites in Atlanta, Los Angeles and Washington, D.C. Once discharged from an inpatient or home-based care setting and following baseline assessment, participants are randomized to one of three outpatient intervention groups: ASAP, DEUCC or UCC. A stratified block randomization schema is used for each site to balance randomization assignment by motor severity and time from stroke onset. To prevent unintended crossover, details of the ASAP protocol are currently embargoed; therapists who provide ASAP sign a confidentiality and nondisclosure agreement and do not provide UCC or DEUCC treatments. There are four time points in ICARE: baseline, completion of treatment, and 6 month and 1-year after randomization. The Wolf Motor Function Test (WMFT) time score at one year is
the primary outcome. The Stroke Impact Scale (SIS) and the SIS hand domain subscale are secondary outcome measures. The design includes concealed allocation during recruitment, screening and baseline, blinded outcome assessment and intention to treat analyses.

Analysis: Our primary hypothesis is that the improvement in log-transformed WMFT time will be greater for the ASAP than the DEUCC group. This pre-planned hypothesis will be tested at a significance level of 0.05. For the secondary outcome measure, the success rate of the SIS hand domain will be calculated as the percent of subjects in the ASAP and DEUCC groups that achieved a 25-point increase in normalized SIS hand function at 1-year post randomization compared to baseline.

Trial Status: Actively enrolling; 92% of sample enrolled to date.

Author Disclosure Block:  C.J. Winstein: Research Grant; Significant; NIH, NIDRR. S.L. Wolf: Research Grant; Significant; NIH. A. Dromerick: Research Grant; Significant; NIH, VA, DoD. S. Blanton: Research Grant; Significant; NIH. M.A. Nelsen: Research Grant; Significant; NIH. C.J. Lane: Research Grant; Significant; NIH. R. Leuthwaite: Research Grant; Significant; NIH. C. Scott: Research Grant; Significant; NIH. A. Reiss: Research Grant; Significant; NIH. S. Cen: Research Grant; Significant; NIH. R. Holley: Research Grant; Significant; NIH. S. Janis: None. S. Azen: Research Grant; Significant; NIH.
**Presentation Number:** CT P18

**Trial Abbreviation:** TEMPO-1

**Trial Contact Information:** Dr. Michael Hill, hillmd@ucalgary.ca  ph:01 403 944 8065

**Trial Email:** tempo1@ucalgary.ca

**Trial Name:** TNK-tPA evaluation for minor stroke with proven occlusion

**Trial Registry Number ID:** NCT01654445

**Trial Sponsor:** University of Calgary

**Trial Web Site:** www.clinicaltrials.gov

**Publishing Title:** Thrombolysis for Minor Ischemic Stroke With Proven Acute Symptomatic Occlusion Using Tnk-tpa (Tempo-1)

**Author Block:** Jennifer L Mandzia, Shelagh B Coutts, Carol Kenney, Michael D Hill, Univ of Calgary, Calgary, AB, Canada

**Abstract Body:**

**Background:** Minor stroke and TIA are associated with a significant risk of early major stroke and this is particularly true if there is an identified major vessel occlusion. Among such patients 10-30% have intracranial occlusions on acute CT angiography or perfusion abnormalities on CTP implying an intracranial occlusion. TNK-tPA (TNKase) compared to alteplase is easier to administer, has a longer half life, higher fibrin specificity, and a possible lower rate of intracranial hemorrhage. Therefore it may be an ideal thrombolytic agent in this patient population.

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

**Results:** The coordinating center will be at the Hotchkiss Brain Institute, Department of Clinical Neurosciences, University of Calgary. Enrollment started in Calgary in July 2012. 6 Canadian centers will be recruited to enroll patients. Two patients have so far been enrolled. A formal DSMB will be convened to review safety after any serious adverse event and cumulatively after 10 and 25 patients have been enrolled. Assuming safety of this approach can be demonstrated in both dose tiers, we will then pick the higher of the two doses and proceed with a randomized trial in this population. Such a trial would need to be run internationally and would require approximately 500 patients to show a 10% treatment effect size.

**Co-PIs:** Drs. Shelagh B. Coutts, Michael D. Hill. Department of Clinical Neurosciences, University of Calgary, Alberta Health Services, Hotchkiss Brain Institute, Calgary Stroke Program. Coordinator: Carol Kenney, Carol.Kenney@albertahealthservices.ca, tel:403-944-4286. Sponsor: University of Calgary. Email: tempo1@ucalgary.ca; www.clinicaltrials.gov

The study is funded by the Heart & Stroke Foundation Alberta, Alberta Innovates Health Solutions. [NCT01654445]

**Author Disclosure Block:** J.L. Mandzia: None. S.B. Coutts: Other Research Support; Significant; Hoffmann-La Roche Canada Ltd.. C. Kenney: None. M.D. Hill: Other Research Support; Significant; Hoffmann-La Roche Canada Ltd.
**Abstract Body:**

**Background:** Over one third of ischemic strokes occur in the posterior circulation, a leading cause of which is vertebrobasilar occlusive disease secondary to atherosclerosis. Symptomatic vertebrobasilar disease (VBD) carries a high annual 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, and the 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 consideration of intervention. Preliminary studies suggest that the risk of stroke in VBD is strongly related to the extent to which intracranial blood flow is compromised.

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

**Design:** VERiTAS is a 5 year multicenter, prospective, observational cohort study, with a recruitment goal of 80 patients.

**Population Studied:** The target population is patients with symptomatic VBD. Inclusion criteria: stroke or transient ischemic attack (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 the ability to return for follow-up assessment; limited life expectancy; known cardiac disease associated with cardioembolic risk (e.g. atrial fibrillation and prosthetic valves); blood dyscrasias; non-atherosclerotic vertebrobasilar disease (e.g. dissection); unilateral vertebral stenosis or occlusion; inability to undergo MRI or cerebral angiography.

**Study Procedures:** Patients will undergo 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 to identify recurrent ischemic events will be performed 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 of the primary endpoint will consist of time-to-event comparison using the log-rank test between patients designated as 'low flow' versus 'normal flow' based upon the enrollment MR imaging.
**Trial status:** The study is open for enrollment at 6 sites (UIC, UCLA, Washington University, Columbia, Mercy, UHN-Toronto Western Hospital). As of November 1, 2012, 77 subjects have been enrolled.

