

Ongoing Clinical Trials Posters II

Thursday, February 12, 2015, 6:15 pm – 6:45 pm

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Presentation Number: CT P1

Trial Abbreviation: REVASCAT

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Trial Name: Randomized trial of reVascularizAtion with Solitaire® device versus best mediCal therapy in the treatment of Acute stroke due to anTerior circulation large vessel occlusion presenting within 8 hours of symptom onset

Trial Registry Number ID: NCT01692379

Trial Sponsor: Fundació ICTUS Malaltia Vascular by means of an unrestricted grant from Covidien-ev3

Trial Web Site: <http://clinicaltrials.gov/ct2/show/record/NCT01692379>

Publishing Title: Randomized Trial Of Revascularization With Solitaire® Device Versus Best Medical Therapy In The Treatment Of Acute Stroke Due To Anterior Circulation Large Vessel Occlusion Presenting Within 8 Hours Of Symptom Onset (REVASCAT)

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Abstract Body: REVASCAT is a multi-center, randomized, sequential, open, blinded-endpoint trial. Subjects presenting with 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 ineligible for IV tPA or have received it without recanalization are randomized following a 1:1 ratio to mechanical embolectomy with the CE MARK approved stentriever Solitaire or medical management alone. Randomization is done under a minimization process using age, baseline NIHSS, therapeutic window, vessel occlusion site and treating center.

The primary endpoint on the basis of intention-to-treat criteria is the modified Rankin Scale score (mRS) at 90 days. The main analysis will estimate a common odds ratio of improvement over mRS cut-points 1 to 4 by a cumulative ordinal logistic regression adjusted by minimization factors and tPA. A central blinded evaluator adjudicates this score using a video recording. Criteria for missing data imputation on mRS is done by the blinded trial steering committee. Maximum sample size is planned to be 690 patients for an estimated common odds ratio of 1.615 that corresponds to an absolute difference in treatment effect of 10%. We have designed efficacy and futility stopping rules when data are available on 174, 346 and 518 patients.

Salvageable brain is evaluated by ASPECTS score on non-contrast CT or DWI-MRI. Secondary endpoints are infarct volume evaluated on CT at 24 h by a central core-lab, dramatic early favorable response as determined by an NIHSS of 0-2 or NIHSS improvement ≥ 8 points at 24 h, vessel recanalization evaluated by CTA or MRA

at 24 h and successful recanalization in the Solitaire arm assessed by mTICI 2b or 3 on the post-procedure angiogram adjudicated by a central core-lab. Safety variables will be mortality at 90 days, symptomatic ICH rates at 24 h and procedural related complications adjudicated by an independent committee.

The trial started on November 2012 and 187 patients have been randomized by mid October 2014. The recommendation of the DSMB of either continuing or stopping the trial for treatment efficacy, safety or trial futility after the first interim analysis will be available at the time of the presentation of the abstract.

Author Disclosure Block: X. Urra: None. Á. Chamorro: None. E. Cobo: None. M. de Miquel: None. C. Molina: None. Á. Rovira: None. L. San Román: None. J. Serena: None. T.G. Jovin: None. A. Dávalos: Research Grant; Significant; Covidien, unrestricted grant for REVASCAT. Consultant/Advisory Board; Modest; Covidien.

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Presentation Number: CT P2

Trial Abbreviation: NAVIGATE ESUS

Trial Contact Information: NAVIGATEESUS@phri.ca

Trial Email: NAVIGATEESUS@phri.ca

Trial Name: New Approach rivaroxaban Inhibition of factor Xa in a Global trial vs ASA to prevent Embolism in Embolic Stroke of Undetermined Source

Trial Registry Number ID: pending

Trial Sponsor: Bayer HealthCare, Janssen Pharmaceuticals

Trial Web Site: pending

Publishing Title: NAVIGATE ESUS: A Multicenter, Randomized, Double-blind, Double-dummy, Active-comparator, Event-driven, Superiority Phase III Study Of Prevention Of Recurrent Stroke And Systemic Embolism In Patients With A Recent Embolic Stroke Of Undetermined Source (ESUS), Comparing Rivaroxaban 15 mg Once Daily With Aspirin 100 mg

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Abstract Body: Rationale: Embolic stroke of undetermined source (ESUS) has been defined as a non-lacunar infarction without proximal arterial stenosis or identified high risk source of cardioembolism. The risk of recurrent stroke in older ESUS patients is substantial. The optimal antithrombotic strategy for prevention of recurrent stroke after ESUS is unknown, but anticoagulation with a factor Xa inhibitor is hypothesized to be more efficacious than aspirin (ASA).

Objective: To determine whether rivaroxaban is superior to ASA for reducing the risk of recurrent stroke and systemic embolism after recent ESUS.

Design: Multicenter, multinational, double-blind, double-dummy, active-controlled randomized clinical trial.

Population:

- 7000 men and women, age ≥ 18 years.
- Embolic stroke of undetermined source, defined by all of the following: non-lacunar ischemic stroke visualized by neuroimaging; absence of relevant extracranial atherosclerotic stenosis $\geq 50\%$ or occlusion; no history/evidence of atrial fibrillation after at least 24 hr of cardiac monitoring; no intracardiac thrombus on echocardiography; no other specific cause of stroke identified.
- Randomization < 6 months of qualifying stroke.
- No specific contraindication to ASA or rivaroxaban.
- No indication for chronic anticoagulation or antiplatelet therapy.
- Estimated GFR ≥ 30 mL/min/1.73 m².

Intervention: Participants will be randomized 1:1 to blinded treatment with either rivaroxaban 15 mg once daily or ASA 100 mg once daily.

Primary outcome: Time to recurrent stroke or systemic embolism. All patients will be followed until 450

confirmed primary outcome events have occurred.

Secondary outcomes: Time to a composite of cardiovascular death, recurrent stroke, systemic embolism, and myocardial infarction, as well as all-cause mortality, and the individual components of the composite. The primary safety outcome is major bleeding (ISTH criteria).

Statistical analysis: The primary efficacy intention-to-treat analyses will compare rivaroxaban to ASA using an age-stratified log-rank test, and Kaplan-Meier curves will be generated.

Trial Status: Enrollment begins in late 2014/early 2015 in 26 countries at ~350 sites.

Author Disclosure Block: **S.E. Kasner:** Consultant/Advisory Board; Modest; AstraZeneca--SOCRATES National Lead Investigator, Novartis-Endpoint Adjudication Committee, Merck-Endpoint Adjudication Committee, Pfizer-Endpoint Adjudication Committee, DaiichiSankyo--Trial Design Consultant, Boehringer Ingelheim--consultant, Medtronic--DSMB, Bayer--Trial Steering Committee, Abbvie-Endpoint Adjudication Committee. Research Grant; Significant; WL Gore--PI REDUCE trial. **K. Muir:** Consultant/Advisory Board; Modest; Bayer. **R.J. Gagliardi:** Consultant/Advisory Board; Modest; Bayer. **S.F. Ameriso:** Consultant/Advisory Board; Modest; Bayer. **P.M. Lavados:** Consultant/Advisory Board; Modest; Bayer. **M. Sharma:** Consultant/Advisory Board; Modest; Bayer. **H. Mundl:** Employment; Significant; Bayer. **S.D. Berkowitz:** Employment; Significant; Bayer. **R.G. Hart:** Consultant/Advisory Board; Modest; Bayer. **S.J. Connolly:** Consultant/Advisory Board; Modest; Bayer.

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Presentation Number: CT P3

Trial Abbreviation: TOBAS

Trial Contact Information: Suzane Nolet, suzanne.nolet@crchum.qc.ca

Trial Email: Suzanne.Nolet@crchum.qc.ca

Trial Name: Treatment of Brain AVMs Study

Trial Registry Number ID: Treatment of Brain AVMs (TOBAS) Study

Trial Sponsor: none

Trial Web Site: ClinicalTrial.gov

Publishing Title: Treatment of Brain AVMs: A Randomized Controlled Trial and Registry (TOBAS)

Author Block: **Naim N Khoury**, Michel W Bojanowski, Elsa Magro, André Lima Batista, Jean-Christophe Gentric, Chiraz Chalaala, Daniel Roy, Alain Weill, Univ de Montréal, Montreal, QC, Canada; Tim E Darsaut, Univ of Alberta, Edmonton, AB, Canada; Jean Raymond, Univ de Montréal, Montreal, QC, Canada

Abstract Body: Title: Treatment of Brain AVMs Study (TOBAS): A randomized controlled trial and registry
Background: The management of AVMs remains controversial. The ARUBA trial suggested that conservative management of unruptured AVMs achieved a better 5-year outcome, but the evidence remains inconclusive. Current treatment modalities include surgical resection, endovascular embolization and radiotherapy, either alone or in combination.

Objectives: To provide a research care context for practicing treatment options that have yet to be validated as beneficial.

Methods: TOBAS is a pragmatic, prospective, randomized controlled trial and a registry. Patients with AVMs eligible to conservative and curative treatment are randomized to an observation or treatment group. Prior to randomization, treatment allocation is predetermined based on best clinical judgement in a multidisciplinary conference. A second randomized trial nested in TOBAS addresses the role of adjunct endovascular embolization prior to surgical resection or radiotherapy in patients eligible to both options (with or without embolization). Patients not eligible to randomization are offered participation in the registry. The primary outcome of the study is death from any cause or disabling stroke (mRS >2) at 10 years.

Expected results: 400 patients are needed to detect a 15% reduction (from 40 to 25%) in primary outcome events in the treatment arm, by intention-to-treat analysis. For the nested study on embolization, 440 patients are required to detect a 10% increase (from 80 to 90%) in the rate of success, defined as complete AVM eradication without disabling complications.

Trial Status: Forty patients have been recruited in one centre since May 2014. Recruitment of additional centers is undergoing.

Conclusion: TOBAS is designed to offer optimal care of AVMs in the presence of uncertainty.

Author Disclosure Block: **N.N. Khoury:** None. **M.W. Bojanowski:** None. **E. Magro:** None. **A. Lima Batista:** None. **J. Gentric:** None. **C. Chalaala:** None. **D. Roy:** None. **A. Weill:** None. **T.E. Darsaut:** None. **J. Raymond:** None.

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Presentation Number: CT P4

Trial Abbreviation: HERO

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Trial Email: jmarti@santpau.cat

Trial Name: Intracerebral Hemorrhage Due to Oral Anticoagulants: Prediction of the Risk by Magnetic Resonance

Trial Registry Number ID: NCT02238470

Trial Sponsor: Ministry of Health (Spain)

Trial Web Site: <http://heropub.pic.es/>

Publishing Title: The HERO Project: Can MR Help in Predicting the Risk of Intracranial Hemorrhage in Patients Treated with Oral Anticoagulants?

Author Block: Joan Martí-Fàbregas, Raquel Delgado-Mederos, Alejandro Martínez-Domeño, Luís Prats-Sánchez, Pol Camps-Renom, Rebeca Marín, Fidel Núñez, José Mateo, Ignasi Gich, Hosp de la Santa Creu i Sant Pau, Barcelona, Spain; Ignacio Casado-Naranjo, Hosp San Pedro de Alcántara, Cáceres, Spain; Blanca Fuentes, Hosp La Paz, Madrid, Spain; Manuel Gómez-Choco, Hosp Moisés Broggi, Sant Joan Despí, Spain; Yolanda Bravo, Hosp de Burgos, Burgos, Spain; Javier Tejada, Hosp de León, León, Spain; Juan Arenillas, Hosp de Valladolid, Valladolid, Spain; Beatriz Zandio, Hosp de Navarra, Pamplona, Spain; Maria José Torres, Hosp Son Espases, Palma de Mallorca, Spain; Ana María De Arce, Hosp de Donostia, Donostia, Spain; Aida Lago, Hosp La Fe, Valencia, Spain; David Cánovas, Parc Taulí, Sabadell, Spain

Abstract Body:

BACKGROUND

By allowing the detection and quantification of leukoaraiosis and microbleeds, Magnetic Resonance (MR) helps in the assessment of hypertensive and/or amyloid angiopathy, two underlying angiopathies that may increase the risk of Intracranial Haemorrhage associated with oral anticoagulants (ICH-OA). The acronym HERO stands for Intracranial HEmorrhage prediction with magnetic Resonance in patients receiving Oral Anticoagulants.

METHODS

Type of study: A prospective, observational, multicenter study of 1000 patients with ischemic stroke, older than 65 y, who are candidates to receive OA indefinitely (either antivitamin K or direct anticoagulants). Patients will be enrolled at >30 Spanish sites.

Exclusion criteria: Patients receiving OA prior to the index stroke, those who have absolute contraindication for OA and when there is a contraindication to perform a MR.

Primary end-point: ICH-OA (intracerebral or extracerebral).

MR: A cerebral MR scan will be obtained within 30 days of stroke onset, although the consent to participate must be obtained before the MR. The presence and severity of leukoaraiosis and microbleeds will be evaluated.

Patients will be followed-up every 3 months during 2 years with phone interviews, to evaluate the appearance of ICH-OA, adherence to treatment, major hemorrhage and ischemic stroke recurrence.

We will register data about demographics, vascular risk factors, anticoagulation, MR, echocardiography and co-morbidity. With those variables associated with ICH-OA in bivariate

analyses, we will perform a logistic regression analysis in which ICH-OA will be the dependent variable. Finally, a predictive score of ICH-OA will be created.

Patients included to date (october 2014): 654 patients from 32 participating centres.

CONCLUSION

The HERO study evaluates whether MR helps in predicting the risk of ICH-OA in patients with ischemic stroke who will receive Oral Anticoagulants (OA) for the secondary prevention of stroke. The results obtained will contribute to improve the safety of oral anticoagulation in patients with a cardiac source of embolism.

Author Disclosure Block: J. Martí-Fàbregas: None. R. Delgado-Mederos: None. A. Martínez-Domeño: None. L. Prats-Sánchez: None. P. Camps-Renom: None. R. Marín: None. F. Núñez: None. J. Mateo: None. I. Gich: None. I. Casado-Naranjo: None. B. Fuentes: None. M. Gómez-Choco: None. Y. Bravo: None. J. Tejada: None. J. Arenillas: None. B. Zandio: None. M. Torres: None. A. De Arce: None. A. Lago: None. D. Cánovas: None.

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Presentation Number: CT P5

Trial Abbreviation: ACTION

Trial Contact Information: Lahar Mehta; lahar.mehta@biogenidec.com; phone: 617-914-1909; fax: 877-284-5968

Trial Email: clinicaltrials@biogenidec.com

Trial Name: A Multicenter, Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Study to Evaluate the Safety and Efficacy of Intravenous Natalizumab (BG00002) on Reducing Infarct Volume in Acute Ischemic Stroke

Trial Registry Number ID: NCT01955707

Trial Sponsor: Biogen Idec

Trial Web Site: <http://clinicaltrials.gov/show/NCT01955707>

Publishing Title: A Multicenter, Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Study to Evaluate the Safety and Efficacy of Intravenous Natalizumab on Reducing Infarct Volume in Acute Ischemic Stroke (ACTION)

Author Block: Lahar Mehta, Biogen Idec, Cambridge, MA; Mitchell Elkind, Columbia Univ, New York, NY; Roland Veltkamp, Imperial Coll London, London, United Kingdom; Joan Montaner, Vall d'Hebron Res Inst, Barcelona, Spain; S. Claiborne Johnston, Univ of Texas, Austin, TX; Bernard Ravina, Voyager Therapeutics Inc, Cambridge, MA; Yun Chen, Jacob S Elkins, Biogen Idec, Cambridge, MA

Abstract Body: Background: Clinical and preclinical data suggest that peri-infarct inflammation can contribute to secondary injury and worsen outcome after brain ischemia. Natalizumab is a recombinant humanized monoclonal antibody that blocks interaction of $\alpha 4\beta 1$ integrin on leukocytes with vascular cell adhesion molecule-1 on endothelial cells, inhibiting transmigration of leukocytes into inflamed parenchymal tissue. Natalizumab treatment results in substantial reductions in measures of CNS inflammation in its approved indication for multiple sclerosis; a single IV infusion achieves rapid and nearly complete saturation of $\alpha 4\beta 1$ integrin that lasts approximately 3 weeks.

Objective: To determine whether in patients with acute ischemic stroke (AIS), a single dose of natalizumab given between 0 and 9 hours from when the patient was last known normal (LKN) reduces the change in infarct volume from baseline to day 5 on MRI.

Design: ACTION is a phase 2, proof-of-concept, multicenter, double-blind, placebo-controlled, randomized, parallel-group study evaluating the efficacy and safety of natalizumab over a 90-day period in patients with AIS. The study is adaptive with a blinded sample size reestimation.

Population: A total of 160 patients (80 in each time window) aged 18–85 years presenting with signs of ischemic stroke, a National Institutes of Health Stroke Score (NIHSS) ≥ 6 , and ≥ 1 acute infarct of > 2 cm (largest diameter) on baseline brain DWI will be enrolled.

Intervention: Eligible patients are randomized 1:1 to receive a single dose of 300 mg IV natalizumab or placebo. Randomization is stratified by treatment window (≤ 6 hours or > 6 to ≤ 9 hours from LKN) and baseline DWI infarct size (< 4 cm or ≥ 4 cm, largest diameter).

Outcome Measures: The primary endpoint is the change in infarct volume from baseline (DWI) to day 5 (FLAIR). Infarct volume is also measured at 24 hours (DWI) and day 30 (FLAIR). Clinical outcomes are measured by modified Rankin Scale, NIHSS, and Barthel Index at days 5, 30, and 90.

Trial Status: As of September 2014, 48 and 73 patients have been enrolled for the ≤ 6 -hour and > 6 - to ≤ 9 -hour

time windows, respectively, across 60 sites in Germany, Spain, and the United States. The sample size was reestimated per protocol. Baseline data are being analyzed.

Author Disclosure Block: **L. Mehta:** Employment; Significant; Biogen Idec. **M. Elkind:** Consultant/Advisory Board; Modest; Biogen Idec. **R. Veltkamp:** Research Grant; Significant; Bayer, Boehringer Ingelheim. Honoraria; Significant; Bayer, Biogen, Boehringer Ingelheim, Daiichi Sankyo. Consultant/Advisory Board; Significant; Bayer, Boehringer Ingelheim, BMS, Daiichi Sankyo, Morphosys. **J. Montaner:** Consultant/Advisory Board; Modest; Steering Committee and National Coordinator (Spain) of ACTION Trial. **S. Johnston:** Other Research Support; Significant; AstraZeneca. **B. Ravina:** Employment; Significant; Voyager Therapeutics Inc, Biogen Idec. Other; Significant; Equity in: Voyager Therapeutics Inc, Biogen Idec. **Y. Chen:** Employment; Modest; Employee of Biogen Idec. **J.S. Elkins:** Employment; Significant; Biogen Idec.

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Presentation Number: CT P6

Trial Abbreviation: TASTE

Trial Contact Information: Mark.parsons@hnehealth.nsw.gov.au

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Trial Name: Tenecteplase versus Alteplase for Stroke Thrombolysis Evaluation Trial

Trial Registry Number ID: ACTRN12613000243718

Trial Sponsor: National Health and Medical Research Council of Australia, Boehringer Ingelheim

Trial Web Site: <http://taste.webmistar.com/>

Publishing Title: Tenecteplase versus Alteplase for Stroke Thrombolysis Evaluation Trial

Author Block: Mark Parsons, **Andrew Bivard**, Univ of Newcastle, Newcastle, Australia; Bruce Campbell, Royal Melbourne Hosp, Melbourne, Australia; Patrick McElduff, Univ of Newcastle, Newcastle, Australia; Chih-Cheng Hsu, Institute of Population Health Sciences, Zhunan, Taiwan; Ken Butcher, Univ of Alberta, Alberta, AB, Canada; Chris Bladin, Flory Neuroscience institute, Melbourne, Australia; Richard Lindley, Univ of Sydney, Sydney, Australia; Werner Hacke, Heidelberg Univ Hosp, Heidelberg, Germany; Greg Albers, Stanford Univ, Stanford, CA; Henry Ma, Than Phan, Flory Neuroscience institute, Melbourne, Australia; Carlos Molina, Hosp Vall d'Hebron-Barcelona, Barcelona, Spain; Vincent Thijs, Univ Hosp Leuven, Leuven, Belgium; Geoffrey Donnan, Flory Neuroscience institute, Melbourne, Australia; Stephen Davis, Royal Melbourne Hosp, Melbourne, Australia; Christopher Levi, Univ of Newcastle, Newcastle, Australia

Abstract Body: In phase II studies, tenecteplase has been shown to result in more complete reperfusion. We have now begun a phase III trial compare Tenecteplase with Alteplase in acute ischemic stroke with onset <4.5 hours in patients clinically eligible for intravenous alteplase who fulfil additional imaging criteria.