**PI/Coordinator name:** Sepideh Amin-Hanjani, MD

**PI/Coordinator Affiliation(s):** University of Illinois at Chicago

**Trial Sponsor:** NIH/NINDS

**Trial Email:** lfinnell@uic.edu

**Trial web site:** http://veritas.neur.uic.edu

**Author Disclosure Information:**

- **Trial Name:** Vertebrobasilar Flow Evaluation and Risk of Transient Ischemic Attack and Stroke
- **Trial Abbreviation:** VERITAS Study
- **Trial Registry Number or 10:** NCT00590980
- **PI/Coordinator Name(s):** Sepideh Amin-Hanjani, MD
- **PI/Coord. Affiliation(s):** University of Illinois at Chicago
- **Trial Sponsor(s):** NINDS
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- **Trial Web Site:** http://veritas.neur.uic.edu

**Author Disclosure Block:**

- **S. Amin-Hanjani:** Research Grant; Significant; NIH/NINDS. Other Research Support; Modest; GE Healthcare, VasSol, Inc.
- **K. Thulborn:** Ownership Interest; Significant; Thulborn Associates, Inc. (owner).
- **D. Pandey:** None.
- **D. Richardson:** None.
- **M.S. Elkind:** None.
- **G.J. Zipfel:** Research Grant; Significant; NIH. Other Research Support; Modest; American Health Assistance Foundation, McDonnell Center Systems Neuroscience and Washington University Institute of Clinical and Translational Sciences.
- **D.S. Liebeskind:** None.
- **F. Silver:** None.
- **J. Kramer:** None.
- **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, W.L. Gore and Associates.
- **P.B. Gorelick:** Other Research Support; Significant; Lundbeck, Inc.
- **F.T. Charbel:** Ownership Interest; Significant; VasSol, Inc.
**Presentation Number:** CT P20

**Trial Abbreviation:** SUSTAIN (Systematic Use of STroke Averting INterventions)

**Trial Contact Information:** Monica Ayala-Rivera, MMAyala@mednet.ucla.edu

**Trial Email:** N/A

**Trial Name:** Randomized, Controlled Trial of an Intervention to Enable Stroke Survivors Throughout the Los Angeles County Safety Net to “Stay With the Guidelines”

**Trial Registry Number ID:** NCT00861081

**Trial Sponsor:** UCLA AHA-PRT SPINA Outcomes Research Center

**Trial Web Site:** N/A

**Publishing Title:** Randomized, Controlled Trial of an Intervention to Enable Stroke Survivors Throughout the Los Angeles County Safety Net to “Stay With the Guidelines”

**Author Block:** Nerses Sanossian, LAC+USC Medical Ctr, Los Angeles, CA; Eric M Cheng, William Cunningham, David Geffen Sch of Med at UCLA, Los Angeles, CA; Amytis Towfighi, Rancho Los Amigos Rehabilitation Ctr, Los Angeles, CA; Robert J Bryg, Olive View-UCLA Medical Ctr, Sylmar, CA; Tom L Anderson, Harbor-UCLA Medical Ctr, Torrance, CA; Jeffery J. Guterman, Olive View-UCLA Medical Ctr, Sylmar, CA; Sandra G Gross-Schulman, Los Angeles County Dept of Health Services, Los Angeles, CA; Sylvia Beanes, American Heart Association, Los Angeles, CA; Andrea S Jones, Healthy African American Families, Los Angeles, CA; Lillie Hudson, Rancho Los Amigos Rehabilitation Ctr, Los Angeles, CA; Monica Ayala-Rivera, Stefanie Vassar, Barbara G Vickrey, David Geffen Sch of Med at UCLA, Los Angeles, CA

**Abstract Body:**

**Title:**
Randomized, Controlled Trial of an Intervention to Enable Stroke Survivors Throughout the Los Angeles County Safety Net to “Stay With the Guidelines”

**Trial Abbreviation:**
SUSTAIN (Systematic Use of STroke Averting INterventions)

**Registry Trial Number:** NCT00861081

**Background:**
Better control of risk factors, especially hypertension, could substantially decrease the incidence of stroke. Effective stroke prevention care is lacking, especially among minority populations.

**Objective:**
To determine whether a chronic care model-based care intervention called SUSTAIN (Systematic Use of Stroke Averting Interventions) reduces the risk of stroke in a county system serving a predominantly minority population, and if so, at what cost.

**Design:**
Randomized-controlled trial.

**Population Studied:**
Patients who have developed a new ischemic stroke or TIA within the past 6 months and possess a systolic blood pressure greater than 120 mm Hg. An inclusion criteria is that subjects expect to obtain health care within the Los Angeles county health care system in the following year.

**Interventions:**
Subjects randomized to the intervention arm will be managed by a care manager - nurse practitioner or physician assistant - following protocols jointly developed by the research team, physicians working in the county system, and directors of community resource programs (see Figure). Subjects are scheduled for three group clinics and two individual clinics. Subjects also receive telephone calls between face-to-face visits to further coordinate their care. Subjects are trained to use self-management tools, including report cards and
home blood pressure monitors. The care managers use database systems that provide decision support and track tasks for each subject. The care managers have clinical privileges to adjust medications relevant to risk factor control. Subjects randomized to the control arm receive a pamphlet on controlling stroke risk factors.

Outcomes Measurements: The primary outcome is control of systolic blood pressure. Secondary outcomes include control of other risk factors, stroke knowledge, and adoption of healthy lifestyle habits and medication adherence.

Analysis:
An intention-to-treat analysis will be used to determine whether persons randomized to the intervention arm achieve better outcomes than persons randomized to the control arm at 12 months after randomization. Further analyses will determine whether variables such as socioeconomic status, stroke severity, medication adherence are predictive of outcomes. In order to perform a cost analysis, direct costs will be calculated with the start-up costs and maintenance costs, including clinic room charges, materials, telephone costs, and intervention care management. Utilization costs will also be calculated using a query of county administrative database.

Trial Status: Enrollment of 410 study participants was completed in August 2012. Follow up data collection will continue through August 2013.

Figure:
Design of RCT and schedule of key activities among subjects randomized to the intervention arm.

Abstract Body:

Rationale: Traditional outcome prediction models suggest that patients with severe intracerebral hemorrhage (ICH) have a high risk of death. Early do-not-resuscitate (DNR) orders and withdrawal or limitation of life sustaining treatment (LST), however, are common after ICH. Predictions of outcome from prognostic models and clinical experience are therefore confounded by the intensity of treatment provided. More data are needed about the survival and functional outcome of patients with ICH treated with full modern neurocritical care and without early limitations of LST.

Study Goal: To compare the 30-day mortality and 90-day functional outcome of patients with severe ICH and without early DNR orders to the predicted outcome based on a published ICH prognostic model.

Eligibility and Design: This is an observational study ongoing at 4 centers (University of Michigan, San Francisco General Hospital, University of Washington, and Providence Sacred Heart Medical Center) where the standard care pattern is to avoid early DNR orders or limitations of LST for ICH. Eligibility criteria include: 1) Age ≥ 18 years; 2) Spontaneous ICH; 3) Initial GCS of ≤ 12; and 4) No plans for DNR orders or withdrawal of LST in the first 5 days of hospitalization. Patients with pre-existing DNR orders or clear prior wishes to refuse aggressive treatment for severe illness are excluded.

The patient’s legally authorized representative is approached to consent for observational data collection only if they have already agreed to a plan of full supportive treatment as part of regular clinical care. No specific treatments are mandated by the study, and the patient or family may request a DNR order or withdrawal of LST at any time. Data on ICH characteristics and inpatient treatment patterns are collected. Patients are contacted at 30 and 90 days to determine vital status and functional outcome (modified Rankin Scale). The predicted probability of death at 30 days for each patient will be calculated based on the ICH Score, and the average predicted mortality for the cohort will be compared to the observed mortality. For the analysis of functional outcome, the observed proportion of cases with severe disability at 90 days (modified Rankin Scale of 5) will be compared to the proportion predicted from prior ICH outcome studies. Pre-defined criteria for a positive study are a 15% absolute reduction in predicted mortality with a less than 10% increase in the proportion of cases with severe disability. A pre-planned interim analysis performed at 61 patients suggested the study should continue, though the planned sample size was increased per the study protocol to 110 patients (from 105) based on the predicted mortality of the enrolled cohort.

Enrollment Progress: As of October 2012, 81 patients have been enrolled at the 4 centers. Any centers wishing to participate should contact Dr. Morgenstern at LMorgens@umich.edu.

Future Directions: This study will provide information on the outcome of severe ICH patients treated without early DNR orders or withdrawal of LST. If there is a reduction in mortality without an increase in severe
disability, future educational intervention studies designed to reduce use of early treatment limitations after ICH should follow.

**Author Disclosure Block:**  
D. Zahuranec: Research Grant; Significant; NIH Grant K23AG038731. J. Hemphill: None. K.J. Becker: None. M.C. Geraghty: None. B.N. Sanchez: None. L.B. Morgenstern: None.
Abstract Body: Background: Many acute ischemic stroke patients are not eligible for intravenous (IV) alteplase or rt-PA therapy because the time of stroke onset cannot be determined or the patient is outside the treatment time window on initial presentation based on last known well (LKW) time. FLAIR signal intensity changes become conspicuous at subacute time points (> 3h) while DWI changes are evident within minutes of ischemia onset. Our goal is to determine if DWI in conjunction with normal FLAIR MRI can be used as a surrogate “witness” when no human witness of stroke onset is available, to safely decide whether to administer IV rt-PA in acute stroke patients who would otherwise not qualify for standard IV rt-PA therapy based on LKW. If our study is successful, we can potentially expand the use of lytics to a stroke patient population for whom little acute intervention is currently offered.

Objectives:
(1) To determine the safety of IV alteplase therapy in subjects with unwitnessed stroke onset with LKW time greater than 3 h, who otherwise would meet thrombolysis therapy guidelines, and exhibit MRI evidence consistent with early stroke.
(2) To validate novel MRI profiles to improve the sensitivity while maintaining high specificity for detecting subjects with stroke duration less than or equal to 3.5 h.
(3) To explore imaging surrogates of clinical efficacy in subjects with unwitnessed stroke onset who are treated with thrombolysis

Design
MR WITNESS is an open-label, single-arm, multi-center Phase IIa safety study of IV alteplase in MRI-selected ischemic stroke subjects with unwitnessed stroke onsets. We propose to extend IV rt-PA treatment to a sub-population of these patients (see Study Population), whose admission MRI, most importantly, would classify them as being an early stage stroke. The algorithm is as follows: FLAIR negative or SIR<1.15, where SIR represents the signal intensity ratio (SIR) of FLAIR signal intensity in lesion region of interest to normal contralateral tissue.

Study Population: Eighty adult subjects 18-85 years of age with acute ischemic stroke who arrive between 4.5 h and 24 h since LKW and be able to receive rt-PA within 4.5 h of symptom discovery. 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.

Procedures: Non-research baseline MRI and 24h post-treatment non-contrast CT. Research MRI will be obtained post-drug infusion and at 30 days. NIHSS scores will be recorded at baseline, post-drug, and prior to...
24 h CT. At 5-days or discharge and at 30 days, NIH SS, Barthel Index (BI), and modified Rankin Scale (mRS) scores will be obtained. At 90 day, mRS and BI will be obtained.

**Outcome Measures:** The primary outcome for this study is safety as evidenced by no significant increase in symptomatic intracranial hemorrhage (SICH) rates at 24 hours using ECASS 2 definition. SICH rates and all serious adverse events (SAE) are monitored by an Independent Medical Monitor and Data and Safety Monitoring Board (DSMB). Only subjects who receive rt-PA are included in the safety analysis. For secondary safety outcomes, other SAE are monitored, such as symptomatic edema or mortality, to investigate whether our rates are significantly higher than those reported by ECASS 3. For secondary outcomes, we will also examine rates of early reperfusion and lesion growth in alteplase treated patients when evaluating for potential benefit.

**Trial Status:** We have undergone our first DSMB review and the DSMB recommended that the study continue without modification. 12 patients have been enrolled to date. Recruiting centers consist of Massachusetts General Hospital, NIH/ NINDS Washington Hospital Center & Suburban Hospital, Washington University in St. Louis. Cedar Sinai Medical Center is expected to begin recruiting by January 1, 2013. 3 additional sites are anticipated to join the trial before end of 2013.

**Author Disclosure Block:** O. Wu: Research Grant; Significant; P50NS051343, R01NS059775, R01NS063925. L.L. Latour: None. S.S. Song: None. K.L. Furie: Research Grant; Significant; P50NS051343. S. Warach: None. L.H. Schwamm: Research Grant; Significant; P50NS051343. Consultant/Advisory Board; Significant; Lifeimage.
Presentation Number: CT P24

Trial Abbreviation: CREST

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Trial Email: brottgt@umdnj.edu

Trial Name: Carotid Revascularization Endarterectomy versus Stenting Trial (CREST): Long Term Follow-up

Trial Registry Number ID: U01 NS038384

Trial Sponsor: NINDS/NIH

Trial Web Site: www.cresttrial.org

Publishing Title: Carotid Revascularization Endarterectomy versus Stenting Trial (CREST): Retention, Data Quality and Productivity in Long Term Follow-up

Author Block: Alice Sheffet, Susan E Hughes, MeeLee Tom, UMDNJ Medical Sch, Newark, NJ; Ariane Mackey, CHA Hop de L'Enfant-Jesus, Quebec, QC, ON, Canada; William Brooks, Central Baptist Hosp, Lexington, KY; Wayne Clark, Oregon Health Science Univ, Portland, OR; Michael D Hill, Univ of Calgary, Calgary, AB, Canada; Vito Mantese, Mercy Hosp St. Louis, St. Louis, MO; Jenifer H Voeks, Medical Univ of South Carolina, Charleston, SC; Mary E Longbottom, Thomas G Brott, for the CREST Investigators, Mayo Clinic Florida, Jacksonville, FL

Abstract Body:

BACKGROUND: NINDS approved CREST follow-up through 2016 for assessment of the longer-term effectiveness of CAS versus CEA. Retention of an aging population (mean age 74.1) at 107 clinical sites in a study for ten years is an increasing challenge.