Design:

Multicentre, prospective, randomised, open-label, blinded endpoint (PROBE) phase III study. Patients will be randomised 1:1 to standard dose intravenous alteplase (0.9 mg/kg) or tenecteplase (0.25 mg/kg as a single bolus). There will be two randomisation strata: first, randomisation will be stratified by the presence or absence of internal carotid artery occlusion (ICAO) on baseline CT or MR angiography; second, randomisation will be stratified by size of infarct core (above or below 25 mL) on baseline CTP or diffusion-weighted MRI (DWI). Patients with ICAO will be capped at a maximum of 25% of the sample size.

Population studied:

Patients aged ≥ 18 years presenting with acute hemispheric ischemic stroke within 4.5 hours of stroke onset who are clinically eligible for IV alteplase. Multimodal CT or MRI including perfusion imaging must be performed before randomization. Infarct core and penumbral volumes will be calculated by automated software, RAPID or MiStar.

Primary Outcome:

Modified Rankin Scale (mRS) 0-1 at 3 months (no disability).

Secondary Outcomes:

Reperfusion at 24 hours post stroke

Early clinical improvement (reduction in acute - 24 hour NIHSS score)

Modified Rankin Scale (mRS) 0-1 at 3 months (adjusted for baseline age and NIHSS)

Modified Rankin Scale 0-2 at 3 months

Categorical shift in mRS at 3 months

Infarct growth at 24 hours

Recanalisation at 24 hours post stroke.

Trial Status:

Commenced August 2015 with 6 centres now open in Australia and a further 17 sites planned to open in 2014 across Taiwan, Canada and Europe.

Author Disclosure Block: **M. Parsons:** None. **A. Bivard:** None. **B. Campbell:** None. **P. McElduff:** None. **C. Hsu:** None. **K. Butcher:** None. **C. Bladin:** None. **R. Lindley:** None. **W. Hacke:** None. **G. Albers:** None. **H. Ma:** None. **T. Phan:** None. **C. Molina:** None. **V. Thijs:** None. **G. Donnan:** None. **S. Davis:** None. **C. Levi:** None.

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Presentation Number: CT P7

Trial Abbreviation: FRONTIER

Trial Contact Information: Colleen North, NorthC@smh.ca

Trial Email: N/A

Trial Name: Field Randomization Of NA-1 Treatment By Early Responders

Trial Registry Number ID: N/A

Trial Sponsor: NoNO Inc.

Trial Web Site: N/A

Publishing Title: The FRONTIER trial: Field Randomization Of NA-1 Treatment By Early Responders

Author Block: Laurie Morrison, St. Michael's Hosp, Toronto, ON, Canada; **Michael D Hill**, Univ of Calgary, Calgary, AB, Canada; Michael Tymianski, Univ of Toronto, Toronto, ON, Canada; Paul Raftis, Garrie Wright, Gary Mcauley, Toronto Paramedic Services, Toronto, ON, Canada; Richard Verbeek, Sheldon Cheskes, Sunnybrook Ctr for Prehospital Med, Toronto, ON, Canada; Peter Dundas, Priya Kakar, Gordon Neville, Peel Regional Paramedic Services, Mississauga, ON, Canada; Jim Christenson, Univ of British Columbia, Vancouver, BC, Canada; Devin Harris, Stroke Services British Columbia, Vancouver, BC, Canada; Paul R Leslie, William Dick, British Columbia Emergency Health Services, Vancouver, BC, Canada; Richard Swartz, Sunnybrook Health Sciences Ctr Regional Stroke Ctr, Toronto, ON, Canada; Daniel Selchen, St. Michael's Hosp Regional Stroke Ctr, Toronto, ON, Canada; Leanne Casaubon, Toronto Western Hosp Regional Stroke Ctr, Toronto, ON, Canada; Manu Mehdiratta, Yael Perez, Trillium Health Partners Regional Stroke Ctr, Mississauga, ON, Canada; Oscar Benavente, Vancouver General Hosp Regional Stroke Ctr, Vancouver, BC, Canada

Abstract Body: Background

Although clinical benefit from a stroke treatment is only achievable if it is given before ischemic damage is complete, all in-hospital neuroprotection trials to date initiated treatment ≥ 4 hr from symptom onset.

FRONTIER will evaluate the PSD95 inhibitor NA-1 when initiated early in the prehospital arena before irreversible stroke damage occurs.

Methods

FRONTIER is a multicenter, randomized, double-blind, placebo-controlled study enrolling patients with suspected acute stroke by paramedics en route to the Stroke Centre within 3h of symptom onset. Subjects with symptoms of acute stroke, age 40-95, ambulatory prior to the event with Los Angeles Motor Scale score of 2-5 at the time of randomization will be enrolled. Waiver of consent for the intervention and deferred consent for continued participation will be used. Exclusions include: lack of IV access, seizure at onset, GCS < 10, recent head trauma, pregnancy or major systemic illness.

Intervention

Intravenous NA-1 2.6mg/kg or saline control over 10 minutes.

Outcomes and Sample Size

The primary outcome is the modified Rankin Score (mRS), analyzed at 90 days using the sliding dichotomy approach according to baseline LAMS. The sample size is 560 subjects, with 1:1 allocation.

Progress

FRONTIER will be conducted in 3 Canadian regions: the city of Toronto, Ontario by Toronto Paramedic Service; the Region of Peel, Ontario by Peel Regional Paramedic Services; and the city of Vancouver, B.C. by

BC Emergency Health Services. These EMS services transport all potential strokes to 5 dedicated stroke centres: Vancouver General, Sunnybrook, St Michael's, University Health Network and Trillium. Regulatory approval has been obtained from Health Canada. Paramedics in participating services are currently undergoing training in the trial protocol. First enrollment is expected in early 2015.

Funding

Frontier is funded by Brain Canada with support from the Canadian Stroke Network, the University of British Columbia Brain Research Centre and Djavad Mowafaghian Centre for Brain Health and NoNO Inc. The trial will be directed by a collaborative interdisciplinary steering committee with support from Rescu, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto.

Author Disclosure Block: **L. Morrison:** None. **M.D. Hill:** None. **M. Tymianski:** Ownership Interest; Significant; CEO of NoNO Inc.. **P. Raftis:** None. **G. Wright:** None. **G. Mcauley:** None. **R. Verbeek:** None. **S. Cheskes:** None. **P. Dundas:** None. **P. Kakar:** None. **G. Neville:** None. **J. Christenson:** None. **D. Harris:** None. **P.R. Leslie:** None. **W. Dick:** None. **R. Swartz:** None. **D. Selchen:** None. **L. Casaubon:** None. **M. Mehdiratta:** None. **Y. Perez:** None. **O. Benavente:** None.

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Presentation Number: CT P8

Trial Abbreviation: TOBC registry

Trial Contact Information: David.Carvel@stryker.com

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Trial Name: TransForm™ Occlusion Balloon Catheter Registry

Trial Registry Number ID: NCT01949779

Trial Sponsor: Stryker

Trial Web Site: none

Publishing Title: A Prospective Multi-center Registry of Transform Occlusion Balloon Catheter Use in the Treatment of Cerebral Aneurysms

Author Block: Muhammad A Taqi, Syed A Quadri, Desert Regional Medical center, Palm Springs, CA; Brian Fred Fitzsimmons, Medical Coll of Wisconsin, Milwaukee, WI; Ansaar Rai, West Virginia Univ, Morgantown, WV; Curtis Given, Central Baptist Hosp, Lexington, KY; Ciaran Powers, Ohio State Univ, Columbus, OH; Javiers Masso, Univrio Donostia, Donostia, Spain

Abstract Body: Background

Balloon-assisted coil embolization (BACE) and Stent-assisted coil embolization play a major role in the treatment of complex cerebral aneurysms. TransForm™ Occlusion Balloon Catheter (TOBC) registry is intended to evaluate safety and performance of TOBC. This is the first prospective registry trial of BACE for intracranial aneurysms.

Hypothesis

BACE using TOBC is safe and effective.

Design

TOBC registry is a prospective multicenter registry trial. Up to 15 sites will enroll up to 140 patients.

Results

Interim analysis was performed on data for 47 patients enrolled from 11/2013 to 09/ 2014. Data were from 5 sites in the U.S. and 1 site in Spain. Mean age was 57 (SD±14.84); 24.4% were males and 75.6% were females. TOBC was used for: BACE 87.5%, test occlusion 4.2%, safety 2.1%, and others (vasospasm and post-flow diverter placement) 6.2%. Most common contrast concentrations used were 70/30 (60.9%) and 50/50 (28.3%). Mean dome-to-neck ratio was 1.37 (SD±0.78).

Following are the mean scores* for balloon performance variables (1=excellent and 5=poor): visibility under fluoroscopy 1.73 (SD±0.87), ability to reach intended site 1.64 (SD±0.87), stability during first positioning 1.50 (SD±0.66), stability during inflation 1.51 (SD±0.70) and deflation 1.51 (SD±0.67), ability to temporarily stop flow 1.42 (SD±0.58), and assist in coil embolization 1.65 (SD±0.83). Mean time for balloon inflation was 4.81 seconds (SD±2.69) and deflation was 4.8 seconds (SD±3.56). Complete obliteration of the aneurysm (Raymond class I) was achieved in 69.2% cases. Thrombus formation occurred in 4/47 (8.5%) cases. Underlying hypercoagulable state from SAH was considered a contributing factor in all 4 cases; in 2 of 4 cases, operators also attributed thrombus formation to TOBC. All thrombus resolved with medication and no patients suffered infarction No vessel rupture/perforation occurred.

Conclusions

BACE using TOBC is safe and effective. The balloon catheter performed as intended and showed good-to-excellent results across all performance measures in the treatment of cerebral aneurysms. Rapid

inflation/deflation was achieved despite use of high contrast concentrations. No serious side effects occurred.

* 1= Excellent, 2=Very good, 3=Good, 4= Fair, 5=poor

Author Disclosure Block: **M.A. Taqi:** Consultant/Advisory Board; Modest; Stryker Neurovascular. **S.A. Quadri:** None. **B. Fitzsimmons:** None. **A. Rai:** Consultant/Advisory Board; Modest; Stryker Neurovascular. **C. Given:** Speakers' Bureau; Modest; Covidien. Consultant/Advisory Board; Modest; Stryker Neurovascular. **C. Powers:** None. **J. Masso:** None.

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Presentation Number: CT P10

Trial Abbreviation: PRISMS

Trial Contact Information: Darren Tayama, MD (tayama.darren@gene.com)

Trial Email: info@prismsstrokestudy.com

Trial Name: A Study of the Efficacy and Safety of Activase (Alteplase) in Patients With Mild Stroke (PRISMS)

Trial Registry Number ID: NCT02072226

Trial Sponsor: Genentech, Inc.

Trial Web Site: <http://www.prisms-stroke-study.com>

Publishing Title: THE PRISMS TRIAL: A Phase 3b, Double-blind, Multicenter Study to Evaluate the Efficacy and Safety of Alteplase in Patients With Mild Stroke: Rapidly Improving Symptoms and Minor Neurologic Deficits

Author Block: Pooja Khatri, Joseph Broderick, Univ of Cincinnati Academic Health Ctr, Cincinnati, OH; Anjan Chatterjee, Univ of Pennsylvania, Cincinnati, OH; Edward C Jauch, Medical Univ of South Carolina, Cincinnati, OH; Steven R Levine, SUNY Downstate Medical Ctr, Brooklyn, NY; Jose F Romano, Univ of Miami, Miami, FL; Jeffrey L Saver, Univ of California, Los Angeles, Los Angeles, CA; Sharon D Yeatts, Medical Univ of South Carolina, Charleston, SC; Yunming Mu, Darren Tayama, Genentech, Inc, South San Francisco, CA; PRISMS Investigators

Abstract Body: BACKGROUND: The balance of risk versus benefit of thrombolysis for acute ischemic stroke patients with mild deficits at the time of the treatment decision is uncertain.
OBJECTIVE: To determine the efficacy and safety of IV alteplase for treatment of acute ischemic stroke (AIS) in patients with mild stroke (“rapidly improving stroke symptoms” and “minor neurologic deficit”).
DESIGN: PRISMS is a double-blind, multicenter, randomized, phase 3b trial of patients with mild ischemic stroke within 3 hours of last known well time. Mild stroke is defined as a National Institutes of Health Stroke Scale (NIHSS) ≤ 5 and not “clearly disabling” (i.e., inability to return to work or perform basic activities of daily living based on current deficits). Patients meeting eligibility criteria are randomized (1:1) to receive either (1) IV alteplase 0.9 mg/kg with oral aspirin placebo or (2) IV alteplase placebo with oral aspirin 325 mg.
SAMPLE SIZE: Approximately 948 patients will be enrolled across 75 sites in North America.
PRIMARY OUTCOME MEASURE: Difference in proportion of a favorable functional outcome between the two treatment groups, defined by a modified Rankin Scale (mRS) score of 0 or 1 at day 90 post-randomization.
STATISTICAL ANALYSIS: The primary efficacy outcome will be analyzed via a Cochran-Mantel-Haenszel test, stratified by pre-treatment NIHSS score (0-2 vs 3-5), age (<65 vs ≥ 65), and last known well time to treatment (0-2 hours vs 2-3 hours).
TRIAL STATUS: As of November 5, 2014, 34 subjects were enrolled.

Author Disclosure Block: P. Khatri: Other Research Support; Modest; Biogen Inc pays my dept for my role as trial DSMB. Other Research Support; Significant; Genentech Inc pays my dept for my role as PRISMS Trial Lead PI, Penumbra Inc pays my dept for my effort as THERAPY Trial Neurology PI. J. Broderick: Research Grant; Significant; Genentech (PRISMS Steering Committee). Other Research Support; Significant; EKOS Corporation, Schering-Plough. Honoraria; Significant; Genentech. A. Chatterjee: Consultant/Advisory Board; Significant; Genentech (PRISMS Steering Committee). E.C. Jauch: Research Grant; Modest; Genentech (PRISMS Steering Committee). S.R. Levine: Research Grant; Significant; Genentech - PRISMS Steering

Committee. **J.F. Romano:** Research Grant; Significant; University of Miami for MaRISS study. Consultant/Advisory Board; Modest; Genentech (PRISMS Steering Committee). **J.L. Saver:** Other; Significant; University of California Regents. **S.D. Yeatts:** Consultant/Advisory Board; Modest; Genentech (PRISMS Steering Committee). **Y. Mu:** Employment; Significant; Genentech. **D. Tayama:** Employment; Significant; Genentech, a member of the Roche Group. Ownership Interest; Significant; Shareholder in Roche.

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Presentation Number: CT P11

Trial Abbreviation: STOP-IT Study

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

Trial Email: carrozj@uc.edu

Trial Name: The Spot Sign for Predicting & Treating ICH Growth Trial

Trial Registry Number ID: NCT00810888

Trial Sponsor: NIH / NINDS

Trial Web Site: www.STOPITSTUDY.org

Publishing Title: The Spot Sign for Predicting and Treating ICH Growth Trial

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

Abstract Body: Background:

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

Objectives:

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

Design:

STOP-IT enrolls patients presenting with acute ICH within five hours of symptom onset. The randomization arm includes subjects with acute ICH and contrast extravasation (spot sign present) on CTA. The observational arm includes subjects with acute ICH without a spot sign. Comparisons will be made: 1) between patients with a spot sign randomized to the placebo arm and patients without a spot sign, and 2) patients with a spot sign between those randomized to rFVIIa and placebo.

Population:

A total of 184 subjects with intracerebral hemorrhage are to be enrolled at ten clinical sites across the United States and Canada.

Interventions:

Eighty-four patients with a spot sign present on CTA will be randomized 1:1 to treatment with either rFVIIa (80 mcg/kg) or placebo. One hundred patients without a spot sign will be enrolled in the prospective observational arm.

Outcome Measures:

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

Trial Status:

Ten clinical sites actively recruiting: 89 subjects enrolled as of 21-Oct-2014

Principal Investigator:

Matthew Flaherty, MD-University of Cincinnati

Trial Sponsor:

NIH/NINDS

Trial Contact Information:

Janice Carrozzella, MSN, CNP, CCRA

Email: carrozj@uc.edu

Trial website: www.STOPITSTUDY.org

Author Disclosure Block: M. Flaherty on Behalf of STOP-IT Investigators: Research Grant; Significant; NIH/NINDS. Other Research Support; Significant; Novo Nordisk providing Recombinant activated factor VII.

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Presentation Number: CT P12

Trial Abbreviation: MR WITNESS

Trial Contact Information: mrwitness@partners.org

Trial Email: mrwitness@partners.org

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

Trial Registry Number ID: NCT01282242

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

Trial Web Site: <http://www.mrwitness.org>

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

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

Abstract Body: Background: Many patients are discovered with acute stroke symptoms whose onset is unwitnessed. Current FDA guidelines exclude them from intravenous (IV) alteplase or rt-PA therapy because it has been more than 3 h since the patient was last known to be well (LKW). We propose to use advanced MRI as the surrogate “witness” when no human witness is available.

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

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

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

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

Outcome Measures: The primary outcome for this study is rt-PA safety as evidenced by no significant increase in symptomatic ICH rates using ECASS 2 definition observed in the ECASS 3 trial (5.3%). Secondary safety outcome will be no significant increases in rate of symptomatic edema.

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

Trial Status: 54/80 (67.5%) subjects have been enrolled to date. Recruiting centers are Massachusetts General Hospital, NIH/NINDS Washington Hospital Center & Suburban Hospital, Washington University in St. Louis, Cedar Sinai Medical Center, UCLA Medical Center, and Seton/UT Southwestern. 5 additional sites are anticipated.

Author Disclosure Block: **O. Wu:** Research Grant; Significant; P50NS051343, R01NS059775, Genentech. Consultant/Advisory Board; Modest; Penumbra. **L.L. Latour:** None. **S.S. Song:** None. **K.L. Furie:** None. **S. Warach:** None. **L.H. Schwamm:** None.

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Presentation Number: CT P13

Trial Abbreviation: BEST MSU

Trial Contact Information: Stephanie Parker, stephanie.a.parker@uth.tmc.edu, 7135007014, 8326218411

Trial Email: stephanie.a.parker@uth.tmc.edu

Trial Name: Benefits of Mobile Stroke Unit

Trial Registry Number ID: NCT02190500

Trial Sponsor: philanthropy

Trial Web Site: n/a

Publishing Title: Stroke Treatment Delivered Using a Mobile Stroke Unit

Author Block: **Stephanie Parker**, Elizabeth Noser, Univ of Texas Medical Sch - Houston, Houston, TX; David Persse, Baylor Coll of Med, Houston, TX; James Grotta, Memorial Hermann-TMC, Houston, TX

Abstract Body: Objectives. The BEST-MSU study aims to answer 3 questions. 1. How much can a Mobile Stroke Unit (MSU) speed and increase treatment of ischemic stroke patients with tissue plasminogen activator (tPA) compared to standard management (SM)? 2. Can the doctor aboard the MSU be replaced by telemedicine (TM)? 3. What are the costs of implementing and maintaining a MSU and the health care costs of patients transported compared to SM.