OBJECTIVE: To extend CREST follow-up (up to ten years) to evaluate the long term clinical and anatomic durability of CAS versus CEA (as assessed by ipsilateral stroke and recurrent stenosis > 50%).

DESIGN: CREST (ClinicalTrials.gov NCT00004732) is an NINDS-funded, randomized, two-arm, multicenter trial with blinded endpoint adjudication. Extended follow-up of CREST CAS and CEA subjects includes annual visits and midpoint telephone visits (maximum 10 years follow-up; average 7.5 years).

POPULATION: Active post-procedure symptomatic and asymptomatic CREST subjects (n=2000) re-consented for up to 10 years of follow-up.

OUTCOMES: The primary aim is to assess CEA versus CAS in the prevention of ipsilateral stroke. Secondary aims will 1) assess if there are effect modifiers of the long-term durability of the two procedures, such as age, sex, pre-procedural degree of stenosis and symptomatic status, 2) assess if there is a temporal change or pattern in the relative efficacy of the two procedures, 3) assess differences between groups in the rates of restenosis or revascularization, 4) link Medicare-eligible CREST participants with inpatient and outpatient CMS data files to assess patient outcomes and utilization of healthcare services.

ANALYSIS: Statistical analysis of the primary aim (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 PROGRESS: Among CREST's accomplishments are 1) retention of participants in long term follow-up 2) improvement of data quality and compliance and 3) publication of trial results. Currently CREST retains 73% of surviving randomized participants at 107 U.S. and Canadian sites who have signed contracts through 2016. There are 1554 subjects actively followed; 727 have granted permission for linkage to CMS data files for study endpoint data. Sites retaining the most active subjects are CHA Hopital de L'Enfant Jesus, Quebec City, QC, Canada; Central Baptist Hospital, Lexington, KY; Oregon Health Science University, Portland, OR; University of Calgary, Calgary, AB, Canada; and Mercy Hospital St. Louis, St. Louis,
New ongoing Retention and Dashboard Reports have resulted in improved visit compliance and data quality: visits completed increased to 85.3%, ultrasounds to 86.1% and TIA Stroke forms to 94.1%; 35 sites have exceeded the mean in all five dashboard compliance categories.


Continuing CREST follow-up will assess the clinical and anatomical durability of CAS and CEA in symptomatic and asymptomatic subjects for the longest period in any carotid trial.

Trial Name: Psychosocial/Behavioral Intervention in Post-Stroke Depression

Trial Abbreviation: PSD2

Background: Post-stroke depression (PSD) affects almost one-third of stroke survivors and can have long-term adverse affects on physical and psychosocial function and recovery. A brief psychosocial/problem-solving treatment has previously been shown to be very effective in reducing PSD in ischemic stroke survivors. It was additionally found that certain serotonin transporter (SERT) gene polymorphisms may predict the response to the intervention.

Objectives: 1) To test the effectiveness of a shortened version of a psychosocial/behavioral intervention delivered in-person or by telephone compared to usual care in ischemic and hemorrhagic stroke survivors in terms of PSD response and outcome; and 2) To explore the role of genetic polymorphisms of SERT and brain-derived neurotrophic factor on treatment response and outcome. Antidepressant therapy will be recommended to patients in all three arms as standard of care.

Design: The study is a RCT with three arms (in-person intervention, telephone intervention, usual care) using a computerized adaptive randomization program to balance the arms in respect to age, gender, stroke subtype, stroke severity, and depression severity. Participants provide a saliva sample for genetic testing.

Population Studied: Individuals aged 21 or older with ischemic or hemorrhagic stroke who are clinically depressed (Geriatric Depression Scale score greater than 10) and within four months of an index stroke. Exclusions: significant receptive or global aphasia, reduced level of consciousness, current substance abuse, or major psychiatric co-morbidity. Target sample size is 225 (75 in each group).

Intervention: The 6 session intervention is delivered by telephone or in-person by psychosocial nurse practitioners and focuses on identifying and incorporating pleasant events into daily activity, and on problem-solving and reframing events. Family members or significant others may participate but are not required to do so.

Outcome Measures: The primary outcomes are percent reduction in depressive symptoms as measured using the Hamilton Depression Rating Scale (HDRS) and percent in remission (HDRS less than 10) at 8 weeks following enrollment and at 12 months post-stroke. Secondary outcomes include limitation in ability (Barthel Index, Stroke Impact Scale [SIS]), limitation in participation (SIS), and overall stroke impact (SIS). Outcomes measures for participating family or significant other include the Geriatric Depression Scale and Bakas Caregiver Outcomes Scale.

Analysis: Regression analysis will be used to test the null hypothesis that percent in remission at one year post-stroke is the same in all three groups, controlling for baseline HDRS score. Analysis of covariance will be used to test the outcome of percent reduction in HDRS score. Randomization group differences in limitation in ability and participation, and overall stroke impact will be evaluated using repeated measures analysis of
variance. Further analyses will explore subgroups for whom the psychosocial treatment has the greatest benefit and test if there is a differential response by gender, major or minor depression, severity of stroke, and level of social support, as well as a significant interaction effect of the genetic polymorphisms. **Trial Status:** Enrolment is currently at one-quarter of the target enrolment (n = 59). The planned study end date is 10/31/2014.

**Author Disclosure Block:**  
**C.J. Kirkness:** Research Grant; Significant; Grant funding for trial being reported.  
**K.J. Becker:** Research Grant; Significant; Grant funding for trial being reported.  
**D.L. Tirschwell:** Research Grant; Significant; Grant funding for trial being reported.  
**R.C. Veith:** Research Grant; Modest; Grant funding for trial being reported.  
**R. Kohen:** Research Grant; Modest; Grant funding for trial being reported.  
**L. Teri:** Research Grant; Modest; Grant funding for trial being reported.  
**K.C. Cain:** Research Grant; Significant; Grant funding for trial being reported.  
**A. Buzaitis:** Research Grant; Significant; Grant funding for trial being reported.  
**P.L. Weisman:** Research Grant; Significant; Grant funding for trial being reported.  
**S.M. McKenzie:** Research Grant; Significant; Grant funding for trial being reported.  
**P.H. Mitchell:** Research Grant; Significant; Grant funding for trial being reported.
Presentation Number: CT P27

Trial Abbreviation: PROTECT DC

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Trial Name: Preventing Recurrence of Thromboembolic Events through Coordinated Treatments in the District of Columbia

Trial Registry Number ID: NCT00703274

Trial Sponsor: NINDS U54 057405

Trial Web Site: http://clinicaltrials.gov/ct2/show/NCT00703274?term=protect+dc&rank=1

Publishing Title: A Phase II RCT of Stroke Navigators to Improve Compliance with Secondary Stroke Prevention: PROTECT DC

Author Block: Alexander W Dromerick, Georgetown Univ Sch of Med/Natl Rehabilitation Hosp, Washington, DC; M Christopher Gibbons, Johns Hopkins Sch of Med, Baltimore, MD; Dorothy F Edwards, Univ of Wisconsin, Madison, WI; Deeonna Farr, Univ of South Carolina, Columbia, SC; Annapurni Jayam-Trouth, Howard Univ Sch of Med, Washington, DC; Nawar M Shara, Georgetown Univ/Medstar Health Res Inst, Washington, DC; Brisa M Sanchez, Jeffrey J Wing, Univ of Michigan, Ann Arbor, MI; Stephen Fernandez, Medstar Health Res Inst, Hyattsville, MD; Regina Coles, Georgetown Univ, Washington, DC; Deirdra Tiffany, Natl Rehabilitation Hosp, Washington, DC; Bruce Ovbiagele, Medical Univ of South Carolina, Charleston, SC; Chelsea S Kidwell, Georgetown Univ, Washington, DC

Abstract Body:

Trial Abbreviation: PROTECT DC
Trial Registry Number: NCT00703274
Background: Despite significant advances in the prevention and treatment of cerebrovascular disease, stroke remains the fourth leading cause of death and a leading cause of adult disability. The initiation of effective secondary prevention strategies is most effective when implemented early (before disabling stroke occurs), monitored frequently, and maintained long-term after a cerebrovascular event. PROTECT DC facilitates the initiation of secondary prevention behaviors in an attempt to prevent the recurrence of stroke among participants. The program trains a lay person, called a stroke navigator, to provide participants with education on secondary prevention behavior and to navigate the health and human service system, which will assist participants in obtaining the necessary services and programs to engage in secondary prevention behaviors.

Population
1. Age ≥ 18 years
2. Hospitalized due to ischemic stroke or intercurrent ischemic stroke event within the past 30 days
3. Large vessel, small vessel, or cryptogenic with stroke risk factor etiologies as defined by TOAST criteria
4. Community dwelling prior to stroke
5. Resides within the District of Columbia or closely in its suburbs
6. Expected to reside after hospital discharge within the District of Columbia or closely in its suburbs
7. Caregiver or interested party available, if moderately or severely disabled (not required to actually reside with participant)
8. Sufficient number of collateral contacts to assure follow-up.
9. NIHSS <20
Objective: To determine whether stroke navigators can improve compliance with secondary stroke prevention measures in an urban underserved population with atherogenic ischemic stroke.
Design: Phase II, single-blind, randomized controlled trial
Interventions:
Experimental: Stroke navigation for a one year period.
Control: Usual and customary care for one year
Outcome Measures:
Primary: Composite score of compliance with objective measures of risk factor control (e.g. systolic blood pressure, HbA1c, LDL, INR, antithrombotic pill count) at one year after stroke onset.
Secondary: Stroke knowledge, exercise, dietary modification, smoking cessation at one year.
Analysis: Intention to treat
Trial status: Enrollment completed, with 116 randomized to the experimental condition and 114 randomized to the control condition. Thus far, 187 participants have completed the primary 1-year time point. Mean age of the enrolled participants is 62 years (SD=12, range 29 - 90), 87% are African-American, 49% are male and the median NIHSS score is 2 (range 0 - 20).

**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 stroke (subtype analysis according to the TOAST classification) or hemorrhagic stroke, cardiovascular events including myocardial infarction, all the cerebrovascular and cardiovascular events, death of stroke, vascular events, and all causes, hospital admission, activity of daily living, modified Rankin Scale, dementia and cognitive impairment.

**Statistical Analysis:** We conducted an interim analysis in 2011. Based on the results, the independent data monitoring committee decided to continue this study. 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 4.4 years at September, 2012). Mean age 66.2 years; 25.4% atherothrombotic infarction, 64.2% lacunar infarction. The latest status including substudies (e.g. J-STARS Echo, hsCRP and Genomics) will be presented at the conference.
Presentation Number: CT P29

Trial Abbreviation: ENOS

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Trial Email: enos@nottingham.ac.uk

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

Author Block: Kailash Krishnan, Sally Utton, Sharon Ellender, Tanya Payne, Aimee Houlton, Philip M Bath, Univ of Nottingham, Nottingham, United Kingdom

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, a multimodal molecule given as glyceryl trinitrate (GTN), is safe and effective in improving outcome after acute stroke. Furthermore, around half of all patients admitted with acute stroke are taking antihypertensive therapy immediately prior to the stroke. No data exist as to whether it is beneficial or safe to stop or continue this treatment during the acute phase.

Design: ENOS is a prospective, international, multicentre, randomised, parallel-group, blinded, controlled trial. 3,500 - 5,000 ischaemic or haemorrhagic stroke patients with systolic BP 140-220 mmHg, and within 48 hours of onset will be included. Subjects will be randomised to 7 days of single-blind treatment with transdermal GTN or control. Those patients taking prior antihypertensive therapy will also be randomised to continue or temporarily stop this for 7 days. ENOS is conducted over a secure internet site. The primary outcome is modified Rankin Scale at 90 days which is carried out by a blinded assessor. The analysis will be by intention to treat.

Trial status: As at 1st November, 2012, 3398 patients had been recruited from 162 centres (Australia, Canada, China, Denmark, Egypt, Georgia, Hong Kong, India, Italy, Malaysia, New Zealand, Norway, Philippines, Poland, Republic of Ireland, Romania, Singapore, Spain, Sri Lanka, Sweden and UK).

Contact information: http://www.enos.ac.uk , E-mail: enos@nottingham.ac.uk Telephone: +44 (0)115 823 1770

Background: Controversy exists over the optimal dose (0.6 vs 0.9 mg/kg) of i.v. rtPA and level of BP in acute ischaemic stroke. Asian studies suggest low dose rtPA is efficacious, while hypertension (>140 mmHg systolic) ‘before’ and ‘after’ rtPA predicts poor outcomes.

Aims: ENCHANTED will assess in rtPA-eligible patients whether: (i) 0.6 mg/kg rtPA is non-inferior and lowers the risk of major intracerebral haemorrhage (ICH) compared to 0.9 mg/kg rtPA; and (ii) early intensive BP lowering (target systolic 140-150 mmHg) provides superior benefits and lower ICH risk compared to BP guideline recommendations (systolic <180-185 mmHg).

Methods: An independent, quasi-factorial, active-comparative, prospective, randomised, open blinded endpoint (PROBE) trial evaluating [a] ‘rtPA dose’ and/or [b] ‘BP control’ with central internet randomisation in patients fulfilling local criteria for rtPA and uncertainty over study treatments. The study is being conducted across an expanding global network (140+ sites) to achieve the required of sample size (5000; 3300 per treatment arm; >90% power) to detect study objectives. The study is funded by the Australian government (NHMRC project grant 1020462) and the UK Stroke Association.