Methods. The Houston MSU is staffed by a vascular neurologist (VN), registered nurse, CT technician, and paramedic and is activated following a 911 call to Emergency Medical Services (EMS) suggesting stroke symptoms, or call from an EMS first responder identifying a stroke patient, from 8 am-6 pm 7 days/week. On 50% of weeks, by blocked randomization, the MSU travels to the site of the call or rendezvous with EMS and evaluates the patient. If the patient meets inclusion criteria (symptom onset within 4.5 hours and meeting guidelines for tPA), they are enrolled into the study and moved into the MSU. If after CT scan and point of care lab testing on the MSU, the patient still fulfills criteria for tPA according to the on-site VN (the patient is simultaneously evaluated via TM with the remote VN making an independent decision), they are immediately given tPA and transported to one of 3 comprehensive stroke centers (CSC). If the patient doesn't meet tPA criteria, they are managed as per best practice for their diagnosis en route to the CSC. On the other 50% of weeks (SM weeks), the nurse meets the patient without the MSU, determines eligibility by the same criteria, but the patient transported and managed per current EMS routine. Informed consent is obtained at the CSC to obtain follow up data at 1, 3, 6 and 12 months in 248 patients to answer the 3 aims.

Results. During a 8 week lead in phase, 13 patients were treated with tPA on the MSU, 31% between 0-60 and 31% 61-80 minutes from onset, average on scene time 26 minutes, and no hemorrhagic or other complications. 11 other patients were enrolled but not treated (4 intracerebral hemorrhages, 3 seizures, 2 too mild, 2 other reasons).

Conclusion. The BEST-MSU trial has begun enrolling patients according to a randomized protocol.

Author Disclosure Block: **S. Parker:** None. **E. Noser:** None. **D. Persse:** None. **J. Grotta:** None.

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Presentation Number: CT P14

Trial Abbreviation: SHINE

Trial Contact Information: Karen C. Johnston University of Virginia email - kj4v@virginia.edu

Trial Email: kj4v@virginia.edu

Trial Name: Stroke Hyperglycemia Insulin Network Effort

Trial Registry Number ID: NCT01369069

Trial Sponsor: NIH-NINDS

Trial Web Site: www.shinetrial.com

Publishing Title: Stroke Hyperglycemia Insulin Network Effort Trial

Author Block: Amy C. Fansler, **Karen C. Johnston**, UVA, Charlottesville, VA; Christiana Hall, UT Southwestern, Dallas, TX; Askiel Bruno, Georgia Regents Univ, Augusta, GA; William G. Barsan, Univ of Michigan, Ann Arbor, MI; Kevin M. Barrett, Mayo Clinic Florida, Jacksonville, FL; Valerie L Durkalski, MUSC, Charleston, SC

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 management of hyperglycemia in acute ischemic stroke patients.

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

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

Population: Adult acute ischemic stroke patients with Type 2 diabetes mellitus and glucose >110 mg/dL or glucose of ≥ 150 mg/dL for patients without diabetes at the time of enrollment. Study participants must be enrolled within 12 hours of stroke symptom onset and are expected to be enrolled within 3 hours of hospital arrival. Study participants will be recruited from approximately 65 sites (50 Neurological Emergencies Treatment Trials (NETT) sites and 15 ancillary sites).

Sample Size: Expected to require 1400 subjects

Intervention: Study participants are randomized to intervention (IV insulin with target glucose 80-130 mg/dL) or control treatment (subcutaneous sliding scale insulin with target glucose 80-179 mg/dL). The intervention group uses the GlucoStabilizer® computerized decision support tool to guide therapy. Treatment continues 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 outcome of $\geq 7\%$. 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 58 of the approximately 65 sites. As of October 2014, 473 subjects have been enrolled.

Sponsor: NIH-NINDS U01NS069498, U01NS056975, U01NS059041

Author Disclosure Block: **A.C. Fansler:** Research Grant; Significant; NIH-NINDS U01NS069498. **K.C. Johnston:** Research Grant; Significant; NIH-NINDS U01NS069498. **C. Hall:** Research Grant; Significant; NIH-NINDS U01NS069498. **A. Bruno:** Research Grant; Significant; NIH-NINDS U01NS069498. **W.G. Barsan:** Research Grant; Significant; NIH-NINDS U01NS069498, NIH-NINDS U01 NS056975. **K.M. Barrett:** Research Grant; Significant; NIH-NINDS U01 NS069498. **V.L. Durkalski:** Research Grant; Significant; NIH-NINDS U01 NS069498, NIH-NINDS U01 NS059041.

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Presentation Number: CT P15

Trial Abbreviation: iDEF

Trial Contact Information: Magdy Selim, MD, PhD (mselim@bidmc.harvard.edu). Tel: 617-632-8913. Fax: 617-632-8920

Trial Email: mselim@bidmc.harvard.edu

Trial Name: INTRACEREBRAL HEMORRHAGE DEFEROXAMINE TRIAL

Trial Registry Number ID: NCT02175225

Trial Sponsor: NIH/NINDS

Trial Web Site: <http://clinicaltrials.gov/show/NCT02175225>

Publishing Title: Intracerebral Hemorrhage Deferoxamine (iDEF) Trial

Author Block: Magdy Selim, **Caroline Feigert**, Beth Israel Deaconess Medical Ctr, Boston, MA; Sharon Yeatts, Medical Univ of Southern Carolina, Charleston, SC; Claudia Moy, NINDS, Bethesda, MD; Aaron Perlmutter, Medical Univ of Southern Carolina, Charleston, SC; Andre Thornhill, medical Univ of Southern Carolina, charleston, NC; Catherine Dillon, Lydia Foster, Medical Univ of Southern Carolina, charleston, SC

Abstract Body: BACKGROUND: The iron chelator, Deferoxamine Mesylate (DFO), exerts diverse neuroprotective effects, reduces perihematoma edema and neuronal damage, and improves functional recovery after experimental ICH. To translate these findings into the clinical setting, we conducted a small Phase I, open-label study to determine the tolerability, safety, and maximum tolerated dose of DFO in patients with ICH, then initiated this Phase II clinical trial.

OBJECTIVES: 1) To assess whether it is futile to move DFO into Phase III evaluation as a therapeutic intervention for ICH; and 2) To assess the safety of DFO in a larger cohort of patients.

METHODS: This is a prospective, multi-center, double-blind, randomized, placebo-controlled, phase-II clinical trial. Approximately, 294 subjects with spontaneous ICH will participate in this study. Participants will be randomized to either DFO at 32 mg/kg/day (up to a maximum daily dose of 6000 mg/day), or saline placebo, given by IV infusion for 3 consecutive days. Treatment will be initiated within 24 hours after ICH symptom onset. Randomization will control baseline imbalances associated with ICH onset-to-treatment time, baseline ICH score, ICH volume, and NIHSS score, and warfarin use. All subjects will be followed for 6 months.

OUTCOME MEASURES: The primary outcome measure is the modified Rankin Scale (mRS), dichotomized to define good functional outcome as mRS score of 0-2 at 90 days. At the conclusion of the study, the proportion of DFO-treated subjects with mRS 0-2 at 3 months will be compared to the placebo proportion in a futility analysis. As secondary analyses of the primary outcome, a dichotomized analysis considering the proportion of DFO- and placebo-treated subjects with mRS 0-3 (still a desirable effect in patients with ICH) will also be performed. Similar analyses at 180 days and ordinal analysis across all mRS scores will be performed. Safety endpoints will include all DFO-related adverse events until day-7 or discharge (whichever is earlier) and serious adverse events through day-90. Mortality (all cause and ICH-related) will be assessed through day 180.

TRIAL STATUS: Enrollment in iDEF began in the fall of 2014 and is ongoing.

Author Disclosure Block: **M. Selim:** Research Grant; Significant; NIH/NINDS. **C. Feigert:** None. **S. Yeatts:** Research Grant; Modest; NIH/NINDS. Consultant/Advisory Board; Significant; Genentech. **C. Moy:** None. **A. Perlmutter:** None. **A. Thornhill:** None. **C. Dillon:** None. **L. Foster:** None.

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Presentation Number: CT P16

Trial Abbreviation: POINT

Trial Contact Information: Mary Farrant, mary.farrant@ucsfmedctr.org, 415-502-7304

Trial Email: mary.farrant@ucsfmedctr.org

Trial Name: Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial

Trial Registry Number ID: NCT00991029

Trial Sponsor: NIH/NINDS

Trial Web Site: POINTtrial.org

Publishing Title: Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial

Author Block: **Mary Farrant**, UCSF, San Francisco, CA; Clay Johnston, UT Austin, Austin, TX; J. Donald Easton, UCSF, San Francisco, CA

Abstract Body: Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial

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

Subjects are 18 years of age or older with high-risk TIA (defined as an ABCD² score \geq 4) or minor ischemic stroke (an NIHSS \leq 3); each subject is followed for 90 days from randomization. A total of 5,840 patients will be recruited and the trial will be completed in 7 years. The first subject was enrolled on May 28, 2010.

International sites joined the POINT trial in August of 2013.

Planned Number of Centers: 350; Present Number: 241

Planned Number of Subjects: 5,840; Present Number: 2,398

Sponsor: University of California, San Francisco (UCSF); National Institute of Neurological Disorders and Stroke (NINDS)

Collaborators: Neurological Emergencies Treatment Trials Network (NETT); Statistics and Data Management Center (SDMC) at Medical University of South Carolina (MUSC); POINT Clinical Research Collaboration (POINT CRC) at EMMES Corporation

Dates of Study: October 2009 - September 2016

ClinicalTrials.gov Identifier: NCT00991029;

<http://clinicaltrials.gov/ct2/show/NCT00991029?term=POINT&rank=1>

Author Disclosure Block: **M. Farrant:** None. **C. Johnston:** None. **J. Easton:** None.

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Presentation Number: CT P17

Trial Abbreviation: CP-01

Trial Contact Information: pbobbitt@cerevast.com

Trial Email: pbobbitt@cerevast.com

Trial Name: Clotbust ER

Trial Registry Number ID: NCT01098981

Trial Sponsor: Cerevast Therapeutics, Inc.

Trial Web Site: www.cerevast.com

Publishing Title: Combined Lysis of Thrombus with Ultrasound and Systemic Tissue Plasminogen Activator for Emergent Revascularization in Acute Ischemic Stroke

Author Block: **Andrei V. Alexandrov**, The Univ of Tennessee Health Science Ctr, Memphis, TN; Peter D. Schellinger, Johannes Wesling Klinikum Minden, Minden, Germany; Andrew Baretto, The Univ of Texas Medical Sch, Houston, TX; Andrew M. Demchuk, The Univ of Calgary, Calgary, AB, Canada; Lauri Soenne, Helsinki Univ Central Hosp, Helsinki, Finland; Martin Köhrmann, Neurologische Univklinik Erlangen, Erlangen, Germany; George Howard, The Univ of Alabama at Birmingham, Birmingham, AL; Carlos Molina, Vall d'Hebron Hosp, Barcelona, Spain

Abstract Body: The CLOTBUST-ER trial - Combined Lysis of Thrombus with Ultrasound and Systemic Tissue Plasminogen Activator (tPA) for Emergent Revascularization in Acute Ischemic Stroke

Background: Continuous exposure of intracranial arterial occlusions to pulsed wave ultrasound enhances tissue plasminogen induced recanalization.

Hypothesis: Sonothrombolysis improves functional outcomes of stroke patients receiving tPA therapy.

Objectives: The primary objective is to assess the efficacy of combined treatment with a novel transcranial ultrasound device and systemic tPA (Target group) compared to systemic tPA alone (Control group) in subjects with acute ischemic stroke.

Methods: Subjects with acute ischemic stroke, pre-morbid mRS of 0 or 1 and NIHSS scores 10 or greater will be randomized (1:1) to the Target and Control groups respectively. Active and sham ultrasound will be delivered via the Clotbust ER device for 2 hours with the first hour overlapping with IV-tPA administration. Subjects will be followed for adverse events through day 7 or hospital discharge, whichever is first and will return 90 days post treatment for their final mRS evaluation. Primary endpoint analysis of 90 day modified Rankin Scores will be assessed utilizing ordinal regression analysis. This phase 3 study is being conducted in over 70 sites in 14 countries. A total of 824 patients will be enrolled with interim analyses at 1/3 and 2/3 of enrollment.

Current Status: As of November 1, 2014 CLOTBUST-ER is ongoing with 492 of 824 planned subjects enrolled to date. Recruitment of new centers is ongoing. The DSMB recommended continuation of the trial as planned without modification after the first interim analysis.

Conclusions: CLOTBUST-ER enrollment is projected to continue into the third quarter of 2015.

The Clotbust ER study is sponsored by Cerevast Therapeutics Inc. For further information please contact John Alleman, COO via email at jalleman@cerevast.com or phone 425-821-1603 ext.

ClinicalTrials.gov Trial Registry ID: NCT01098981

Author Disclosure Block: **A.V. Alexandrov:** Ownership Interest; Modest; Cerevast Therapeutics. Consultant/Advisory Board; Modest; Cerevast Therapeutics. **P.D. Schellinger:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc., Coaxia Inc., Photothera, Sanofi Aventis, Ferrer, EV3/Covidien, GSK, Haemonetics, Bayer Healthcare, BMS-Pfizer. Other; Modest; Travel Grants and Consulting Fees Cerevast Therapeutics Inc., Boehringer Ingelheim, Coaxia, Photothera, Sanofi Aventis, Ferrer, EV3/Covidien, Haemonetics, Bayer Healthcare, BMS-Pfizer. **A. Baretto:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc. **A.M. Demchuk:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc. **L. Soinne:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc. **M. Köhrmann:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc., Coaxia, Inc., Photothera, Bayer Healthcare, BMS-Pfizer. Other; Modest; Travel Grants and Consulting Fees Cerevast Therapeutics, Inc., Boehringer Ingelheim, Coaxia, Inc., Photothera, Bayer Healthcare, BMS-Pfizer. **G. Howard:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc. **C. Molina:** Consultant/Advisory Board; Modest; Cerevast Therapeutics, Inc.. Other; Modest; Travel Grants and Consulting Fees, Cerevast Therapeutics, Inc., Travel Grants and Consulting Fees, Boehringer Ingelheim.

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Presentation Number: CT P19

Trial Abbreviation: HEALS

Trial Contact Information: Natalie Valle, nvalle@dhs.lacounty.gov

Trial Email: nvalle@dhs.lacounty.gov

Trial Name: HEALS (Healthy Eating And Lifestyle after Stroke): A Pilot Trial of a Multidisciplinary Lifestyle Intervention Program for Stroke Survivors

Trial Registry Number ID: NCT01550822

Trial Sponsor: American Heart Association National Scientist Development Grant

Trial Web Site: clinicaltrials.gov

Publishing Title: HEALS (Healthy Eating And Lifestyle after Stroke): A Pilot Trial of a Multidisciplinary Lifestyle Intervention Program for Stroke Survivors

Author Block: Amytis Towfighi, Valerie Hill, Univ of Southern California, Los Angeles, CA; Eric Cheng, VA Greater Los Angeles Healthcare System, Los Angeles, CA; Natalie Valle, Monica Ayala-Rivera, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Karina Martinez, Beatrice Martinez, Cynthia Munoz, Rancho Los Amigos Natl Rehabilitation Ctr, Los Angeles, CA; Lilian Moreno, Heidi Dombish, Annaliese Charlton, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Deborah Wang, Rancho Los Amigos Natl Rehabilitation Ctr, Los Angeles, CA; Dina Ochoa, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Barbara G. Vickrey, Univ of California Los Angeles, Los Angeles, CA

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

Objective: To conduct a pilot test of an outpatient post-stroke lifestyle intervention in a safety-net healthcare system to 1) determine feasibility of the program; 2) conduct a formative evaluation to assess adherence and implementation; and 3) estimate and compare effect sizes for short-term changes in BMI, diet, and physical activity.

Design: Randomized control trial

Population studied: One hundred adults (≥ 40 years of age) with ischemic stroke or TIA ≥ 90 days prior to study enrollment, systolic blood pressure > 120 mm Hg, English- or Spanish-speaking, recruited from one Los Angeles County-Department of Health Services safety net hospital.

Intervention: Six week lifestyle intervention with weekly 2-hour group sessions led by occupational therapists focusing on goal setting, health education, peer exchange, participation in healthy activities, overcoming potential obstacles, self-efficacy and self-management skills. Control group receives usual care.

Outcome Measures: (1) maintaining a BMI of 18.5-24.9 kg/m², (2) eating ≥ 5 servings fruits/vegetables per day, (3) exercising ≥ 12 times per month.

Analysis: Intention-to-treat analysis to determine whether persons randomized to intervention achieve better outcomes than persons randomized to usual care, at 6 months.

Trial Status: Enrolled 65 of 100 study participants.

Author Disclosure Block: **A. Towfighi:** None. **V. Hill:** None. **E. Cheng:** None. **N. Valle:** None. **M. Ayala-Rivera:** None. **K. Martinez:** None. **B. Martinez:** None. **C. Munoz:** None. **L. Moreno:** None. **H. Dombish:** None. **A. Charlton:** None. **D. Wang:** None. **D. Ochoa:** None. **B.G. Vickrey:** None.

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Presentation Number: CT P20

Trial Abbreviation: WEB-IT

Trial Contact Information: Thomas McCarthy, tomm@sequentmedical.com

Trial Email: tomm@sequentmedical.com

Trial Name: The WEB Intrasaccular Therapy Study

Trial Registry Number ID: NCT02191618

Trial Sponsor: Sequent Medical, Inc.

Trial Web Site: www.sequentmedical.com

Publishing Title: The WEB Intrasaccular Therapy Study (WEB-IT)

Author Block: Adam Arthur, Semmes-Murphey Clinic, Memphis, TN; David Fiorella, SUNY-Stony Brook, Stony Brook, NY; Thomas McCarthy, Sequent Medical, Inc., Aliso Viejo, CA

Abstract Body: Introduction: The Woven Endobridge (WEB) is an intra-aneurysmal flow diverter intended for use in the endovascular embolization of intracranial, wide-necked, bifurcation aneurysms (WNBA). In the United States (US) the WEB has recently been granted an Investigational Device Exemption (IDE) for use within the WEB-IT Study. We present the design and enrollment status of the WEB-Intrasaccular Therapy (WEB-IT) study.

Methods: WEB-IT is a prospective, multicenter, single-arm interventional trial designed to evaluate the safety and effectiveness of the WEB device for the treatment of ruptured and unruptured WNBA arising from the basilar apex, middle cerebral artery, internal carotid artery terminus, and anterior communicating artery complex. The primary effectiveness endpoint is complete angiographic occlusion of the targeted aneurysm at 1 year as determined by an independent core laboratory. The primary safety endpoint is the proportion of subjects with death or any major stroke within the first 30 days after treatment or major ipsilateral stroke or death due to a neurological cause from day 31 to 1 year. Both effectiveness and safety endpoints will be compared with a performance goal or Objective Performance Characteristic (OPC) derived from the available clinical literature for the treatment of WNBA. The study will be interpreted as a success if both endpoints are met. The aneurysms to be treated should be saccular in shape, have a neck size ≥ 4 mm or a dome-to-neck ratio < 2 , and a diameter of approximately 5-11 mm at screening. Ruptured patients must have a Hunt & Hess score of I or II. Patients will be followed for 5 years after the procedure.

Results: The WEB-IT trial was initiated on August 19, 2014. The trial will include 20 United States (US) centers and 5 centers outside of the US. To date 10 of 139 subjects have been enrolled. All subjects enrolled thus far have had unruptured aneurysms.

Conclusions: The WEB-IT trial will provide an assessment of the safety and efficacy of the WEB device for the treatment of WNBA.

Author Disclosure Block: **A. Arthur:** Consultant/Advisory Board; Significant; Study PI; Sequent Medical. **D. Fiorella:** Consultant/Advisory Board; Significant; Study Co-PI, Sequent Medical. **T. McCarthy:** Employment; Significant; Sequent Medical.

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Presentation Number: CT P21

Trial Abbreviation: SCENT

Trial Contact Information: rpaparazzo@boston-biomedical.com

Trial Email: rpaparazzo@boston-biomedical.com

Trial Name: Surpass intraCranial aneurysm Embolization system pivotal Trial to treat large or giant wide neck aneurysms

Trial Registry Number ID: NCT01716117

Trial Sponsor: Stryker Neurovascular

Trial Web Site: <http://clinicaltrials.gov/ct2/show/NCT01716117?term=surpass&rank=5>

Publishing Title: Surpass Intracranial Aneurysm Embolization System Pivotal Trial To Treat Large Or Giant Wide Neck Aneurysms (SCENT Trial)

Author Block: **Ricardo A Hanel**, Lyerly Neurosurgery, Jacksonville, FL; Philip Meyers, Columbia Univ, New York City, NY; Ajay K Wakhloo, for SCENT Investigators, Univ of Massachusetts Medical Sch, Worcester, MA

Abstract Body: Background: Large and giant intracranial aneurysms remain challenging lesions for endovascular treatment. The Surpass device is a braided endoprosthesis designed to achieve a precise delivery with a more uniform and consistent mesh configuration for flow diversion and treatment of intracranial aneurysms.

Methods: The SCENT trial is an international multi-center, prospective, non-randomized trial to evaluate safety and effectiveness of the Surpass Flow Diverter (Stryker Neurovascular, Fremont, CA) compared to a historical control in the treatment of large or giant wide neck intracranial aneurysms. Eligible subjects should be 19 to 80 years, have a single targeted intracranial aneurysm that is located in the internal carotid artery (ICA) distribution up to the terminus with a neck ≥ 4 mm or no discernible neck and an aneurysm size ≥ 10 mm (including saccular, fusiform and dissecting configuration). Primary safety end-point: percent of subjects experiencing neurologic death or major ipsilateral stroke through 12 months. Primary effectiveness end-point: percent of subjects with 100% occlusion (Raymond Class 1) without clinically significant stenosis (defined as $< 50\%$ stenosis) of the parent artery and without any subsequent treatment of the target aneurysm at 12 months. Results: 23 sites are currently enrolling patients (22 in the US, 1 in Europe). A total of 137 patients have been enrolled, with 127 already treated (29 as roll-in cases; 98 as protocol cases).

Conclusion: The SCENT trial is currently enrolling and is expected to complete enrollment by mid-2015.

Author Disclosure Block: **R.A. Hanel:** None. **P. Meyers:** None. **A.K. Wakhloo, for SCENT Investigators:** Consultant/Advisory Board; Significant; Stryker Neurovascular.

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Presentation Number: CT P22

Trial Abbreviation: ESCAPE

Trial Contact Information: esctril@ucalgary.ca

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

Trial Registry Number ID: NCT01778335

Trial Sponsor: University of Calgary

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

Publishing Title: Endovascular Treatment For Small Core And Anterior Circulation Proximal Occlusion With Emphasis On Minimizing Ct To Recanalization Times (escape)

Author Block: **Michael D HILL**, Mayank Goyal, Andrew M Demchuk, Bijoy K Menon, Muneer Eesa, Karla J Ryckborst, Privia A Randhawa, Noreen Kamal, Univ of Calgary, Calgary, AB, Canada; Daniel Roy, CHUM, Montreal, QC, Canada; Robert Willinsky, UHN, Toronto Western Hosp, Toronto, ON, Canada; Walter Montanera, St. Michael's Hosp, Toronto, ON, Canada; Frank L Silver, UHN, Toronto Western Hosp, Toronto, ON, Canada; Ashfaq Shuaib, Jeremy Rempel, Univ of Alberta, Edmonton, AB, Canada; Tudor Jovin, UPMC, Pittsburgh, PA; Donald Frei, Swedish Medical Ctr, Denver, CO; Biggya Sapkota, Erlanger Medical Ctr, Chattanooga, TN; M John Thornton, Beaumont Hosp, Dublin, Ireland; Alexandre Poppe, CHUM, Montreal, QC, Canada; Donatella Tampieri, McGill Univ, Montreal, QC, Canada; Cheemun Lum, Univ of Ottawa, Ottawa, ON, Canada; Alain Weill, CHUM, Montreal, QC, Canada; Tolulope Sajobi, Univ of Calgary, Calgary, AB, Canada

Abstract Body: Background: There is no convincing, randomized trial evidence that modern endovascular therapy is better than routine care, including routine intravenous thrombolysis, for acute ischemic stroke. Objective: To show that rapid endovascular revascularization amongst radiologically selected (small core/proximal anterior circulation occlusion) patients with ischemic stroke results in improved outcome compared to patients treated in clinical routine. The secondary objectives are to demonstrate the safety and feasibility of achieving rapid endovascular revascularization in this population of patients. Design: A Phase 3, randomized, open-label study with blinded outcome evaluation.

Main Inclusion criteria:

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

Main Exclusion criteria:

1. Baseline NCCT reveals moderate to large core of early ischemic changes in the territory of the symptomatic intracranial occlusion (ASPECTS<6),
2. Baseline venous weighted CTA reveals insufficient collaterals in the symptomatic MCA territory as determined by a collateral certified physician interpretation using MIP images and compared to the contralateral side, OR CT perfusion CBF or CBV ASPECTS < 6.

3. Chronic intracranial occlusion,

4. Pre-stroke functional dependence for ADLs or major co-morbid illness

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

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

Trial Status: Active, Recruiting. Estimated final total site number: 22 in Canada, US, Europe, Asia.

Author Disclosure Block: **M.D. Hill:** Research Grant; Significant; Grant support from Covidien. **M. Goyal:** None. **A.M. Demchuk:** None. **B.K. Menon:** None. **M. Eesa:** None. **K.J. Ryckborst:** None. **P.A. Randhawa:** None. **N. Kamal:** None. **D. Roy:** None. **R. Willinsky:** None. **W. Montanera:** None. **F.L. Silver:** None. **A. Shuaib:** None. **J. Rempel:** None. **T. Jovin:** None. **D. Frei:** None. **B. Sapkota:** None. **M.J. Thornton:** None. **A. Poppe:** None. **D. Tampieri:** None. **C. Lum:** None. **A. Weill:** None. **T. Sajobi:** None.

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Presentation Number: CT P23

Trial Abbreviation: DAWN

Trial Contact Information: patricia.morgan@stryker.com

Trial Email: patricia.morgan@stryker.com

Trial Name: DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention

Trial Registry Number ID: NCT02142283

Trial Sponsor: Stryker Neurovascular

Trial Web Site: DAWNTRIAL.com

Publishing Title: DAWN TRIAL: DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention

Author Block: Raul G Nogueira, Emory Univ/Grady Memorial Hosp, Atlanta, GA; Jeffrey L. Saver, Stroke Ctr and Dept of Neurology, Univ of California, Los Angeles, Los Angeles, CA; Scott Berry, Berry consultants, LLC, Austin, TX; Kennedy Lees, Inst of Cardiovascular and Medical Sciences, Univ of Glasgow, Glasgow, United Kingdom; Anthony Furlan, Dept of Neurology, Case Western Reserve Univ, Cleveland, OH; Blaise Baxter, Dept of Interventional Radiology, Univ of Tennessee, Chattanooga, TN; Marc Ribo, Stroke Unit, Dept of Neurology, Univ Hosp Vall d'Hebron, Spain, Barcelona, Spain; Olav Jansen, Dept of Radiology and Neuroradiology, Univ of Kiel, Germany, Kiel, Germany; Rishi Gupta, Wellstar Kennestone Hosp, Marietta, GA; Vitor M Pereira, Univ of Toronto, Toronto, ON, Canada; Greg Albers, Stanford Stroke Ctr, Dept of Neurology, Palo Alto, CA; Wade Smith, Univ of California, San Francisco, Medical Ctr, San Francisco, CA; Tudor G. Jovin, UPMC Stroke Inst, Univ of Pittsburgh Medical Ctr, Pittsburgh, PA

Abstract Body: DAWN is a multi-center, prospective, randomized, controlled, blinded-endpoint, phase II/III (feasibility/pivotal) trial of embolectomy for wake up ischemic stroke that follows an adaptive design based on Bayesian predictive probabilities allowing population enrichment.

Subjects presenting with acute ischemic stroke beyond 6 hours from time last seen well (TLSW) with CTA or MRA proven arterial occlusion of the intracranial internal carotid or proximal MCA (M1) are randomized in a 1:1 ratio to mechanical embolectomy with the Trevo® Retriever vs. medical therapy.

First interim analysis is planned at 180 patients. The maximum allowed sample size is 500. Selection is based on clinical/core mismatch (CCM) and age. Core is measured using FDA approved automated volumetric analysis software (RAPID) on baseline DWI MRI or CT Perfusion. Patients will be included based on the following CCM/age scenarios: 0-20 cc core, NIHSS \geq 10 and age \geq 80; 0-30 cc core, NIHSS \geq 10 and age $<$ 80 years old; 31 cc to $<$ 50 cc core, NIHSS \geq 20 and age $<$ 80. Randomization is stratified by CCM subgroups, TLSW to Treatment (12 hours cut-off) and Baseline Occlusion Location.

The primary endpoint on the basis of intention-to-treat criteria is the difference between the average weighted modified Rankin Scale score at 90 days between the treatment and control groups. Secondary endpoints are proportion of subjects with good functional outcome at 90 days, proportion of subjects with "early response" at day 5-7, difference in all-cause mortality rates, difference in median final infarct size at 24 hours, difference in revascularization rates at 24 hours and analysis of reperfusion rates (mTICI \geq 2b) post device and post procedure. Primary safety outcome measure: stroke related mortality at 90 days. Secondary safety outcome measures: symptomatic ICH rates at 24 hrs., incidence of neurological deterioration and procedural related

complications.

Enrollment started in October 2014. Estimated study duration is approximately 3 years.

Author Disclosure Block: R.G. Nogueira: None. J.L. Saver: None. S. Berry: None. K. Lees: None. A. Furlan: None. B. Baxter: None. M. Ribo: None. O. Jansen: None. R. Gupta: None. V.M. Pereira: None. G. Albers: None. W. Smith: None. T.G. Jovin: None.

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Presentation Number: CT P24

Trial Abbreviation: GAMES RP

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Trial Name: GAMES (Glyburide Advantage in Malignant Edema and Stroke) RP

Trial Registry Number ID: NCT01794182

Trial Sponsor: Remedy Pharmaceuticals, Inc

Trial Web Site: None

Publishing Title: GAMES (Glyburide Advantage In Malignant Edema And Stroke) RP

Author Block: Kevin N Sheth, Yale Univ, New Haven, CT; Jordan Elm, Medical Univ of South Carolina, Charleston, SC; Sven Jacobson, Remedy Pharmaceuticals, Inc, New York, NY; W. Taylor Kimberly, Massachusetts General Hosp, Boston, MA; GAMES Investigators

Abstract Body: Background: Malignant infarction is characterized by the formation of rapidly accumulating cerebral edema, and decompressive craniectomy (DC) is the only proven therapy for this syndrome. An IV formulation of glyburide (RP-1127) was tested in GAMES Pilot, which suggested feasibility for a phase II study. Objective: The primary objective is to assess the safety and efficacy of RP-1127 compared to placebo in severe anterior circulation ischemic stroke patients who are at high risk for developing malignant edema. Design: This is a randomized, multi-center, double blind, phase II trial. Population studied: Eligible patients will have a baseline MRI DWI lesion between 82 cm³ and 300 cm³, age 18-80 years, and time from symptom onset to drug infusion of ≤ 10 hours. Patients who receive intra-arterial reperfusion therapy or are on sulfonylurea treatment at presentation are excluded. Intervention: Enrolled patients are randomly assigned to either RP-1127 or placebo bolus and continuous infusion for 72 hours. Subjects undergo MRI at baseline and at 72-96 hours. Neurological assessments and safety parameters, including frequent glucose monitoring, are performed during the first 7 days. Modified Rankin Scale (mRS) assessment occurs at days 30 and 90, and at 6 and 12 months. Outcome measure: The primary outcome will be assessed by the incidence of mRS ≤4 without DC at 90 days. Safety will be assessed by the frequency/severity of adverse events, hypoglycemia (<55 mg/dL) and symptomatic hypoglycemia, and incidence of QTc interval prolongation > 500 ms. Analysis Plan: An interim analysis will be conducted after stage 1 to re-estimate the sample size and assess futility. The primary analysis will be ITT and will combine patients enrolled in both stages using a weighted combination test (two-sided alpha= 0.05). As demonstrated by simulation, the design has 80% power under a 20-percentage-point effect size. Trial Status: To date, across 17 US sites, 53 patients have been enrolled. There have been no episodes of symptomatic hypoglycemia. There have been two drug related significant adverse events, defined as glucose below 70 mg/dL. No patients have been lost to follow up.

Author Disclosure Block: **K.N. Sheth:** Research Grant; Significant; Remedy Pharmaceuticals. Other; Modest; AHA Get with the Guidelines Stroke. **J. Elm:** Other Research Support; Significant; Remedy Pharmaceuticals, Inc, NIH. **S. Jacobson:** Employment; Significant; Remedy. **W.T. Kimberly:** Other Research Support; Significant; Remedy Pharmaceuticals, Inc, NIH.

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Presentation Number: CT P25

Trial Abbreviation: NEWTON

Trial Contact Information: Herb Faleck, hfaleck@edgetherapeutics.com, +18002083343 ext103

Trial Email: hfaleck@edgetherapeutics.com

Trial Name: NEWTON - Nimodipine microparticles to Enhance recovery While reducing TOxicity after subarachnoid hemorrhage

Trial Registry Number ID: NCT01893190

Trial Sponsor: Edge Therapeutics

Trial Web Site: www.edgetherapeutics.com

Publishing Title: Newton - Nimodipine Microparticles To Enhance Recovery While Reducing Toxicity After Subarachnoid Hemorrhage

Author Block: Daniel Hanggi, **Nima Etminan**, Hans Jakob Steiger, Heinrich-Heine-Univ Duesseldorf, Duesseldorf, Germany; Robert Loch Macdonald, St. Michaels Hosp, Toronto, ON, Canada; NEWTON Investigators

Abstract Body: Aneurysmal subarachnoid hemorrhage (aSAH) is associated with high morbidity and mortality. EG-1962 is a sustained release microparticle formulation of nimodipine that has shown preclinical efficacy when administered intraventricularly or intracisternally to dogs with SAH, with no evidence for toxicity at potentially therapeutic doses. Thus, there is rationale for conducting a study administering EG-1962 to humans in order to assess safety and tolerability and determine a dose to investigate efficacy in subsequent clinical studies. We describe a Phase 1/2a multicenter, controlled, randomized, open label, dose escalation study to determine the maximum tolerated dose (MTD) and assess the safety and tolerability of EG-1962 in patients with aSAH. The study is ongoing and is comprised of 2 parts: a dose escalation period (Part 1) to determine the MTD of EG-1962 and a treatment period (Part 2) to assess the safety and tolerability of the selected dose of EG 1962. Patients with a ruptured saccular aneurysm treated by neurosurgical clipping or endovascular coiling will be considered for enrollment in this study. Patients will be randomized in cohorts of 12 patients to receive either EG-1962 (study drug: nimodipine microparticles, n = 9 per cohort) or nimodipine 60 mg (active control, n = 3 per cohort) within 60 hours of aSAH. Primary objectives are to determine the MTD and the safety and tolerability of the selected dose of intraventricular EG 1962 as compared to enteral nimodipine in patients with aSAH. The secondary objective is to measure plasma and CSF concentrations of nimodipine. Exploratory objectives are to determine the incidence of delayed cerebral infarction on computed tomography, clinical features of delayed cerebral ischemia, angiographic vasospasm, incidence of rescue therapy and clinical outcome. Thus far cohorts of 12 patients have been administered 100 mg or 200 mg EG-1962 (n = 9 each) and enrollment is ongoing in the third cohort at 400 mg.

Author Disclosure Block: **D. Hanggi:** Consultant/Advisory Board; Significant; Scientific Advisor of EDGE Therapeutics. **N. Etminan:** Consultant/Advisory Board; Modest; Edge Therapeutics. **H. Steiger:** None. **R. Macdonald:** Other; Significant; Chief Scientific Officer of Edge Therapeutics.

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Presentation Number: CT P26

Trial Abbreviation: ATTEND TRIAL

Trial Contact Information: Mohammed Alim, malim@georgeinstitute.org.in, phone +91 40 6731 4444

Trial Email: info@georgeinstitute.org.in

Trial Name: Family-led rehabilitation after stroke in India

Trial Registry Number ID: U1111-1138-6707

Trial Sponsor: National Health and Medical Research Council of Australia

Trial Web Site: www.georgeinstitute.org.in

Publishing Title: Family-led Rehabilitation After Stroke In India: Attend Trial

Author Block: **Cynthia Felix**, Jeyaraj D Pandian, Christian Medical Coll, Ludhiana, India; Mohammed Alim, George Inst for Global Health, Hyderabad, India; Dorcas Bc Gandhi, Christian Medical Coll, Ludhiana, India; Anuradha Syrigapu, Deepak K Tugnawat, Indian Inst of Public Health, Hyderabad, India; Shweta Verma, Christian Medical Coll, Ludhiana, India; Lisa Harvey, Univ of Sydney, Sydney, Australia; G V Murthy, Indian Inst of Public Health, Hyderabad, India; Pallab K Maulik, George Inst for Global Health, Hyderabad, India; Richard I Lindley, George Inst for Global Health, Sydney, Australia; ATTEND Trial Collaborators

Abstract Body: Background: Stroke is one of the leading causes of death and disability globally and majority of the 17 million strokes occur in lower middle income countries. It is challenging in countries like India to establish stroke units with adequate skilled staff required for comprehensive care, as many of these patients currently receive little or no rehabilitation. The novel concept of trained caregiver acting as the 'multidisciplinary team' delivering stroke rehabilitation as a cost-efficient model of care can help in creating sustainable and multi-professional rehabilitation systems in these countries, including provision of services to rural population.

Objective: To evaluate, a family-led caregiver-delivered home-based rehabilitation intervention compared to usual care is an effective, affordable early supported discharge strategy for those with disabling stroke in India.

Design: Investigator Initiated, Prospective, Randomized, Open Blinded Endpoint assessment (PROBE design) Phase 3 study.

Population Studied: 1200 patients with acute stroke having mild to moderate disability will be enrolled from 14 centers across India.

Intervention: Patients randomized (web based randomization) to intervention arm will have their family nominated caregiver trained by a specially trained stroke coordinator (i.e. nurse, physiotherapist) using a structured assessment (cognition, language, function and mobility) and rehabilitation package based on best evidence adapted for the Indian environment.

Outcome Measure: Primary outcome is the modified Rankin Scale score at 6 months post randomization and secondary outcomes include quality of life, depression and anxiety, and health costs.

Analysis: The intention to treat principle will be applied in all analyses.

Trial Status: 362 patients have been enrolled from January to October 2014 from 13 centers.

Collaborators

1. The George Institute for Global Health, Hyderabad, India
2. Christian Medical College, Ludhiana, India
3. Indian Institute of Public Health, Hyderabad, India
4. University of Sydney, Australia.
5. The George Institute of Global Health, Sydney, Australia.

Author Disclosure Block: C. Felix: None. J.D. Pandian: None. M. Alim: None. D.B. Gandhi: None. A. Syrigapu: None. D.K. Tugnawat: None. S.J. Verma: None. L. Harvey: None. G.V.S. Murthy: None. P.K. Maulik: None. R.I. Lindley: None.