Results: Following study in March, 205 patients have been randomised from 30 active sites at early November 2012. Roll-out of ethics applications continues in the UK, Europe, Australia-Asia and South America.

Conclusions: Low-dose rtPA and early intensive BP lowering could provide more affordable and safer thrombolysis treatment of ischaemic stroke worldwide.
**Presentation Number:** CT P31

**Trial Abbreviation:** INTERACT2

**Trial Contact Information:** canderson@georgeinstitute.org.au

**Trial Email:** interact@georgeinstitute.org.au

**Trial Name:** INTEnsive blood pressure Reduction in Acute Cerebral haemorrhage Trial

**Trial Registry Number ID:** NCT00716079

**Trial Sponsor:** NHMRC of Australia

**Trial Web Site:** www.interact2.org

**Publishing Title:** Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT2): Recruitment Complete

**Author Block:** Craig Anderson, George Inst Intl Hlth, Sydney NSW, Australia; Yining Huang, Dept of Neurology, Peking Univ First Hosp, Beijing, China; Jiguang Wang, Ctr for Epidemiological Studies and Clinical Trials, Rui Jin Hosp, Shanghai Jiaotong Univ, Shanghai, China; Emma Heeley, Hisatomi Arima, Candice Delcourt, Richard Lindley, George Inst Intl Hlth, Sydney NSW, Australia; Mark Parsons, Dept of Neurology, John Hunter Hosp, Newcastle NSW, Australia; Christian Stapf, Dept of Neurology, Lariboisière Hosp, Paris, France; Pablo Lavados, Dept of Neurology, Clinica Alemana, Santiago, Chile; Tom Robinson, Dept of Cardiovascular Sciences, Univ of Leicester, Leicester, United Kingdom; John Chalmers, George Inst Intl Hlth, Sydney NSW, Australia

**Abstract Body:** Background: INTERACT2 is an open, randomised, blind end-point, multicentre clinical trial to establish the effectiveness of early intensive blood pressure (BP) lowering treatment in acute intracerebral haemorrhage (ICH), the most serious and least treatable form of stroke. Methods: A total of 2800 ICH patients with elevated systolic BP (150-220 mmHg) and capacity to receive intensive BP lowering treatment <6 hours of onset are required to be included from ~140 sites worldwide. Simple electronic data collection procedures are used and patients are centrally randomly assigned to intensive (target systolic <140 mmHg) or conservative (target systolic <180 mmHg) BP management using routine intravenous agents. Vital status and disability is assessed at 28 and 90 days. CT digital images are analysed centrally and there is central and site monitoring of data quality. The trial is registered (ACTRN1260800036239, NCT00716079, ISRCTN73916115).

Results: The study completed recruitment of 2839 patients from 144 sites worldwide at 31 August 2012. Blinded data indicates adequate BP separation between randomised groups and primary 90-day event rates as expected. Close-out of sites will be complete in December 2012. Joint publication/presentation of the main results is planned for ESC in London 2013.

Conclusions: INTERACT2 is on schedule to achieve its goals and provide definitive evidence for any beneficial effects of early, more intensive, blood pressure control in ICH.

**Presentation Number:** CT P32

**Trial Abbreviation:** ALISAH II

**Trial Contact Information:** Jose I Suarez, MD, e-mail: jisuarez@bcm.edu  phone: 713-798-8472

**Trial Email:** jisuarez@bcm.edu

**Trial Name:** The Albumin In Subarachnoid Hemorrhage (ALISAH) II Study

**Trial Registry Number ID:** Pending at the time of abstract submission

**Trial Sponsor:** NINDS (resubmission underway); BAXTER (study drug supply); IND approval from FDA (BB-IND #13022)

**Trial Web Site:** Under construction

**Publishing Title:** The Albumin in Subarachnoid Hemorrhage (ALISAH) II Study

**Author Block:** Jose I Suarez, Baylor Coll of Med, Houston, TX; Renee H Martin, Medical Univ of South Carolina, Charleston, SC; Eusebia Calvillo, Baylor Coll of Med, Houston, TX; The ALISAH II Study Investigators

**Abstract Body:**

Background: 25% Human Albumin (ALB) has been associated with better clinical outcomes and decreased costs in patients with subarachnoid hemorrhage (SAH). In addition the NINDS-funded Phase I ALISAH study studied several doses of ALB prospectively for safety and treatment effects. ALISAH showed that doses up to 1.25 g/kg/d x 7 days were well tolerated and patients achieved excellent clinical outcome. Further prospective studies are needed to confirm this finding. Objective: To determine the futility of 2 dosages of ALB (0.9375 and 1.25 g/kg/d x 7 days) compared to placebo. ALISAH II focuses on a futility analysis and the selection of the appropriate dose to carry forward to Phase III testing. Design: ALISAH II is a prospective, multi-center, Phase II clinical trial. Subjects will be randomized in a blinded fashion in a 2:2:1 ratio to receive one of two active study drugs or a saline placebo for 7 days. Population Studied: Adult patients with aneurysmal SAH will be enrolled. Subjects will be included within 72 hours of symptoms onset and after ruptured aneurysms have been treated. Subjects with known history of decompensated heart failure or left-ventricular ejection fractions < 40% will be excluded. The total sample size required is 250 subjects with SAH. Interventions: ALB 0.9375 or 1.25 g/kg/day or saline placebo (equivolume) for 7 days. All interventions will be specially packaged and administered blindly as a continuous infusion over 6 hours daily. Outcome measures: Primary Outcome Measure: proportion of poor outcome as defined by the Glasgow Outcome Scale (GOS ≤ 2) at 3 months after treatment. Secondary Outcome Measures: mRs, BI, MOCA, and EUROQOL at 3 months, and frequency of cardiopulmonary complications up to 48 hours after study drug infusion. Analysis: The futility of each albumin dose will be determined independently. The futility analysis [Ravina B., Palesch Y. The phase II futility clinical trial design. Progress in Neurotherapeutics and Neuropsycharmacology. 2007;2:1,27-38] will be conducted with level of significance (the probability that an effective intervention will be called ineffective, or futile) set at 0.10. The primary null hypothesis is that the intervention (albumin) reduces the proportion of patients with poor outcome compared to the hypothesized poor outcome rate of 0.357, by a clinically meaningful threshold of at least 0.10. Specifically, the futility hypothesis specifies that if the proportion of albumin-treated subjects with poor outcome is greater than 0.257 (H₀: p>0.257), it might be futile to move albumin forward to phase III testing. The test for futility (H₀: p>0.257) requires 100 albumin-treated subjects, based on a one sample test of binomial proportions to detect an absolute difference of 0.10, when compared to a pre-specified threshold value of 0.357, with one-sided level of significance 0.10 and power 0.80. The pre-specified threshold value is based on the assumed control proportion (0.357) and a clinically meaningful decrease in the proportion of subjects with a poor outcome (0.10). The control proportion of 0.357 is based on the estimated poor outcome(GOS ≥ 2 at 90 days) proportion from the IHAST trial [Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med.* 2005; 352: 135-145; Macdonald RL, Higashida RT, Keller Emanuela, et al. Clasozentan, an endothelin receptor antagonist, in
patients with aneurysmal subarachnoid haemorrhage undergoing surgical clipping: (CONSCIOUS-2) a randomised, double-blind, placebo-controlled Phase 3 clinical trial. *Lancet Neurol* 2011;10:618-25]. Trial Status: We are currently finalizing site recruitment and are preparing resubmission to NINDS for final review and funding approval.