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Presentation Number: CT P27

Trial Abbreviation: LSS

Trial Contact Information: bsamson@seton.org

Trial Email: bsamson@seton.org

Trial Name: Lone Star Stroke

Trial Registry Number ID: LSS-1

Trial Sponsor: State of Texas

Trial Web Site: <http://lonestarstroke.org>

Publishing Title: A State-Wide Tele-Stroke Research Initiative: The Lone Star Stroke Network

Author Block: **Thomas A Kent**, BAYLOR COLLEGE OF MEDICINE, Houston, TX; Robin L Brey, Univ of Texas Health Science Ctr at San Antonio, San Antonio, TX; Salvador Cruz-Flores, Texas Tech Univ Health Sciences Ctr-El Paso, El Paso, TX; Mark Goldberg, Univ of Texas Southwestern Medical Ctr, Dallas, TX; James C Grotta, Memorial Hermann Hosp-Texas Medical Ctr, Houston, TX; Patricia D Hurn, Univ of Texas System, Austin, TX; Sean I Savitz, Univ of Texas Medical Sch in Houston, Houston, TX; Steven J Warach, UT Southwestern Medical Ctr, Austin, TX

Abstract Body: Introduction: Better access to stroke care in rural regions and in high risk patient populations is a major health care need. Two consequence of this lack is reduced opportunity to participate in research protocols and insufficient information about the feasibility of new therapies in such populations. To address this gap, the Texas State Legislature funded establishment of the Lone Star Stroke Research Network (LSS) to address research in all aspects of stroke care to rural centers in Texas connected to major academic institutions performing clinical stroke research. The goal is that both extramurally funded multi-center trials will utilize LSS to enhance recruitment and pilot studies will generate data for investigator-initiated projects. Objective: Inaugurated in 2013, LSS consists of 5 academic center hubs (Baylor College of Medicine in Houston, University of Texas Health Science Centers in Houston, San Antonio and Dallas, and the Seton Healthcare Family in Austin), each with 4 identified tele-stroke spokes interested and capable of conducting stroke research. Spoke sites include regions identified with a high incidence of stroke and reduced access to acute and secondary prevention therapies. The LSS infrastructure supports equipment and personnel at the hubs and spokes. An External Advisory Committee (EAC) has been established with the participation of 4 experienced stroke researchers outside of Texas to evaluate the appropriateness and scientific validity of each pilot proposal to the mission of LSS.

Status: The EAC has initially approved 3 projects. These are: NASCARE, a quality improvement project utilizing lean management techniques to address processes for tPA administration in the Emergency Department; V-STOP II, a project to adapt individual cardiovascular self-management processes to a group, tele-medicine approach within a rural setting; and pharmaceutical-sponsored CLOTBUSTER trial of adjunctive ultrasound to tPA. Initiation of recruitment is anticipated to begin early 2015.

Conclusions: LSS should provide a model for acceleration of recruitment for clinical trials and the enhanced inclusion of populations that traditionally are under-represented.

LSS website: <http://lonestarstroke.org>

Author Disclosure Block: **T.A. Kent:** Research Grant; Significant; Texas Department of State Health Services. **R.L. Brey:** Research Grant; Significant; Texas Department of State Health Services. **S. Cruz-Flores:**

Research Grant; Significant; Texas Department of State Health Services. **M. Goldberg:** Research Grant; Significant; Texas Department of State Health Services. **J.C. Grotta:** Research Grant; Significant; Texas Department of State Health Services. **P.D. Hurn:** Research Grant; Significant; Texas Department of State Health Services. **S.I. Savitz:** Research Grant; Significant; Texas Department of State Health Services. **S.J. Warach:** Research Grant; Significant; Texas Department of State Health Services.

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Presentation Number: CT P28

Trial Abbreviation: RE-VERSE AD

Trial Contact Information: Boehringer Ingelheim Call Center, 1-800-243-0127 clintriage.rdg@boehringer-ingelheim.com

Trial Email: clintriage.rdg@boehringer-ingelheim.com

Trial Name: Reversal of Dabigatran Anticoagulant Effect With Idarucizumab

Trial Registry Number ID: NCT02104947

Trial Sponsor: Boehringer Ingelheim

Trial Web Site: <http://clinicaltrials.gov/ct2/show/NCT02104947?term=NCT02104947&rank=1>

Publishing Title: A Phase III Clinical Trial To Evaluate The Reversal Effects Of Idarucizumab On Active Dabigatran (RE-VERSE AD)

Author Block: Charles Pollack, Univ of Pennsylvania, Philadelphia, PA; R Dubiel, Boehringer Ingelheim Pharmaceutical Inc, Ridgefield, CT; John Eikelboom, McMaster Univ, Hamilton, ON, Canada; Menno Huisman, Leiden Univ, Leiden, Netherlands; Elaine Hylek, Boston Univ, Boston, MA; C W Kam, Tuen Mun Hosp, Hong Kong City, Hong Kong; P Kamphuisen, Univ Medical Ctr Groningen, Groningen, Netherlands; Jörg Kreuzer, Boehringer Ingelheim, Ingelheim, Germany; J Levy, Duke Univ, Durham, NC; Paul Reilly, B Wang, S Wang, Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT; J Weitz, McMaster Univ, Hamilton, ON, Canada; R Bernstein, North Western Univ, Chicago, IL

Abstract Body: Introduction: Anticoagulation therapy is a mainstay in the treatment and prevention of thromboembolic events. Bleeding complications are a relevant side effect and immediate, reliable reversal of an oral anticoagulant (OAC) without additive prothrombotic effect may be beneficial in critical situations. To date, specific reversal options for OAC do not exist. Idarucizumab, a monoclonal antibody fragment, immediately reverses the effect of dabigatran after IV administration in healthy volunteers with a good safety profile.

Objective: The aim of RE-VERSE AD (NCT02104947) is to demonstrate the ability of idarucizumab to reverse anticoagulant effect in patients treated with dabigatran etexilate (DE) who need emergent stabilization or medical or invasive intervention. **Design:** RE-VERSE AD is a multicenter, open label, single arm phase III trial with a target sample size of 200 - 300 patients. This design was selected since withholding an effective antidote to DE in clinically critical situations would be unethical. Two study groups are included:

- a.) Patients treated with DE who have uncontrolled bleeding or bleeding into a critical space
- b.) Patients treated with DE who require emergency surgery or a procedure for a condition other than bleeding, in whom adequate hemostasis is required

All patients in the study will receive 5g of idarucizumab, administered as two separate infusions of 2.5g, no more than 15 minutes apart. Blood samples for coagulation studies and PK/PD measurements will be taken at baseline before first infusion, just prior to the second infusion, and at multiple predefined time points after the second infusion. The patient will be monitored for bleeding, adverse events, and clinical status throughout the study (90 days). The primary endpoint is reversal of DE, based on dTT or ECT from the completion up to 4h after completion of the second infusion. Key secondary endpoints include bleeding and hemodynamic status, antidote safety, and pharmacokinetics of DE in the presence of idarucizumab.

Conclusion: RE-VERSE AD will evaluate the efficacy of idarucizumab to rapidly reverse DE-induced anticoagulation in critical clinical situations.

Author Disclosure Block: **C. Pollack:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **R. Dubiel:** Employment; Significant; Boehringer Ingelheim. **J. Eikelboom:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **M. Huisman:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **E. Hylek:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **C.W. Kam:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **P. Kamphuisen:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **J. Kreuzer:** Employment; Significant; Boehringer Ingelheim. **J. Levy:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **P. Reilly:** Employment; Significant; Boehringer Ingelheim. **B. Wang:** Employment; Significant; Boehringer Ingelheim. **S. Wang:** Employment; Significant; Boehringer Ingelheim. **J. Weitz:** Consultant/Advisory Board; Significant; Boehringer Ingelheim. **R. Bernstein:** Consultant/Advisory Board; Significant; Boehringer Ingelheim.

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Presentation Number: CT P29

Trial Abbreviation: CTorMRI

Trial Contact Information: Christine Krarup Hansen, christinekraruphansen@gmail.com, +45 35313733, +45 22705664

Trial Email: christinekraruphansen@gmail.com

Trial Name: CT or MRI in evaluation for i.v. thrombolysis: a single-centre quasi randomized trial

Trial Registry Number ID: H-4-2013-118

Trial Sponsor: Tryg Foundation

Trial Web Site: www.bispebjerghospital.dk

Publishing Title: CT or MRI In Evaluation Of Patients For I.v. Thrombolysis: A Single-centre Quasi Randomized Trial

Author Block: **Christine Krarup Hansen**, Anders Christensen, Inger Havsteen, Hanne Christensen, Bispebjerg Univ Hosp, Copenhagen, Denmark

Abstract Body: Background: The issue if Computer Tomography (CT) or Magnetic Resonance Imaging (MRI) is the 'best' primary image modality in evaluation of patients with symptoms of acute stroke, and thus candidates for i.v thrombolysis, has been discussed by stroke scientists for more than a decade. Access to primary acute MRI evaluation is frequently regarded as a token of high treatment quality; nevertheless, few centres worldwide are really primarily MRI based. MRI is superior in detecting acute ischaemia and CT is faster and has no contraindications. As the efficacy of thrombolysis decreases with time to treatment one must if use of MRI is only of academic interest.

Aim: The aim of this ongoing study is to determine if choice of primary imaging modality (CT versus MRI) affects efficacy and safety of i.v thrombolysis.

Method: An open quasi-randomised design, where imaging allocation is based on the date of admission. The 3 following items will be compared:

Safety; Exclusion of other causes of symptoms than acute cerebral ischemia and contraindications to scanning method (contraindications to use of contrast or magnetism).

Effect; Delay to treatment, acquisition of imaging in diagnostic quality and identification of stroke mechanism.

Applicability; Patient experience, experience of decision support for treating physician, deviation from radiological Standard Operational Plan (SOP) and use of resources.

Inclusion & exclusion criteria: Clinical suspicion of stroke <4.5 hours, NIHSS \geq 1, admission in the daytime at weekdays and informed consent by patient or proxy. Patients in whom the stroke diagnosis is refuted on arrival and patients not providing informed consent are excluded from the study.

Time schedule: Inclusion of patients was initiated in December 2013 and is expected to comprise 600 patients during a period of 24 months. By October 2014 230 patients had been evaluated.

Author Disclosure Block: **C. Hansen:** Research Grant; Significant; A grant from the Danish nonprofit Tryg Foundation. **A. Christensen:** None. **I. Havsteen:** None. **H. Christensen:** None.

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Presentation Number: CT P30

Trial Abbreviation: TICH-2

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Trial Email: tich-2@nottingham.ac.uk

Trial Name: Tranexamic Acid for IntraCerebral Haemorrhage 2

Trial Registry Number ID: ISRCTN93732214

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.tich-2.org

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

Author Block: Philip M. Bath, Kailash Krishnan, Hayley Foster, Tanya Payne, Margaret Adrian, Joanne Keeling, Harriet Howard, Michael Stringer, Katie Robson, **Nikola Sprigg**, Univ of Nottingham, Nottingham, United Kingdom

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

Design: Patients will be randomised (1:1) to receive either tranexamic acid or placebo (0.9 % saline) within 8 hours of acute primary intracerebral haemorrhagic stroke.

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

Trial status: The start-up phase of the trial commenced on 1 March 2013 and ran for 1 year, and the main phase commenced 1st April 2014. The recruitment target was 300 participants in the start up phase and 2,000 in the main phase. As at 3rd November, 2014 650 patients have been recruited from 72 centres (UK, Georgia, Italy). The objective is to have 80 UK centres and 40 international centres.

Funding: The National Institute of Health Research, Health and Technology Assessment Programme

Contact information: <http://tich-2.org>, E-mail: tich-2@nottingham.ac.uk, Telephone: +44 (0)115 823 1770

Author Disclosure Block: **P.M.W. Bath:** None. **K. Krishnan:** None. **H. Foster:** None. **T. Payne:** None. **M. Adrian:** None. **J. Keeling:** None. **H. Howard:** None. **M. Stringer:** None. **K. Robson:** None. **N. Sprigg:** None.

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Presentation Number: CT P31

Trial Abbreviation: I-SPOT Trial

Trial Contact Information: Nina T. Gentile, ph. 215-707-8402, email ngentile@temple.edu

Trial Email: ngentile@temple.edu

Trial Name: Insights on Selected Procoagulation markers and Outcomes in Stroke Trial (I-SPOT)

Trial Registry Number ID: NCT01811550

Trial Sponsor: NIH-NINDS

Trial Web Site: <http://www.shinetrial.org/ispot>

Publishing Title: Insights on Selected Procoagulation markers and Outcomes in Stroke Trials (I-SPOT)

Author Block: **Nina T. Gentile**, A. Koneti Rao, Hannah Reimer, Temple Univ Sch of Med, Philadelphia, PA; Askiel Bruno, Georgia Regents, Augusta, GA; Viswanathan Ramakrishnan, Medical Univ of South Carolina, Charleston, SC; William G. Barsan, Univ of Michigan, Ann Arbor, MI

Abstract Body: Background: Markers of blood coagulation are elevated in hyperglycemia and in acute ischemic stroke (AIS). The effect of blood glucose control after AIS on levels of markers of tissue factor pathway of blood coagulation and their relationship to stroke outcomes is unknown. Objectives: To determine the relationships between levels of blood coagulation markers and hyperglycemia control and functional neurological outcome in SHINE treatment and control patients. Design: The I-SPOT Trial is designed to accompany the Stroke Hyperglycemia Insulin Network Effort (SHINE) clinical trial. SHINE is a multicenter, randomized, controlled trial with 2 treatment arms: glucose control (80 - 130 mg/dL) using insulin infusion versus standard sliding scale insulin with target glucose <180 mg/dL. Population: SHINE enrolled subjects (adult AIS patients with hyperglycemia) who have not received fibrinolytics, anticoagulants, have no severe liver disease nor hypercoagulable disorders are eligible for I-SPOT. Sample Size: 315 Subjects Intervention: Blood coagulation marker levels [tissue factor procoagulant activity (TF-PCA); coagulation factors VII, VIIa, and VIII, TAT, D-dimer, tissue factor pathway inhibitor (TFPI), plasminogen activator inhibitor-1 (PAI-1)] will be measured before and at 48 hrs after the start of glucose control treatment. Outcome Measures: At 90 days participants have modified Rankin Scale (mRS) and Questionnaire for Verifying Stroke Free Symptoms (QVSFS) assessments performed. Statistical Analysis: Baseline and 48-hour changes in biomarkers levels will be compared between SHINE treatment groups and between groups by clinical outcome. The baseline NIHSS stroke severity adjusted difference in favorable outcome between the treatment groups will be used to assess the relationships between markers of blood coagulation and clinical outcome and to determine if hyperglycemia control modulates the relationship between these biomarkers and clinical outcome in patients with hyperglycemia after stroke. Trial Status: Enrollment is ongoing at 49 of the approximately 60 SHINE sites. As of November 1, 2014, 58 subjects have been enrolled. Sponsor: NIH-NINDS 1U01NS079077

Author Disclosure Block: **N.T. Gentile:** Research Grant; Significant; NINDS research grants. Other; Significant; AstraZeneca research study. **A.K. Rao:** Research Grant; Significant; NINDS research grant. **H.**

Reimer: Research Grant; Significant; NINDS research grant. **A. Bruno:** Research Grant; Significant; NINDS research grants. **V. Ramakrishnan:** Research Grant; Significant; NINDS research grant. **W.G. Barsan:** Research Grant; Significant; NINDS research grants.

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Presentation Number: CT P32

Trial Abbreviation: SUCCEED

Trial Contact Information: Monica Ayala-Rivera, mmayala@mednet.ucla.edu, (562) 401-8446

Trial Email: mmayala@mednet.ucla.edu

Trial Name: Secondary stroke prevention by Uniting Community and Chronic care model teams Early to End Disparities: the SUCCEED Trial

Trial Registry Number ID: NCT01763203

Trial Sponsor: NIH, NINDS

Trial Web Site: <http://clinicaltrials.gov/ct2/show/NCT01763203?term=NCT01763203&rank=1>

Publishing Title: Secondary Stroke Prevention By Uniting Community And Chronic Care Model Teams Early To End Disparities: The Succeed Trial

Author Block: Amytis Towfighi, Univ of Southern California, Los Angeles, CA; Eric M. Cheng, Univ of California - Los Angeles, Los Angeles, CA; Nerses Sanossian, Univ of Southern California, Los Angeles, CA; Robert Bryg, Olive View-UCLA Medical Ctr, Sylmar, CA; Bijal Mehta, Harbor-UCLA Medical Ctr, Torrance, CA; Ali Razmara, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Lillie Hudson, Rancho Los Amigos Natl Rehabilitation Ctr, Los Angeles, CA; Heather McCreath, Univ of California - Los Angeles, Los Angeles, CA; Monica Ayala Rivera, Theresa Sivers-Teixera, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Jamie Tran, Harbor-UCLA Medical Ctr, Torrance, CA; Marilyn Corrales, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Elizabeth Mojarro-Huang, Univ of Southern California, Los Angeles, CA; Ana Montoya, Harbor-UCLA Medical Ctr, Torrance, CA; Beatrice Martinez, Univ of Southern California, Los Angeles, CA; Cynthia Munoz, Rancho Los Amigos Natl Rehabilitation Ctr, Downey, CA; Phyllis Willis, Watts Labor Community Action Committee, Watts, CA; Mireya Macias, Worker Education And Resource Ctr, Los Angeles, CA; Nancy Ibrahim, Esperanza Community Housing, Los Angeles, CA; Shinyi Wu, Magaly Ramirez, Univ of Southern California, Los Angeles, CA; Jeremy Wacksman, Dimagi, Inc., Cambridge, MA; Brian Mittman, Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, CA; William Cunningham, Frances Barry, Honghu H. Liu, David Ganz, Univ of California - Los Angeles, Los Angeles, CA; Diane Factor, Worker Education and Resource Ctr, Los Angeles, CA; Barbara G. Vickrey, Univ of California - Los Angeles, Los Angeles, CA

Abstract Body: Background: Recurrent stroke risk is substantially reduced by controlling risk factors such as hypertension, diet, physical activity, diabetes, and smoking; yet these factors are sub-optimally controlled in most stroke survivors, particularly among indigent, minority populations, who have barriers to accessing care. Objective: Develop and test the impact of a community-based, Chronic Care Model intervention on control of systolic blood pressure (SBP) among individuals with recent stroke or TIA, enrolled from 4 safety-net hospitals of the 2nd largest municipal health system in the U.S.

Design: Randomized-controlled trial.

Population Studied: 500 adults (>40 yrs) with stroke or TIA (<90 days prior), recruited from 4 Los Angeles County-Department of Health Services hospitals. Individuals with SBP <120 mm Hg, who do not speak English, Spanish, Korean, Mandarin, or Cantonese or are unable to comprehend the study are excluded.

Interventions:

Subjects randomized to intervention are managed by a care manager (nurse practitioner or physician's assistant)- community health worker (CHW) team, using evidence-based algorithms and supervised by a physician. Subjects receive self-management tools including goal cards and BP monitors. CHWs lead Chronic

Disease Self-Management classes and conduct home visits to: (1) reinforce self-management skills; (2) assist in healthcare system navigation; and (3) assess for social isolation and depression. CHWs use tablets with an application that provides decision support, tracks tasks, and guides care management. Subjects randomized to control receive usual care and handouts on controlling risk factors.

Outcomes Measurements: Primary: SBP control. Secondary: control of risk factors, stroke knowledge, healthy lifestyle habits, medication adherence.

Analysis: Intention-to-treat analysis will be conducted to determine whether persons in the intervention achieve better outcomes than persons in the control arm at 12 months. A cost analysis and sustainability plan will be developed.

Trial Status: Enrolling subjects

Author Disclosure Block: A. Towfighi: None. E.M. Cheng: None. N. Sanossian: None. R. Bryg: None. B. Mehta: None. A. Razmara: None. L. Hudson: None. H. McCreath: None. M. Ayala Rivera: None. T. Sivers-Teixera: None. J. Tran: None. M. Corrales: None. E. Mojarro-Huang: None. A. Montoya: None. B. Martinez: None. C. Munoz: None. P. Willis: None. M. Macias: None. N. Ibrahim: None. S. Wu: None. M. Ramirez: None. J. Wacksman: None. B. Mittman: None. W. Cunningham: None. F. Barry: None. H.H. Liu: None. D. Ganz: None. D. Factor: None. B.G. Vickrey: None.

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Presentation Number: CT P33

Trial Abbreviation: none

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Trial Email: mai.n.nguyen-huynh@kp.org

Trial Name: Shake Rattle & Roll

Trial Registry Number ID: NCT01892592

Trial Sponsor: NINDS

Trial Web Site: www.bringitdownstudy.org

Publishing Title: Shake, Rattle & Roll Trial

Author Block: Mai N Nguyen-Huynh, Nolle T Blick, Joseph D Young, Bette Caan, Susan Brown, Julie Schmittdiel, Stephen Sidney, Kaiser Permanente, Oakland, CA

Abstract Body: Background: In the US, blacks have a higher prevalence of hypertension (HTN) and a higher incidence of ischemic stroke compared to whites. In Kaiser Permanente Northern California (KPNC), a setting where all members have similar access to healthcare and a very high overall rate of HTN control, blacks still had poorer blood pressure (BP) control than whites (77% vs 82% controlled). It has been suggested that greater difficulty in controlling BP and lifestyle differences may account for this difference. The “Shake, Rattle and Roll” trial is named for: 1) “shake” the salt habit; 2) “rattle” the intensity of current BP management; and 3) adapt and “roll” out the interventions to other communities.

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

Design: a pragmatic clustered randomized controlled trial

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

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

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

Analysis: No final analysis yet because the trial is in follow-up phase.

Trial Status: We cluster randomized 107 PCPs and their panels to one of 3 arms. To date, we have identified 3599 black patients with uncontrolled BP for the usual care arm, 3940 for enhanced monitoring, and 3475 for lifestyle arm. We have completed enrollment with 3113 enrolled in usual care, and 349 consented to be in the enhanced arm and 305 in the lifestyle arm. Median age across all arms was 62 with a range of 20 to 85 years old.

Author Disclosure Block: M.N. Nguyen-Huynh: None. N.T. Blick: None. J.D. Young: None. B. Caan: None. S. Brown: None. J. Schmittdiel: None. S. Sidney: None.

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Presentation Number: CT P34

Trial Abbreviation: StrokeNet

Trial Contact Information: Judith Spilker, RN, BSN Administrative Director Spilkeja@ucmail.uc.edu (513) 558-5430

Trial Email: spilkeja@ucmail.uc.edu

Trial Name: The NIH StrokeNet

Trial Registry Number ID: none

Trial Sponsor: NINDS

Trial Web Site: <https://nihstrokenet.org/>

Publishing Title: The National Institutes of Health Stroke Network (NIH StrokeNet)

Author Block: **Joseph P Broderick**, Univ of Cincinnati Academic Health Ctr, Cincinnati, OH; **Yuko Y Palesch**, Medical Univ of South Carolina, Charleston, SC; for the NIH StrokeNet

Abstract Body: Background

The 2012 Stroke Progress Review Group and National Institute of Neurological Disorders and Stroke (NINDS) identified the need for a highly collaborative multi-center stroke trial network infrastructure that would provide a robust, standardized, and accessible infrastructure to facilitate rapid development and implementation of NINDS-funded stroke trials focused on key interventions in stroke prevention, treatment, and recovery.

Objective

The network is designed to increase the efficiency and prioritization of stroke clinical trials by facilitating patient recruitment and retention, supporting novel methodologies and streamlined approaches to accelerate the development of promising stroke therapies.

Network Organization

In 2013 the NINDS awarded 25 Regional Coordinating Stroke Centers, a National Clinical Coordinating Center at the University of Cincinnati, and a National Data Management Center at the Medical University of South Carolina, to form the NIH StrokeNet. Efficiencies of the network are fostered through master trial agreements, central IRB, central pharmacy and investigational product distribution, common data elements, standard operating procedures, web-based Clinical Trial Management System, and clinical trials statistical expertise. The StrokeNet is poised to collaborate with other national and international consortia and includes a robust training program directed for stroke research.

Clinical Trials Proposal Processing through the StrokeNet

StrokeNet is an open network. Interested Investigators should contact the NINDS to determine whether a proposed stroke clinical trial is appropriate to be conducted within the network. Concepts approved by NINDS are referred to the StrokeNet to assess feasibility of implementation. Working with the Network, Investigators whose proposal is deemed feasible would then submit a full grant application in response to one of the StrokeNet Funding Opportunity Announcements for review by NINDS.

Discussion

StrokeNet provides a large efficient infrastructure to foster development and rapid implementation of NINDS-funded stroke trials.

Author Disclosure Block: **J.P. Broderick:** Research Grant; Modest; PRISMS Trial. Honoraria; Modest; Boehringer Ingelheim. Consultant/Advisory Board; Modest; Pfizer, Inc., The George Institute for Global Health. **Y.Y. Palesch:** None.

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Presentation Number: CT P35

Trial Abbreviation: CMOSS

Trial Contact Information: CMOSS,
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Trial Email: jiaoliquan@gmail.com

Trial Name: Carotid and Middle cerebral artery Occlusion Surgery Study

Trial Registry Number ID: NCT01758614

Trial Sponsor: 'Five-twelfth' National Science and Technology Support Program

Trial Web Site: <http://www.clinicaltrials.gov/ct2/show/NCT01758614?term=CMOSS&rank=2>

Publishing Title: Carotid And Middle Cerebral Artery Occlusion Surgery Study - New Trial Post 'COSS' In China

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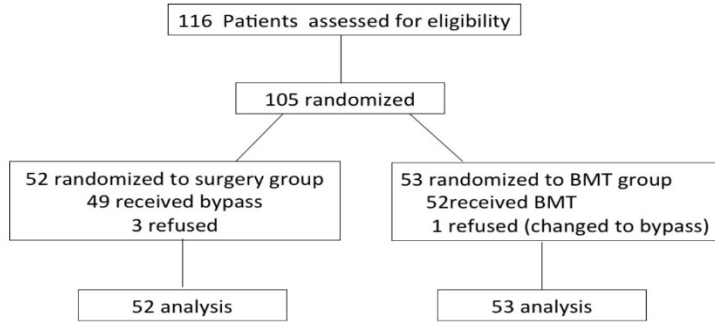
Abstract Body: CMOSS is designed to compare the safety and efficacy of EC-IC bypass surgery with medical therapy in patients with symptomatic ICA or MCA occlusion. It is the sub-project of 'Five-twelfth' National Science and Technology Support Program funded by Chinese government. It is a randomized single-blinded controlled trial and plans to enroll 330 patients with equal randomization to surgical and optimal medical treatment groups. The cerebrovascular hemodynamic is evaluated by CTP. CMOSS is the first RCT to evaluate the EC-IC bypass surgery sponsored by developing country. It is also the first RCT to evaluate the cerebrovascular hemodynamics by CTP in patients with ICA or MCA occlusion. Intracranial occlusion in Asia is much more popular than that in European or North America which could be the guarantee for patients' enrollment. It also selects more experienced neurosurgeons (acting as chief surgeon in at least 15 consecutive previous EC-IC bypass surgery with graft patency greater than 95% and perioperative stroke and death rate less than 10%) to attend the trial to minimize the perioperative complications. Because of the continuity of 'Five-twelfth' Program, the follow-up for these patients might be prolonged to more than 2 years. That could disclose more information after 'crossing-over curves' in COSS. Till 1st OCT 2014, there were 116 patients enrolled in it.



Chinese Doctors' Duty & Honor
Opportunity for Bypass surgery
We hope a satisfied result in 2yrs
We need your help

CMOSS

Current status of CMOSS enrollment



Author Disclosure Block: Y. Ma: None. Y. Gu: None. X. Tong: None. Z. Tong: None. D. Wang: None. J. Wang: None. L. Duan: None. D. Kuai: None. M. AiLi: None. J. Ren: None. Y. Huang: None. C. Huang: None. X. Wang: None. J. Yu: None. Y. Huang: None. Y. Cai: None. F. Ling: None.

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Presentation Number: CT P36

Trial Abbreviation: NeuSTART 2

Trial Contact Information: Harmon Moats, hlm9@columbia.edu, 2123051658, 2123051710

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Trial Name: Neuroprotection With Statin Therapy for Acute Recovery Trial Phase 2

Trial Registry Number ID: NCT01976936

Trial Sponsor: NINDS

Trial Web Site: none

Publishing Title: Neuroprotection with Statin Therapy for Acute Recovery Trial 2

Author Block: **Mitchell S. Elkind**, Ken Cheung, Harmon Moats, Rebeca Aragon Garcia, Howard Andrews, Greg Neils, Tomoko Kitago, Alberto Canaan, Wayna Paulino, Columbia Univ, New York, NY; Mandip S. Dhamoon, Emma Karlin, Icahn Sch of Med at Mount Sinai, New York, NY; Steven K. Feske, Sarah J. Clark, Harvard Medical Sch, Boston, MA; Sidney Starkman, Judy Guzy, Univ of California-Los Angeles, Los Angeles, CA; Jose Romano, Andrea Escobar, Univ of Miami, Miami, FL; Michael T. Mullen, Nichole Gallatti, Univ of Pennsylvania, Philadelphia, PA

Abstract Body: Background: Statins, due to anti-inflammatory and other pleiotropic effects, have dose-dependent neuroprotective effects when administered acutely after ischemic stroke. The role of statins at high doses administered immediately after acute ischemic stroke has not been determined.

Objectives: Primary Aim: To determine whether lovastatin 640 mg daily for 3 days beginning within 24 hours after acute stroke can be administered safely (<10 percentage points higher risk of myotoxicity and/or hepatotoxicity).

Secondary Aim: To assess efficacy of lovastatin administered at high doses.

Design and Outcomes: A phase 2 safety study in which ischemic stroke patients will be randomized within 24 hours of symptom onset to placebo (or the dose equivalent of lovastatin for those already on statins) or oral lovastatin 640 mg per day for 3 days. The primary outcome of this Phase 2 safety study will be musculoskeletal and hepatic toxicity, defined by clinical and laboratory criteria, with a 3 month follow-up period. Secondary outcomes will include neurological outcome (NIH Stroke Scale), functional outcomes (Barthel Index), and handicap (modified Rankin scores). Effects on inflammatory markers, lipid levels, and coagulation effects will also be assessed.

Interventions and Duration: Either (1) placebo or (for those already on statins) standard dose lovastatin 80 mg daily versus (2) short-term high-dose lovastatin 640 mg per day for 3 days. Patients will be followed for 90 days for clinical outcome events and laboratory tests. After three days, patients are treated with standard statin therapy.

Sample Size and Population: One hundred sixty eight patients with acute ischemic stroke presenting within 24 hours of stroke symptom onset.

Study Update: After performance of *in vitro* clot lysis assays, the FDA granted permission to include patients receiving intravenous tissue plasminogen activator. As of November 5, 2014, 104 patients had been enrolled at 7 participating sites. Two DSMB meetings have permitted continuation of the study with a minor modification (ensuring that patients after stroke receive statin medications and other secondary preventive treatments according to currently accepted guidelines).

Author Disclosure Block: **M.S.V. Elkind:** Expert Witness; Significant; Merck/Organon. Consultant/Advisory Board; Modest; BMS/Pfizer Partnership, Boehringer-Ingelheim, Inc., Janssen Pharmaceuticals, Daichii-Sankyo, Biogen IDEC. **K. Cheung:** None. **H. Moats:** None. **R. Aragon Garcia:** None. **H. Andrews:** None. **G. Neils:** None. **T. Kitago:** None. **A. Canaan:** None. **W. Paulino:** None. **M.S. Dhamoon:** None. **E. Karlin:** None. **S.K. Feske:** None. **S.J. Clark:** None. **S. Starkman:** None. **J. Guzy:** None. **J. Romano:** None. **A. Escobar:** None. **M.T. Mullen:** None. **N. Gallatti:** None.

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Presentation Number: CT P37

Trial Abbreviation: TARDIS

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Trial Email: tardis@nottingham.ac.uk

Trial Name: Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke

Trial Registry Number ID: ISRCTN47823388

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.tardistrial.org

Publishing Title: Triple Antiplatelets for Reducing Dependency after Ischaemic Stroke (TARDIS). A randomised controlled trial.

Author Block: Kailash Krishnan, Hayley Foster, Tanya Payne, Margaret Adrian, Joanne Keeling, Harriet Howard, Michael Stringer, Katie Robson, **Philip M Bath**, Univ of Nottingham, Nottingham, United Kingdom

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

Design: TARDIS is a multicentre, parallel-group, prospective, randomised, open-label, blinded-endpoint, controlled trial. In the start-up (3 years) phase, we assessed the safety, tolerability and feasibility of intensive antiplatelet therapy (ACD) versus guideline therapy given for 1 month in 902 patients with acute stroke/TIA. The main 5 year phase will assess the safety and efficacy of intensive or guideline therapy in up to 4,100 patients. The primary outcome is ordinal stroke severity (fatal/severe non-fatal/mild/TIA/none) at 90 days. Secondary outcomes include death, myocardial infarction (MI), vascular events, function, bleeding, serious adverse events; sub-studies will assess cerebral emboli and platelet function.

Trial status: The main phase of the trial commenced on 1st October, 2012, and will run for 5 years. As of 3rd November, 2168 patients have been recruited from 102 centres (UK, Denmark, Georgia, New Zealand).

Funding: The National Institute of Health Research, Health and Technology Assessment Programme

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Author Disclosure Block: **K. Krishnan:** None. **H. Foster:** None. **T. Payne:** None. **M. Adrian:** None. **J. Keeling:** None. **H. Howard:** None. **M. Stringer:** None. **K. Robson:** None. **P.M.W. Bath:** None.

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Presentation Number: CT P38

Trial Abbreviation: REM-PROTECT

Trial Contact Information: Latisha K. Ali, Latisha K Ali, MD 310-794-6379 lali@mednet.ucla.edu Contact: Johanna Avelar, BA 310-825-6930 LAvelar@mednet.ucla.edu

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Trial Name: Remote Preconditioning Over Time to Empower Cerebral Tissue

Trial Registry Number ID: NCT02169739

Trial Sponsor: AHA Bugher Foundation

Trial Web Site: <http://bugher.healthsciences.ucla.edu/>

Publishing Title: Remote Preconditioning Over Time to Empower Cerebral Tissue (REM-PROTECT) Study

Author Block: **Latisha Ali**, UCLA STROKE CENTER, Los Angeles, CA; David S Liebeskind, Neurovascular Imaging Res Core Univ of California Los Angeles, Los Angeles, CA; Johanna L Avelar, Jeffrey L Saver, UCLA STROKE CENTER, Los Angeles, CA

Abstract Body: Background and Objective: Remote ischemic preconditioning (RPreC) activates multiple endogenous cellular and molecular mechanisms that protect brain tissues against ischemia by applying repetitive short ischemic periods to a patient's limbs. RPreC has shown preliminary signals of efficacy in preventing ischemic stroke in small pilot trials in large artery atherosclerotic stroke and in cerebral vasospasm after subarachnoid hemorrhage. We plan to evaluate RPreC as a novel therapeutic strategy to prevent stroke, progressive ischemic brain injury and cognitive decline in patients with moderate to severe cerebral small vessel ischemic disease.

Design: This is a single site, feasibility dose-ranging randomized trial of ischemic preconditioning. 60 enrolled patients will be randomized to best standard medical care (BSMC) plus active RPreC versus BSMC alone.

Intervention: During periods of active treatment, RPreC will be induced using a device which delivers four remote ischemic conditioning cycles of 5 minute intervals followed by 5 minutes of normal blood flow around both upper body extremities. The RPreC intervention will be add-on therapy to guideline-based BSMC.

Outcome Measures: Primary outcome measures will be obtained at the end of the first randomized year.

Successful completion of this trial will delineate the feasibility and safety. We plan to explore biomarker indicators of potential efficacy, of inducing brain ischemic tolerance by measuring volumetric progression of white matter ischemic injury on diffusion tensor imaging and cognitive battery performance, ecologic ambulation assessment, and recurrent stroke events.

Analysis: The primary endpoints are descriptive statistics describing the implementation of the RPreC procedure, including behavioral adherence to treatment, physiologic attainment of limb ischemia, and patient self-reported comfort-discomfort during treatment. The procedure will be considered adequately feasible if adherence and physiologic targets are attained in 75% or more of cases. At this early stage of development, observations and lessons from individual cases may warrant procedural protocol changes to optimize the intervention.

Trial Status: Actively recruiting as of October 2014. (NCT02169739)

Author Disclosure Block: **L. Ali:** Research Grant; Modest; AHA Bugher Foundation Award. **D.S.**

Liebeskind: Consultant/Advisory Board; Modest; Consultant to Stryker and Covidien. **J.L. Avelar:** None. **J.L.**

Saver: Employment; Modest; Dr. Saver is an employee of the University of California. The University of

California, Regents receive funding for Dr Saver's services as a scientific consultant regarding trial design and conduct to. Research Grant; Modest; Dr Saver has served as an unpaid site investigator in multicenter trials run by Lundbeck for which the UC Regents received payments on the basis of clinical trial contracts for the number of subjects. Consultant/Advisory Board; Modest; Dr. Saver serves as an unpaid consultant to Genentech advising on the design and conduct of the PRISMS trial; neither the University of California nor Dr. Saver received any payments for this voluntar. Other; Modest; The University of California has patent rights in retrieval devices for stroke.

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Presentation Number: CT P39

Trial Abbreviation: WEAVE

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Trial Email: Lisha.Capucion@Stryker.com

Trial Name: Wingspan StEnt System Post Market SurVEillance Study

Trial Registry Number ID: NCT02034058

Trial Sponsor: Stryker Neurovascular

Trial Web Site: <http://clinicaltrials.gov/show/NCT02034058>

Publishing Title: Interim Report on the WEAVE Trial: Wingspan StEnt System Post Market SurVEillance Study

Author Block: **Michael J. Alexander**, Cedars-Sinai Medical Ctr, Los Angeles, CA; Alois Zauner, Santa Barbara Cottage Hosp, Santa Barbara, CA; John C. Chaloupka, Mount Sinai Medical Ctr, Miami, FL; Blaise Baxter, Erlanger Medical Ctr, Chattanooga, TN; Richard Callison, SSM DePaul Medical Ctr, St. Louis, MO; Wengui Yu, Cedars-Sinai Medical Ctr, Los Angeles, CA

Abstract Body: Introduction: Indications for revascularization of symptomatic high grade intracranial atherosclerotic stenoses with the Wingspan Stent system were initially defined by the HDE approval of the device. The subsequent SAMMPRIS trial investigated the off-label use of the device under an IDE, but did not show beneficial outcomes. The FDA and the manufacturer have revised the indications for use to be limited to patients who present with a stroke with greater than 70% stenosis, who have failed medical therapy. The WEAVE Trial is a prospective, consecutive enrollment, single-arm, post market surveillance trial evaluating peri-procedural outcomes in patients with this revised indication for use. The total target enrollment for the study is 389 patients.