**Author Disclosure Block:** J.I. Suarez: None. R.H. Martin: None. E. Calvillo: None.
**Presentation Number:** CT P33

**Trial Abbreviation:** MAESTRO

**Trial Contact Information:** Kyung-Yul Lee, kylee@yuhs.ac fax: 822-3462-5904, phone: 822-2019-3325

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**Trial Name:** Comparison of Triflusal and Clopidogrel Effect in Secondary Prevention of Stroke Based on the Cytochrome P450 2C19 Genotyping

**Trial Registry Number ID:** NCT01174693

**Trial Sponsor:** Gangnam Severance Hospital

**Trial Web Site:** none

**Publishing Title:** Comparison of Triflusal and Clopidogrel Effect in Secondary Prevention of Stroke Based on the Cytochrome P450 2C19 Genotyping (MAESTRO), A Prospective Randomised Phase IV Clinical Trial

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**Abstract Body: **Background: Clopidogrel is widely used in the patients with ischemic stroke and cardiovascular disease. Clopidogrel need to be converted into active metabolite by the cytochrome P450 enzymes. Among the various cytochrome P450 enzymes, cytochrome P450 2C19 polymorphism is reported to relate to antplatelet activity of clopidogrel. In coronary artery disease, patients with poor or intermediate metabolizer of cytochrome P450 2C19 had more risk of major cardiovascular event including stroke than extensive metabolizer. However, the role of cytochrome P450 2C19 genotype in the cerebrovascular disease is not defined yet. Objective: To determine triflusal prevents recurrent stroke and cardiovascular event in comparison with clopidogrel in the patients with poor or intermediate metabolizer of cytochrome P450 2C19. Design: Prospective, randomized, open-label, multicenter phase IV clinical trial. Population studied: Patients with acute ischemic stroke within 30 days of stroke onset, 20 years of age or older, and classified to non-cardiogenic etiology according to the TOAST classification are enrolled. The study plans to enroll 640 patients with poor or intermediate metabolizer to prove superiority of triflusal over clopidogrel. Assume that 59% of Koreans are estimated to be poor or intermediate metabolizer, estimated total number of patient is 1080. Intervention(s): Subject is randomized to the group receiving clopidogrel 75mg/day or triflusal 600mg/day. Subjects are evaluated 2 weeks and then every 3 months after randomization until the end of study. Outcome Measure(s): The primary outcome for this study is recurrent stroke in the patients with genotype of poor or intermediate metabolizer. The secondary outcomes are composite cardiovascular events, myocardial infarction or coronary revascularization, and ischemic stroke in patients with poor or intermediate metabolizer. Same primary outcome and secondary outcomes are used in the analysis of subgroup. Analysis: Primary outcome will be analyzed by using the log-rank test between patients with poor or intermediate metabolizer dichotomized receiving triflusal or clopidogrel. Second outcome will be analyzed by using the log-rank test also. All analyses of the outcomes are conducted under the intention-to-treat principle. Trial Status: This study started in March 2010. The study is open for enrollment at 18 sites in Korea. As of October 2012, 762 subjects have been enrolled. Funding: This study is supported by Myung In Pharmaceutical Company, Republic of Korea.

**Author Disclosure Block:** K. Seo: None. K. Lee: None. S. Han: None. Y. Kim: None. S. Ahn: None. W. Seo: None.
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 600 patients. The main phase will assess the efficacy of intensive treatment in a further 2,800 patients over 8 years in total. 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 53 patients to date.
**Objective:** To evaluate the safety and tolerability of dalfampridine extended release tablets (D-ER; prolonged-release fampridine in Europe) 10 mg twice daily administered to patients with chronic stroke deficits, and to perform an exploratory assessment on sensorimotor function.

**Background:** Ischemic stroke is a major cause of sensorimotor deficits leading to persistent disability, which could be moderate to severe in up to 45% of survivors. Dalfampridine improved neurobehavioral measures in rats when initiated between 4-8 weeks after middle cerebral artery occlusion, suggesting that dalfampridine may improve sensorimotor function in patients after stroke. D-ER is used to improve walking in patients with multiple sclerosis.

**Design:** The study design is a multi-center, 8-week, double-blind, placebo-controlled, 2-period crossover. The study scheme is 2-week screening, 2-week treatment (Period-1), 1-week placebo washout and crossover, 2-week treatment (Period-2), and 1-week follow-up; 3 assessment visits per period. Patients (18-85 years) with a history of ischemic stroke ≥6 months prior to enrollment and experiencing stable sensorimotor deficits, with a lower extremity Fugl-Meyer Assessment (FMA) score ≤27 and able to complete the Timed 25-foot walk (T25FW), are eligible. Those with moderate or severe renal impairment, history of non-febrile seizures, or prior dalfampridine use will be excluded. Sixty-six patients are planned to be enrolled. Safety and tolerability will be assessed by reviewing adverse events, physical examinations, vital signs, and laboratory results. Exploratory clinical measures will include intra-subject and between treatment group assessment of walking speed (T25FW), manual dexterity (Box and Block tests), hand strength (grip and pinch tests), motor and sensory function (FMA), activities of daily living (functional independence measure scale), clinician global impression and subject global impression scales.

**Conclusions:** Currently, there is no approved therapy for the management of chronic sensorimotor deficits after stroke. This study will test whether treatment with D-ER is tolerable and improves neurological function in patients after stroke. Supported by Acorda Therapeutics, Inc.
Consultant/Advisory Board; Significant; NeurogeX, Astellas, Eli Lilly, Pfizer, Merz, Ipsen, Acorda Therapeutics, Inc., Depomed, Syntaxin, Viromed, Allergan. **M. Reding:** Research Grant; Significant; Acorda Therapeutics, Inc.. Consultant/Advisory Board; Significant; Acorda Therapeutics, Inc.. Other; Significant; American Society of Neurorehabilitation.
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**Trial Abbreviation:** HeadPoST pilot

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**Trial Name:** Head Position in Stroke Trial (HeadPoST) pilot phase

**Trial Registry Number ID:** NCT01706094

**Trial Sponsor:** None

**Trial Web Site:** None

**Publishing Title:** Head Position in Stroke Trial (HeadPoST) Pilot Phase

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**Abstract Body:**

Background: Several lines of investigation indicate there to be potential beneficial effects of interventions that augment cerebral blood flow (CBF) to irrigate the ischemic penumbra in acute ischemic stroke. The simplest manner to do this is to place the patient in a ‘flat down’ rather than upright head position. However, any potential benefits on the brain may be offset by an increased hazard of aspiration pneumonia or exacerbation of cardiac failure in vulnerable patients. Given uncertainty over the balance of potential modest benefits and risks, and variability regarding the ideal head position policy for patients with acute ischemic stroke around the world, reliable randomized evidence is required to standardize clinical practice.