Methods: Investigators are trained regarding best practices for the intervention and periprocedural patient management, and are advised to treat patients on-label. Based on prior study data, Investigators are advised to delay intervention until greater than 7 days following the patient's last stroke. Selected sites are assessing anti-platelet function studies to verify therapeutic effects. Separate data are being collected regarding perforator proximity to the target lesion, vessel tortuosity, and hemodynamic status based on perfusion studies. Primary outcomes include any peri-procedural stroke, death, or symptomatic hemorrhage in patients treated for the on-label indication. Formal clinical assessments in the peri-procedural period within the first four days are performed by an independent Neurologist.

Results: Currently 25 sites have been approved for patient enrollment in this first year of the study. The mean case experience of Wingspan stents that the site principal investigators had at the initiation of the study was 61 cases. Thusfar, with the initial patient enrollment, safety parameters defined by the FDA review for the study have been met, and greater than 90% of the study cases have been on label. Outlier cases are closely reviewed by the study's Medical Advisory Committee.

Conclusions: WEAVE will help define patient selection criteria and safety parameters for on label intracranial stenting for patients who have failed medical therapy for intracranial atherosclerotic disease.

Author Disclosure Block: **M.J. Alexander:** Research Grant; Significant; Stryker Neurovascular. **A. Zauner:** Consultant/Advisory Board; Modest; Stryker Neurovascular. **J.C. Chaloupka:** Consultant/Advisory Board;

Modest; Stryker Neurovascular. **B. Baxter:** Consultant/Advisory Board; Modest; Stryker Neurovascular. **R. Callison:** None. **W. Yu:** Research Grant; Modest; Stryker Neurovascular.

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Presentation Number: CT P40

Trial Abbreviation: ENCHANTED

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Trial Email: ENCHANTED@georgeinstitute.org.au

Trial Name: The ENhanced Control of Hypertension ANd Thrombolysis stroke stuDy

Trial Registry Number ID: NCT01422616; ACTRN12611000236998; ISRCTN82387104; EudraCT 2011-005545-12

Trial Sponsor: National Health and Medical Research Council (NHMRC) of Australia; Stroke Association of the UK

Trial Web Site: <http://enchanted.org.au>

Publishing Title: Low-dose Rtpa In Acute Ischemic Stroke: The Enhanced Control Of Hypertension And Thrombolysis Stroke Study (enchanted)

Author Block: **Craig Anderson**, George Inst Intl Health, Sydney NSW, Australia; Pablo Lavados, Clinica Alemana-Univ del Desarrollo, Santiago, Chile; Vijay Sharma, Natl Univ Hosp, Singapore, Singapore; Yining Huang, Peking Univ First Hosp, Beijing, China; Nguyen Thang, 115 Hosp, Ho Chi Minh city, Viet Nam; Tom Robinson, Univ Leicester, Leicester, United Kingdom; Tsong-Hai Lee, Chang Gung Memorial Hosp, Taipei, Taiwan; Jong Sun Kim, Asun Med Ctr, Seoul, Korea, Democratic People's Republic of; Richard Lindley, Hisatomi Arima, George Inst Global Health, Sydney NSW, Australia; Mark Parsons, Chris Levi, John Hunter Hosp, Univ of Newcastle, Newcastle, Australia; Sheila Martins, Hosp das Clinicas, Porto Alegre, Brazil

Abstract Body: Background: Controversy exists over the optimal dose (0.6 vs 0.9 mg/kg) of intravenous (IV)-rtPA in acute ischemic stroke. Studies indicate that low-dose IV-tPA improves outcomes through lower risk of intracerebral haemorrhage.

Aims: ENCHANTED will assess in IV-rtPA-eligible patients whether 0.6 mg/kg IV-rtPA provides equivalent benefits and lower risk of ICH than 0.9 mg/kg IV-rtPA.

Methods: An independent, quasi-factorial, active-comparative, prospective, randomised, open, blinded endpoint (PROBE), clinical trial evaluating IV-rtPA dose and level of BP control using central internet randomisation of patients who fulfil local criteria for rtPA. Since the study commenced in March 2012, 2153 patients have been included in the rtPA dose arm as of November 3 2014 across a global network (100+ sites; 13 countries), to achieve the required sample size of ~3300 (1650 per treatment arm) to provide >90% power to detect non-inferiority of low-dose IV-tPA. The study is funded by the Australian government (NHMRC project grant 1020462).

Conclusions: Recruitment is ahead of schedule and due for completion at the end of 2014, with results announced in 2016. Low-dose IV-rtPA as well as early intensive BP lowering (trial arm B) could provide more affordable, safer and more effective thrombolytic treatment in ischaemic stroke worldwide.

Author Disclosure Block: **C. Anderson:** Speakers' Bureau; Modest; Takeda China, Covidien. Consultant/Advisory Board; Modest; Pfizer, The Medicines Company. Research Grant; Significant; National Health and Medical Research Council (NHMRC) of Australia. **P. Lavados:** None. **V. Sharma:** None. **Y. Huang:** None. **N. Thang:** None. **T. Robinson:** Research Grant; Significant; Stroke Association of the UK. **T. Lee:** None. **J. Kim:** None. **R. Lindley:** Research Grant; Significant; NHMRC. **H. Arima:** Research Grant;

Significant; NHMRC. **M. Parsons:** Research Grant; Significant; NHMRC. Other Research Support; Modest; Boehringer Ingelheim. **C. Levi:** Research Grant; Significant; NHMRC. Other Research Support; Modest; Boehringer Ingelheim. **S. Martins:** None.

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Presentation Number: CT P41

Trial Abbreviation: NONE

Trial Contact Information: kathreen jane a. Lara, kathreenjane@yahoo.com, (+63)917-599-2012

Trial Email: kathreenjane@yahoo.com

Trial Name: Efficacy of Nimodipine+Cilostazol in prevention of vasospasm after aneurysmal SAH

Trial Registry Number ID: Control # 15-ISC-CT-5136-AHA

Trial Sponsor: --

Trial Web Site: NONE

Publishing Title: Efficacy Of Cilostazol+ Nimodipine In Cerebral Vasospasm Following Aneurysmal Subarachnoid Haemorrhage: A Prospective, Randomized, Single-blind Trial Preliminary Results

Author Block: **Kathreen Jane A Lara**, Jose R. Reyes Memorial Medical Ctr, Tuguegarao City, Philippines; Jose Navarro, Jose R. Reyes Memorial Medical Ctr, Manila, Philippines

Abstract Body: Vasospasm has been one of the major complications of aneurysmal SAH that gives poorer prognosis amongst patients suffering from it. Although among cerebrovascular diseases, SAH accounts for only 2-5%, a higher mortality and morbidity rate is accounted for by its complications, ie. vasospasm. Objective. This clinical trial aimed to determine the efficacy of oral nimodipine+cilostazol in reducing vasospasm following aneurysmal SAH as compared to using nimodipine alone.

Design. This is an on-going prospective, randomized, single- blind, with intention-to-treat analysis. To have a 95% chance, with a significance level of 0.05, of detecting a 50% reduction in an incidence of cerebral vasospasm following aneurysmal SAH, a minimum of 44 patients were required. As of the time being, only 14 patients were recruited.

Patients and randomization. A computer generated ID was drawn to identify to which treatment will a patient be grouped.

Intervention. Group A received nimodipine 60mg q4 x 21days alone, while Group B received nimodipine 60mg q4 x 21days plus cilostazol 100mg q12 x 14days.

Monitoring and End points. Monitoring of the Lindegaard index (LI) from days 4 to 14 post ictus was done by a blinded technician. An LI > 3 indicates vasospasm (primary end point).

Preliminary results. This is an on-going study; hence statistical analyses have not been employed due to insufficient number of samples recruited at the present time being. Initial findings revealed lower mean values for LI of patients taking both nimodipine+cilostazol compared to those on nimodipine alone. Also, symptomatic vasospasm occurred more on those taking nimodipine alone.

Author Disclosure Block: **K.A. Lara:** None. **J. Navarro:** None.

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Presentation Number: CT P42

Trial Abbreviation: n/a

Trial Contact Information: Caryn McAllister, Caryn@HQHTherapy.com, NEICR.com, 203-914-1907 and phone 203-914-1903

Trial Email: n/a

Trial Name: PT and OT perception of usefulness of PSC in Home Environment

Trial Registry Number ID: n/a

Trial Sponsor: NEICR

Trial Web Site: n/a

Publishing Title: Usefulness of the Post Stroke Checklist in the Home Environment

Author Block: Caryn B McAllister, Peter J McAllister, New England Inst for Clinical Res, Stamford, CT

Abstract Body: The overall aim of this study is to evaluate the PSC with PTs and OTs. Specific aims of pilot testing the PSC in this sample are to evaluate the feasibility of incorporating the PSC into physical therapy/occupational therapy practice, and specifically in the home care environment, to evaluate PT/OTs perceptions of the usefulness of the PSC in physical therapy and occupational therapy practice (i.e. the extent to which the PSC helps PTs and OTs identify and manage post stroke problems), and to assess the relevance of the PSC to the practice of physical and occupational therapy for PT/OTs working with patients who have experienced a cerebral vascular event. One hundred home care OT/PTs will be targeted for recruitment in this study. Prior to administering the PSC to patients, PT/OTs will have training accredited by the Connecticut and New York Physical Therapy Associations (CPTA and NYPTA) on stroke and use of the PSC. PT/OTs will evaluate patients incorporating the PSC in homes. Following the PSC administration, PT/OTs will be asked to complete a satisfaction questionnaire and the pragmatic face and content validity test (PRAC-Test)¹⁶. Quantitative data including the PSC responses, time taken to complete the PSC, number of referrals made and data collected from the satisfaction questionnaire and PRAC test will be analyzed using SPSS software and descriptive statistics. Participation will be entirely voluntary and PTs/OTs will be reassured that their usual work will be unaffected if they choose not to participate in the study. Patients involved in this study will have experienced a stroke, and will be willing and able to participate, and have sufficient understanding of the aims of the study. Patients will be excluded with very severe neurological deficits or uncontrolled psychiatric conditions. Training for PT/OTs who agree to participate will include training on use of the PSC. Usefulness of the PSC will be measured via the pragmatic face and content validity test (PRAC-Test)¹⁶, which will be completed by the PT/OT following individual assessments with at least four patients. One PRAC-Test will be completed per clinician. A satisfaction questionnaire will also be completed by the PT/OT for each patient, following each PSC assessment .

Author Disclosure Block: **C.B. McAllister:** Research Grant; Modest; Allergan. Consultant/Advisory Board; Modest; Allergan and Ipsen. **P.J. McAllister:** Research Grant; Significant; Allergan. Speakers' Bureau; Significant; Allergan, Ipsen. Consultant/Advisory Board; Modest; Allergan, Ipsen, Acorda.

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Presentation Number: CT P43

Trial Abbreviation: BASE

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Trial Email: jeff.june@iscdx.com

Trial Name: Biomarkers of Acute Stroke Etiology

Trial Registry Number ID: NCT02014896

Trial Sponsor: Ischemia Care LLC

Trial Web Site: <http://clinicaltrials.gov/show/NCT02014896>

Publishing Title: Biomarkers of Acute Stroke Etiology

Author Block: Jeffrey June, Ischemia Care, Cincinnati, OH

Abstract Body: Background

The cause of ischemic stroke (IS) remains uncertain (or cryptogenic) in up to 40% of cases. Undetected atrial fibrillation (AF) during evaluation for cause of IS is a significant risk factor for recurrent events. A blood test based upon RNA expression could be used to stratify IS patients by cause and reduce the number of cryptogenic events to ensure appropriate treatment regimens are adopted to prevent recurrence.

Objectives

Clinically validate a blood test to:

1. Differentiate between clinically diagnosed cardioembolic and large artery atherosclerotic IS.
2. Categorize cryptogenic strokes, as cardioembolic or large artery atherosclerotic when standard clinical testing cannot determine the cause.
3. Further sub classify cardioembolic strokes into those caused by AF and those not caused by AF.

Design

800 subject multi-site observational prospective study. Serial samples are drawn at enrollment, 24h and 48h. 60 day follow up. Samples are run on microarrays and analyzed in the Ischemia Care (CLIA) laboratory.

Study Population

1. IS patients
2. Normal controls matched with patients for age, race, gender, smoking, plus vascular risk factors

Inclusion Criteria

- Patients >18 years of age
- Symptoms suggestive of IS
- Arrival to hospital within 8h of symptom onset or last known normal time
- CT/ MRI ruling out other pathology

Exclusion Criteria

- Central nervous system infection (30 day)
- Head trauma, stroke or intracranial hemorrhage (30 day)
- Cancer
- Autoimmune or infectious diseases
- Major surgery (90 day)

Outcome

Clinically validated algorithm.

Status

Enrolling at 6 stroke centers and ~ 130 subjects enrolled through Oct 2014

Author Disclosure Block: J. June: Employment; Significant; CEO Ischemia Care. Ownership Interest; Significant; Founder / CEO Ischemia Care.

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Presentation Number: CT P44

Trial Abbreviation: RIGHT-2

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Fax: +44 (0)115 8231771

Trial Email: Philip.bath@nottingham.ac.uk

Trial Name: Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2

Trial Registry Number ID: CRM 0022101

Trial Sponsor: University of Nottingham, United Kingdom

Trial Web Site: www.right2-trial.org

Publishing Title: Rapid Intervention With Glyceryl Trinitrate In Hypertensive Stroke Trial-2 (right-2): Assessment Of Safety And Efficacy Of Transdermal Glyceryl Trinitrate, A Nitric Oxide Donor, And Of The Feasibility Of A Multicentre Ambulance-based Stroke Trial.

Author Block: Timothy England, Univ of Nottingham, Nottingham, United Kingdom; Malcolm Jarvis, Private, Nottingham, United Kingdom; Alan Montgomery, Univ of Nottingham, Nottingham, United Kingdom; Stuart Pocock, London Sch of Hygiene and Tropical Med, London, United Kingdom; John Potter, Univ of East Anglia, Norwich, United Kingdom; Christopher Price, Univ of Newcastle, Newcastle, United Kingdom; Tom Robinson, Univ Hosp of Leicester, Leicester, United Kingdom; Christine Roffe, Keele Univ, Keele, United Kingdom; Niroshan Siriwardena, Univ of Lincoln, Lincoln, United Kingdom; Nikola Sprigg, Univ of Nottingham, Nottingham, United Kingdom; Joanna Wardlaw, Univ of Edinburgh, Edinburgh, United Kingdom; Hayley Foster, **Philip M Bath**, Univ of Nottingham, Nottingham, United Kingdom

Abstract Body: Rationale:

High blood pressure (BP) is common in acute stroke and is associated with poor outcome. Previous hospital-based trials testing the effects of BP lowering on functional outcome have been inconclusive. The PIL-FAST and RIGHT pilot trials confirmed the feasibility of performing single centre UK ambulance-based stroke trials. In both RIGHT and in a subgroup of patients recruited within 6 hours into the large ENOS trial, transdermal glyceryl trinitrate (GTN), a nitric oxide donor, lowered BP and reduced death or disability. Based on these results, RIGHT-2 aims to test the safety and efficacy of transdermal GTN in the pre-hospital setting.

Methods

Paramedics from 5 UK ambulance services serving 30 comprehensive or primary stroke care centres will screen, consent, randomise and treat 850 patients presenting within 4 hours of FAST-positive stroke and with systolic BP >120 mmHg. Treatment will comprise GTN or similar sham patch, and will be continued in hospital for 3 days. The primary outcome will be the modified Rankin Scale at day 90. Secondary outcomes include vascular events, disability, quality of life, mood and cognition. Neuroimaging and biomarkers will examine potential mechanisms of action. Recruitment will commence in quarter 1/2 2015.

Funding: British Heart Foundation

Author Disclosure Block: T. England: None. M. Jarvis: None. A. Montgomery: None. S. Pocock: None. J. Potter: None. C. Price: None. T. Robinson: None. C. Roffe: None. N. Siriwardena: None. N. Sprigg: None. J. Wardlaw: None. H. Foster: None. P.M.W. Bath: None.

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Presentation Number: CT P45

Trial Abbreviation: HeadPoST

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Trial Email: headpost@georgeinstitute.org.au

Trial Name: Head Position in Acute Stroke

Trial Registry Number ID: NCT02162017; ACTRN12614000483651

Trial Sponsor: National Health and Medical Research Council (NHMRC) of Australia

Trial Web Site: <http://www.headpost.org.au>

Publishing Title: Head Position in Stroke Trial (HeadPoST)

Author Block: **Craig Anderson**, George Inst Global Health, Sydney NSW, Australia; Verónica Olavarría, Clínica Alemana de Santiago, Univ del Desarrollo, Santiago, Chile; Hisatomi Arima, Maree Hackett, George Inst Global Health, Sydney NSW, Australia; Sandy Middleton, Australian Catholic Univ & St Vincent's Health, Sydney NSW, Australia; Caroline Watkins, Univ of Central Lancashire, Preston, United Kingdom; Thompson Robinson, Univ of Leicester, Leicester, United Kingdom; Alejandro Brunser, Clínica Alemana de Santiago, Univ del Desarrollo, Santiago, United Kingdom; Bin Peng, Liying Cui, Dept of Neurology, Peking Union Medical Coll Hosp, Chinese Academic Medical Science, Beijing, China; Pablo Lavados, Clínica Alemana de Santiago, Univ del Desarrollo, Santiago, Chile

Abstract Body: Background: There is insufficient evidence to recommend a specific head position in patients with either acute ischemic stroke (AIS) or intracerebral hemorrhage (ICH). Observational data indicate potential benefits of lying flat in AIS and conversely sitting up in ICH, but these may be offset by increased risks of aspiration pneumonia and cardiac-respiratory failure.

Aims: To compare the effects of lying flat (0°) with sitting up (≥30°) head position applied in the first 24 hours of admission for patients presenting with acute stroke on poor outcome (death or disability) at 90 days. Key secondary aims are to determine: if lying flat is superior to sitting up on poor outcome at 7 days in AIS; and if sitting up is superior to lying flat on these outcomes in acute ICH.

Methods: A multicenter, prospective, cluster randomized, crossover, blinded outcome assessed, clinical trial through a 140 hospitals in Australia, China, Chile, Brazil, and United Kingdom. Eligibility criteria will evaluate the treatment effect in a broad range of patients with AIS and ICH. Sample size is calculated on each hospital recruiting 140 consecutive patients (2 x 70 per randomized arm). Set-up of the study has been undertaken through 2014; patient recruitment will occur during 2015-2016. The study is funded by the National Health and Medical Research Council (NHMRC) of Australia.

Conclusions: Given uncertainty over benefits/risks, and variability regarding the ideal head position for stroke patients around the world, reliable randomized evidence is required to standardize clinical practice to produce optimal outcomes.

Author Disclosure Block: **C. Anderson**, Takeda China, Covidien, Modest, Speakers' Bureau; Pfizer, The Medicines Company, Modest, Consultant/Advisory Board; National Health and Medical Research Council (NHMRC) of Australia, Significant, Research Grant; **V. Olavarría**, None; **H. Arima**, National Health and Medical Research Council (NHMRC) of Australia, Significant, Research Grant; **M. Hackett**, Research Fellowship of the National Health and Medical Research Council (NHMRC) of Australia, Significant, Employment; National Health

and Medical Research Council (NHMRC) of Australia, Significant, Research Grant; **S. Middleton**, NHMRC, Significant, Research Grant; **C. Watkins**, None; **T. Robinson**, Stroke Association of the UK, Significant, Research Grant; **A. Brunser**, None; **B. Peng**, None; **L. Cui**, None; **P. Lavados**, None.

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Presentation Number: CT P46

Trial Abbreviation: BEST-MSU study

Trial Contact Information: Stephanie Parker RN, stephanie.a.parker@uth.tmc.edu

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Trial Name: Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit Compared to Standard Management--BEST-MSU Study

Trial Registry Number ID: Clinicaltrials.govNCT02190500

Trial Sponsor: none

Trial Web Site: none

Publishing Title: Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit

Author Block: Stephanie A Parker, Ritvij Bowry, Tzu-Ching Wu, Elizabeth Noser, David Persse, Univ of Texas-Houston Medical Sch, Houston, TX; **James C Grotta**, Memorial Hermann Hosp, Houston, TX

Abstract Body: Objectives. The BEST-MSU study aims to answer 3 questions. 1. How much can a Mobile Stroke Unit (MSU) speed and increase treatment of ischemic stroke patients with tissue plasminogen activator (tPA) compared to standard management (SM)? 2. Can the doctor aboard the MSU be replaced by telemedicine (TM)? 3. What are the costs of implementing and maintaining a MSU and the health care costs of patients transported compared to SM.

Methods. The Houston MSU is staffed by a vascular neurologist (VN), registered nurse, CT technician, and paramedic and is activated following a 911 call to Emergency Medical Services (EMS) suggesting stroke symptoms, or call from an EMS first responder identifying a stroke patient, from 8 am-6 pm 7 days/week. On 50% of weeks, by blocked randomization, the MSU travels to the site of the call or rendezvous with EMS and evaluates the patient. If the patient meets inclusion criteria (symptom onset within 4.5 hours and meeting guidelines for tPA), they are enrolled into the study and moved into the MSU. If after CT scan and point of care lab testing on the MSU, the patient still fulfills criteria for tPA according to the on-site VN (the patient is simultaneously evaluated via TM with the remote VN making an independent decision), they are immediately given tPA and transported to one of 3 comprehensive stroke centers (CSC). If the patient doesn't meet tPA criteria, they are managed as per best practice for their diagnosis en route to the CSC. On the other 50% of weeks (SM weeks), the nurse meets the patient without the MSU, determines eligibility by the same criteria, but the patient transported and managed per current EMS routine. Informed consent is obtained at the CSC to obtain follow up data at 1, 3, 6 and 12 months in 248 patients to answer the 3 aims.

Results. During a 8 week lead in phase, 13 patients were treated with tPA on the MSU, 31% between 0-60 and 31% 61-80 minutes from onset, average on scene time 26 minutes, and no hemorrhagic or other complications. 11 other patients were enrolled but not treated (4 intracerebral hemorrhages, 3 seizures, 2 too mild, 2 other reasons).

Conclusion. The BEST-MSU trial has begun enrolling patients according to a randomized protocol.

Clinicaltrials.govNCT02190500

Author Disclosure Block: **S.A. Parker:** None. **R. Bowry:** None. **T. Wu:** None. **E. Noser:** None. **D. Persse:** None. **J.C. Grotta:** Research Grant; Modest; Genentech, Covidien. Consultant/Advisory Board; Modest; Frazer Ltd.

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Presentation Number: CT P47

Trial Abbreviation: ENCHANTED

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Trial Email: enchanted@georgeinstitute.org.au

Trial Name: The ENhanced Control of Hypertension ANd Thrombolysis stroke stuDy

Trial Registry Number ID: NCT01422616; ACTRN12611000236998; ISRCTN82387104; EudraCT 2011-005545-12

Trial Sponsor: National Health and Medical Research Council (NHMRC) of Australia

Trial Web Site: <http://www.enchanted.org.au>

Publishing Title: Intensive Blood Pressure Lowering In Acute Ischemic Stroke: Enchanted Trial

Author Block: **Craig Anderson**, George Inst Global Health, Sydney NSW, Australia; Pablo Lavados, Clinica Alemana-Univ del Desarrollo, Santiago, Chile; Vijay Sharma, Natl Univ Hosp, Singapore, Singapore; Huang Yining, Peking Univ First Hosp, Beijing, China; Nguyen Thang, 115 Hosp, Ho Chi Minh city, Viet Nam; Tom Robinson, Univ Leicester, Leicester, United Kingdom; Tsong-Hai Lee, Chang Gung Memorial Hosp, Taipei, Taiwan; Jong Sun Lim, Asun Med Ctr, Seoul, Korea, Democratic People's Republic of; Richard Lindley, Hisatomi Arima, George Inst Global Health, Sydney NSW, Australia; Mark Parsons, Chris Levi, John Hunter Hosp, Univ of Newcastle, Newcastle, Australia; Sheila Martins, Hosp das Clinicas, Clinicas Porto Alegre, Brazil

Abstract Body: Background: Controversy exists over the level of blood pressure (BP) control in the hyperacute phase of acute ischemic stroke. Studies indicate that more intensive control of elevated BP improves outcomes by reducing intracerebral hemorrhage (ICH) after rtPA.

Aims: ENCHANTED will assess in IV-rtPA-eligible patients whether intensive BP lowering (target systolic <140 mmHg) provides superior benefits and lower risk of any ICH compared to current BP guideline recommendations (systolic <180-185 mmHg).

Methods: An independent, quasi-factorial, active-comparative, prospective, randomised, open, blinded endpoint (PROBE), clinical trial evaluating both IV-rtPA dose and BP control using central internet randomisation of patients who fulfil local criteria for rtPA. Since the study commenced in March 2012, 660 patients have been included in the BP arm as of November 3 2014 across a global network (100+ sites; 13 countries), for a required sample of 2400 (1200 per arm) for >90% power to detect superiority of intensive BP lowering. The study is funded by the Australian government (NHMRC project grant 1020462).

Conclusions: Early intensive BP lowering and low-dose IV-rtPA (trial arm A) could provide more safer and more effective use of thrombolytic treatment in ischaemic stroke worldwide.

Author Disclosure Block: **C. Anderson:** Speakers' Bureau; Modest; Takeda China, Covidien. Consultant/Advisory Board; Modest; Pfizer, The Medicines Company. Research Grant; Significant; National Health and Medical Research Council (NHMRC) of Australia. **P. Lavados:** None. **V. Sharma:** None. **H. Yining:** None. **N. Thang:** None. **T. Robinson:** Research Grant; Significant; Stroke Association of the UK. **T. Lee:** None. **J. Lim:** None. **R. Lindley:** Research Grant; Significant; NHMRC. **H. Arima:** Research Grant; Significant; NHMRC. **M. Parsons:** Research Grant; Significant; NHMRC. **C. Levi:** Research Grant; Significant; NHMRC. **S. Martins:** None.

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Presentation Number: CT P48

Trial Abbreviation: CREST

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Trial Name: Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST): Long Term Follow-up (<= 10 Years)

Trial Registry Number ID: U01 NS038384

Trial Sponsor: NINDS/NIH

Trial Web Site: www.cresttrial.org

Publishing Title: Carotid Revascularization Endarterectomy Vs Stenting Trial (CREST): Progress Toward Publication Of 10-year Results

Author Block: Alice J Sheffet, Rutgers, The State Univ of New Jersey-New Jersey Medical Sch, Newark, NJ; George Howard, Virginia Howard, Univ of Alabama at Birmingham, Birmingham, AL; Ariane Mackey, CHU de Quebec, Quebec City, QC, Canada; William Brooks, Baptist Health Lexington, Lexington, KY; Michael D. Hill, Univ of Calgary, Calgary, AB, Canada; Judith Lichtman, Yale Univ, New Haven, CT; Jenifer H. Voeks, Medical Univ of South Carolina, Charleston, SC; Susan E. Hughes, MeeLee Tom, Rutgers, The State Univ of New Jersey-New Jersey Medical Sch, Newark, NJ; James F. Meschia, Thomas G. Brott, for the CREST Investigators, Mayo Clinic Florida, Jacksonville, FL

Abstract Body: BACKGROUND: NINDS extended CREST followup (F/U) to 10 years through 2016. Median F/U will be 7.5 years compared to 2.5 as originally reported.

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

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

POPULATION: 2502 symptomatic and asymptomatic CREST subjects

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

ANALYSIS: Statistical analysis (time-to-event modeling with adjustment for major baseline covariates) will assess post procedural treatment differences from Day 31 up to 10 years, providing 90% power to detect a hazard ratio of 1.67.

TRIAL STATUS: At 103 US and Canadian sites, 1303 (69.4% of surviving subjects) are active; 68 completed 10 years' F/U, and 1152 have consented to CMS database linkage to compare CREST patient outcomes to those in national databases for future publication.

Primary and secondary aims have been published in the New England Journal, Lancet Neurology, Circulation, Stroke, Clinical Trials and the Journal of Vascular Surgery. Recent articles appear in Stroke, the Journal of the American Heart Association and the International Journal of Stroke. CREST investigators are collaborating with European investigators (Carotid Stenting Trialists' Consortia) to merge data for meta-analysis and publications relating to carotid disease. We continue to focus on retention, data compliance and quality in

preparation for publication of the long term follow-up results planned in 2016.
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Author Disclosure Block: **A.J. Sheffet:** None. **G. Howard:** None. **V. Howard:** None. **A. Mackey:** None. **W. Brooks:** None. **M.D. Hill:** None. **J. Lichtman:** None. **J.H. Voeks:** None. **S.E. Hughes:** None. **M. Tom:** None. **J.F. Meschia:** None. **T.G. Brott, for the CREST Investigators:** None.

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Presentation Number: CT P49

Trial Abbreviation: CREST-2

Trial Contact Information: Dale Gamble, gamble.dale@mayo.edu, 844-956-1826

Trial Email: gamble.dale@mayo.edu

Trial Name: Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial

Trial Registry Number ID: NCT02089217

Trial Sponsor: NINDS

Trial Web Site: www.crest2trial.org

Publishing Title: Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis: CREST-2 Update

Author Block: **James F Meschia**, Mayo Clinic Jacksonville, Neurology, Jacksonville, FL; **Brajesh K Lal**, Univ of Maryland, Baltimore, MD; **George Howard**, Univ of Alabama Birmingham, Birmingham, AL; **Gary S Roubin**, Cardiovascular Associates of the Southeast., Birmingham, AL; **Robert D. Brown, Jr**, Mayo Clinic Rochester, Neurology, Rochester, MN; **Kevin M Barrett**, Mayo Clinic Jacksonville, Neurology, Jacksonville, FL; **Seemant Chaturvedi**, Univ of Miami Medical Sch, Miami, FL; **Marc Chimowitz**, Medical Univ of South Carolina, Charleston, SC; **Bart Demaerschalk**, Mayo Clinic Arizona, Neurology, Scottsdale, AZ; **Virginia J Howard**, Univ of Alabama Birmingham, Birmingham, AZ; **John Huston, III**, Mayo Clinic Rochester, Rochester, MN; **Ronald M Lazar**, Columbia Univ, New York, NY; **Wesley Moore**, UCLA, Los Angeles, CA; **Claudia Scala Moy**, NINDS, Bethesda, MD; **Tanya N Turan**, Jenifer Voeks, Medical Univ of South Carolina, Charleston, SC; **Thomas G Brott**, Mayo Clinic Jacksonville, Neurology, Jacksonville, FL; for the CREST-2 Investigators.

Abstract Body: Over 100,000 carotid revascularization procedures are done annually in the US for asymptomatic carotid arterial stenosis. The safety of carotid endarterectomy (CEA) and carotid stenting (CAS), and the efficacy of medical therapy in altering the progression of atherosclerosis have improved. Therefore, the applicability of prior randomized trials in asymptomatic carotid stenosis to current treatment decisions has been called into question.

The aim of the NINDS-funded CREST-2 is to compare CEA and optimal medical therapy (OMT) versus OMT alone (n=1240), and CAS and OMT versus OMT alone (n=1240), through two parallel randomized clinical trials at approximately 120 medical centers, including collaboration with NIH-StrokeNet. The composite primary outcome is any stroke or death within 44 days after randomization or ipsilateral ischemic stroke thereafter up to 4 years. Cognitive status will be assessed on a regular schedule through computer-assisted telephone interview. OMT is directed centrally and will include tight control of blood pressure (systolic target < 140 mm Hg) and cholesterol (LDL target < 70 mg/dl) as well as lifestyle coaching.

As of November 4, 2014, 73 centers have been approved by the CREST-2 Site Selection Committee.

Credentialing of surgeons and stent operators is ongoing, with 21 approved interventionalists, 64 conditionally approved interventionalists, and 92 approved surgeons. Conditionally approved interventionalists will be able to submit additional cases for review by performing CAS under the CREST-2 Registry. The first patient is expected to be randomized in winter, 2014. An update regarding the numbers of centers certified, surgeons and interventionalists credentialed, and cases randomized will be provided.

Author Disclosure Block: **J.F. Meschia:** None. **B.K. Lal:** None. **G. Howard:** None. **G.S. Roubin:** None. **R.D. Brown, Jr:** None. **K.M. Barrett:** None. **S. Chaturvedi:** None. **M. Chimowitz:** None. **B.**

Demaerschalk: None. **V.J. Howard:** None. **J. Huston, III:** None. **R.M. Lazar:** None. **W. Moore:** None. **C.S. Moy:** None. **T.N. Turan:** None. **J. Voeks:** None. **T.G. Brott:** None.

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Presentation Number: CT P50

Trial Abbreviation: C2R

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Trial Email: gamble.dale@mayo.edu

Trial Name: CREST-2 Companion Registry

Trial Registry Number ID: NCT02240862

Trial Sponsor: TBD

Trial Web Site: NA

Publishing Title: The CREST-2 Companion Registry: Quality Control For Carotid Stenting And Pathway To Reimbursement

Author Block: **Brajesh K. Lal**, Univ of Maryland, Baltimore, MD; Kenneth Rosenfield, Massachusetts General Hosp, Boston, MD; Donald Heck, Novant Health Forsyth Medical Ctr, Jacksonville, FL; Sean Tunis, Ctr for Medical Technology Policy, Baltimore, MD; Anthony Furlan, Univ Hosp Case Medical Ctr, Case Western Reserve Univ, Cleveland, OH; Gary Roubin, Cardiovascular Associates of the Southeast., Birmingham, AL; James F Meschia, Mayo Clinic Jacksonville, Jacksonville, FL; George Howard, Univ of Alabama, Birmingham, AL; Claudia Scala Moy, NINDS, Bethesda, MD; Robert Conley, Ctr for Medical Technology Policy, Baltimore, MD; Thomas G Brott, Mayo Clinic Jacksonville, Jacksonville, FL; for the CREST-2 Investigators.

Abstract Body: **PURPOSE:** The CREST-2 Companion Registry (C2R) was developed through multi-specialty input and collaboration with NINDS and the Centers for Medicare and Medicaid Services (CMS). The objective of C2R is to promote the rapid initiation and completion of enrollment in CREST-2.

METHODS AND MATERIALS: Interventionist eligibility for C2R will be determined by the multi-specialty CREST-2 Interventional Management Committee. Approved interventionists will enter individual patient data into 2 ongoing registries operated by the Society for Vascular Surgery (SVS) and the American College of Cardiology (ACC). The SVS and ACC registries will transfer the data to C2R. Patient eligibility will include symptomatic and asymptomatic patients, both standard CEA risk and high CEA risk, with severe carotid artery stenosis that is appropriate for stenting with an embolism protection device. The primary outcome will be the occurrence of any stroke or death within the 30-day period following the stenting procedure. Individual interventionists' C2R outcomes and procedural performance will help guide selection of interventionists for participation in the CREST-2 randomized clinical trial. Continued participation in the C2R will be contingent on optimal outcomes and satisfactory enrollment in the randomized CREST-2 Trial.

RESULTS: On September 17, 2014, CMS approved reimbursement for stenting performed on patients enrolled in CREST-2 and in C2R. Because CREST-2 and the C2R are covered under a national coverage determination, C2R-patient coverage by CMS does not require study sites to obtain approval from the CMS administrative contractors. Enrollment guidelines include 1) at least one operator must receive credentialing into CREST-2 within the first 75 total C2R cases or 30 CREST-2 eligible cases at the operator's site and 2) once the first interventionist at a site is credentialed to randomize into CREST-2, other operators may work toward credentialing, but the site must maintain an overall enrollment ratio of 1:1 into C2R versus CREST-2.

CONCLUSIONS: Enrollment into the C2R has been recently approved by NINDS and CMS to begin in 2014. Enrollment into C2R can continue until publication of the primary results from CREST-2.

Author Disclosure Block: **B.K. Lal:** None. **K. Rosenfield:** Other; Significant; – Abbott Vascular, – Atrium, – NIH, – InspireMD, – Lutonix-Bard. **D. Heck:** None. **S. Tunis:** None. **A. Furlan:** None. **G. Roubin:** Other; Modest; Medicines Co. Advisory Board. Other; Significant; Cook Inc. Royalties,, Essential Medical Equity. **J.F. Meschia:** None. **G. Howard:** None. **C.S. Moy:** None. **R. Conley:** None. **T.G. Brott:** None.

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Presentation Number: CT P51

Trial Abbreviation: CREST-2

Trial Contact Information: Dale Gamble, gamble.dale@mayo.edu, 844-956-1826

Trial Email: gamble.dale@mayo.edu

Trial Name: Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial

Trial Registry Number ID: NCT02089217

Trial Sponsor: NINDS

Trial Web Site: www.crest2trial.org

Publishing Title: CREST-2 and StrokeNet Collaboration - Early Experience

Author Block: Kevin M Barrett, Mayo Clinic, Jacksonville, FL; Claudia Scala Moy, NINDS, Bethesda, MD; Robert D Brown, Jr, Mayo Clinic, Rochester, MN; Joseph Broderick, Michael Linke, Univ of Cincinnati, Cincinnati, OH; Brajesh K Lal, Univ of Maryland, Baltimore, MD; George Howard, Univ of Alabama, Birmingham, AL; Sarah K. Morabito, NIH StrokeNet Natl Coordinating Ctr, Cincinnati, OH; Thomas G. Brott, James F. Meschia, Mayo Clinic, Jacksonville, FL; for the CREST-2 Investigators.

Abstract Body: The NIH StrokeNet is a clinical trials network designed to conduct Phase I/II and III trials in the areas of stroke prevention, treatment, and recovery. The recruitment capacity of StrokeNet derives from a hub-and-spoke model: 25 Regional Coordinating Centers acting as hubs. CREST-2 is a set of two parallel multicenter randomized clinical trials comparing optimal medical therapy (OMT) alone to either OMT plus carotid stenting (n=1240) or OMT plus carotid endarterectomy (n=1240) in patients with asymptomatic high-grade carotid stenosis (>70%). CREST-2 utilizes the StrokeNet central Institutional Review Board (IRB) based at the University of Cincinnati. The central IRB has agreed to establish reliance agreements delineating responsibilities between itself and local center IRBs for all StrokeNet centers participating in CREST-2 as well as all non-StrokeNet centers that are participating in CREST-2 to the extent that are willing to accept the agreements. Here we report our initial experience with the CREST-2-StrokeNet collaboration.

The StrokeNet central IRB approved the CREST-2 protocol on September 24, 2014. Twenty-two of 25 (88%) StrokeNet Regional Coordinating Centers have responded with interest in participating in CREST-2 and have received invitation packets for initiation in the trial. Reliance agreements have been executed for 16 CREST-2 centers and are pending for 6 CREST-2 centers.

As of November 5, 2014, The CREST-2 Site Selection Committee has approved 43 centers for randomizing patients into the trial. Twenty-three of 43 (53%) CREST-2 approved centers have agreed to utilize the StrokeNet central IRB for protection of human subjects. 20 of 43 (47%) CREST-2 centers have declined utilization of the central IRB (1 Canadian and 19 US).

Early experience indicates enthusiasm among StrokeNet RCCs for participation in the CREST-2 stroke prevention trial. Although not all CREST-2 sites are participating in the central IRB, the added efficiencies of StrokeNet superimposed on the strengths of the existing CREST-2 network are expected to build a strong and effective collaboration to support recruitment and retention of study participants.

Author Disclosure Block: K.M. Barrett: None. C.S. Moy: None. R.D. Brown, Jr: None. J. Broderick: None. M. Linke: None. B.K. Lal: None. G. Howard: None. S.K. Morabito: None. T.G. Brott: None. J.F. Meschia: None.