Aims: The main objectives of this pilot phase clinical trial are to determine the feasibility, safety and potential efficacy of a large-scale cluster randomized clinical trial to assess whether a simple nursing care policy - ‘flat down head position’ - provides beneficial effects as compared to the standard upright head position in patients with acute ischemic stroke. The main efficacy outcome of the pilot phase is demonstration of increased mean cerebral blood flow velocity (CBFV) in the flat down compared to the upright head position, as assessed by transcranial Doppler (TCD) to the medial cerebral arteries of patients with anterior circulation infarction. Secondary efficacy objectives are to demonstrate that the flat down head position improves neurological status at 7 days and disability at 90 days.

Methods: Inclusion criteria include consecutive adult patients with acute ischemic stroke within 12 hours of onset admitted to participating centers. A cluster (month) method of randomization to flat down or upright head position for 48 hours, stratified by site. The primary outcome is change in mean CBFV measured by TCD at 24 hours. Secondary outcomes include proportion of adverse events at 7 days, distribution of NIHSS at 7 days, and distribution of mRS disability scale scores at 90 days. Sample size is 16 clusters of 12 patients totaling approximately 200 patients to detect an increase of 8.3 (±17) cm/sec in average CBFV from 30° to 0° head position. This sample size will also allow detection of a 30% increase in average CBFV from baseline with 80% power at a 5% significance level.

Conclusions: The flat head position is a potential low cost, widely applicable, nursing intervention to increase cerebral blood flow and improve clinical outcomes in the acute phase of ischemic stroke.

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**Trial Abbreviation:** TARDIS

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**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](http://www.tardis.org)

**Publishing Title:** Triple Antiplatelets for Reducing Dependency After Ischaemic Stroke (TARDIS). Safety and Efficacy of Intensive vs Guideline Antiplatelet Therapy in High Risk Patients With Recent Ischaemic Stroke or Transient Ischaemic Attack: A Randomised Controlled Trial

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**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 start-up phase of the trial started in April 2009, and the main phase 1st October, 2012. As of 2nd November, 2012, 940 patients have been recruited from 58 live centres within the UK Stroke Research Network.

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**Presentation Number:** CT P38

**Trial Abbreviation:** WASSABI

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**Trial Name:** Wake Up Symptomatic Stroke in Acute Brain Ischemia

**Trial Registry Number ID:** NCT01455935

**Trial Sponsor:** Genentech Medical Education Department.

**Trial Web Site:** [http://clinicaltrials.gov/ct2/show/NCT01455935](http://clinicaltrials.gov/ct2/show/NCT01455935)

**Publishing Title:** Wake Up Symptomatic Stroke in Acute Brain Ischemia

**Author Block:** Tareq Kass-Hout, Emory, Atlanta, GA; Kenneth Snyder, Adnan Siddiqui, Elad Levy, Univ at Buffalo, Buffalo, NY

**Abstract Body:**

**TRIAL TITLE:** Wake Up Symptomatic Stroke in Acute Brain Ischemia  
**TRIAL ABBREVIATION:** WASSABI  
**TRIAL REGISTRY NUMBER:** NCT01455935  

**BACKGROUND:** Acute stroke is the fourth leading cause of mortality and the major cause of long-term disability in the developed world. Approximately 25% of ischemic stroke patients awaken with stroke symptoms, this subset of patients are ineligible to thrombolysis therapy simply because the time of onset is not known. Perfusion studies help to identify patients with preserved salvageable tissue that might benefit from acute intervention therapy.

**OBJECTIVE:** To study the safety and effectiveness of using CT Perfusion studies as an indicator to treat stroke patients with unknown time of onset.

**METHODS:** Single center, randomized, single blinded and prospective study to compare between medical therapy and interventions with patients with wake up stroke. Ninety patients 18-80 years of age presenting with wake up ischemic stroke and considerable salvageable tissue on perfusion studies (defined as TTP> 8 Sec and volume loss < 20% of the size of the penumbra) and a NIHSS 8-22 will be considered for enrollment. Patients will be randomized into one of three prospective groups: Best medical therapy (standard of care with anti-platelets and statins), intravenous thrombolysis (total dose of 0.9 mg/kg) or intra-arterial intervention (IA t-PA and/or MERCI device and/or PENUMBRA device). The primary end point (mRs-90 days) will be compared among the different subgroup, initially using Analysis of Variance (ANOVA) using SAS v9.1. If the ANOVA analysis provides us with statistically significant results suggesting significant difference in Binary comparisons among our groups then we will proceed with Binary comparisons between the groups using the t-Student test for means comparisons. Secondary outcomes including NIHSS at 24 hours post therapy and at discharge, MRS-30 days, Thrombolysis In Myocardial Infarction (TIMI) post procedure and Thrombolysis In Cerebral Ischemia (TICI) post procedure will be compared between the three groups. Also safety measurement defined by ECASS III criteria as a symptomatic intracranial hemorrhage will be compared between the three groups.

**TRIAL STATUS:** Recruiting patients.

**TRIAL SPONSOR:** Genentech Medical Education Department.

**Author Disclosure Block:**  
**T. Kass-Hout:** None.  
**K. Snyder:** None.  
**A. Siddiqui:** None.  
**E. Levy:** None.
Study objective: The distinction between hemorrhagic and ischemic stroke has critical implications for management. For that purpose, clinical scores have been proposed to be used in areas with limited health care resources where brain computed tomographic (CT) scan is not readily available. We conducted this study to evaluate the predictive value of the Allen and Siriraj scores in the differential diagnosis of stroke subtypes.

Methods: We retrospectively collected data for 5 years on the clinical characteristics of patients with stroke in a local medical center study. For all patients, we calculated the Allen and the Siriraj scores and we assessed their accuracy in predicting stroke subtypes with receiver operating characteristics (ROC) curves.

Results: We assessed 300 patients. Of these, 70% (n=210) had ischemic stroke. The area under the ROC curve was higher for Siriraj score compared with the Allen score. Using the original cutoff points, Siriraj score has a sensitivity for the diagnosis of hemorrhage of 60% and a specificity of 95%; the corresponding values for the Allen score are 55% and 70%, respectively. The negative predictive value was higher for Siriraj score compared to the Allen score (90% versus 80%).

Conclusion: Siriraj score is a valid and useful tool for predicting stroke subtype in a clinical setting in which financial constraints make systematic brain CT scan unfeasible.

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