

Ongoing Clinical Trials Posters II

Thursday, February 23, 2017, 6:15 PM – 6:45 PM

International Stroke Conference 2017 abstracts and presentations are embargoed for release at the date and time of presentation or time of AHA/ASA news event. Ongoing Clinical Trials abstracts are embargoed until the date and start time of the Ongoing Clinical Poster Session start time. No information may be released before then.

Presentation Number: CTP1

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

Author Block: Raul Nogueira, Emory Univ, Atlanta, GA; Tudor Jovin, UPMC, Pittsburgh, PA; DAWN Trial Investigators

Abstract Body: Background: Whether the treatment window for endovascular therapy can be expanded in properly selected patients remains to be established. **Objective:** To evaluate the hypothesis that Trevo thrombectomy plus medical management leads to superior clinical outcomes at 90 days as compared to medical management. **Design:** Multi-center, prospective, randomized, controlled, blinded-endpoint, phase II/III (feasibility/pivotal) trial of thrombectomy for wake-up and late presenting AIS that follows an adaptive design based on Bayesian predictive probabilities allowing population enrichment. **Population Studied and Intervention:** Subjects presenting 6-24 hours from TLSW with ICA/MCA-M1 occlusion are randomized 1:1 to embolectomy vs. medical therapy. Selection is based on clinical imaging mismatch (CIM) and age: 0-20 cc core, NIHSS \geq 10, age \geq 80; 0-30 cc core, NIHSS \geq 10, age < 80 years old; 31 cc to < 50 cc core, NIHSS \geq 20, age < 80. Core is measured with RAPID software. Randomization is stratified by CIM subgroups, TLSW and Occlusion Site. Max sample size is 500. **Outcome Measures & Analysis:** Primary endpoint: average weighted 90-day mRS. Secondary endpoints: good outcome at 90 days, "early response" at day 5-7, all-cause mortality, median final infarct size, revascularization at 24 hours, symptomatic ICH. **Trial Status:** Enrollment began Sept 2014. As of Nov 2016, 163 patients have been randomized across 23 centers globally. **Principal Investigators:** Raul Nogueira (Emory University, GA) and Tudor Jovin (University of Pittsburgh, PA) **Trial Sponsor:** Stryker Neurovascular **Trial Contact Information:** Christine Toruno (christine.toruno@stryker.com)

Author Disclosure Block: R. Nogueira: Consultant/Advisory Board; Significant; Study PI, Consultant for Sponsor. T. Jovin: Consultant/Advisory Board; Significant; Study PI, Consultant for Sponsor.

Presentation Number: CTP2

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

Author Block: Philip M Bath, Jason Appleton, Hayley Foster, Margaret Adrian, Michael Stringer, Jamie Longmate, James Kirby, Katie Flaherty, Polly Scutt, Azlinawati Ali, Stefan Pszczolkowski Parraguez, **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 spontaneous intracerebral haemorrhage (SICH). The results will determine whether tranexamic acid should be used to treat ICH. **Design:** Patients will be randomised (1:1) to receive either tranexamic acid or placebo (0.9 % saline) within 8 hours of acute SICH. 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, 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 1st March 2013, 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 of 3rd October 2016, 1729 patients have been recruited from 110 centres (UK, Georgia, Italy, Malaysia, Switzerland, Republic of Ireland, Turkey, Sweden and Denmark). The objective was to have 80 UK centres and 40 international centres. **Funding:** This project is funded by the National Institute for Health Research, HTA Programme (11/129/109) **Disclaimer:** The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Health and Technology Assessment Programme, NIHR, NHS or the Department of Health. **Contact information:** E-mail: tich-2@nottingham.ac.uk, Telephone: +44 (0)115 823 1770

Author Disclosure Block: P.M.W. Bath: None. J. Appleton: None. H. Foster: None. M. Adrian: None. M. Stringer: None. J. Longmate: None. J. Kirby: None. K. Flaherty: None. P. Scutt: None. A. Ali: None. S. Pszczolkowski Parraguez: None. N. Sprigg: None.

Presentation Number: CTP3

Publishing Title: PRACTISE Trial: Penumbra & Recanalisation Acute Computed Tomography in Ischaemic Stroke Evaluation

Author Block: **Salwa El Tawil**, Alicia Murray, Univ of Glasgow, Glasgow, United Kingdom; Joanna Wardlaw, Univ of Edinburgh, Edinburgh, United Kingdom; Lalit Kalra, King's Coll London, London, United Kingdom; Ian Ford, Univ of Glasgow, Glasgow, United Kingdom; Thompson Robinson, Univ of Leicester, Leicester, United Kingdom; Elizabeth Warburton, Univ of Cambridge, Cambridge, United Kingdom; Janet Freeman, None, None, United Kingdom; Keith Muir, Univ of Glasgow, Glasgow, United Kingdom

Abstract Body: Background The use of multimodal brain imaging, including CTP and CTA provides valuable information on tissue viability and vascular anatomy that may be helpful in patient stratification for revascularisation therapy. However, it is currently unknown whether benefits from potentially improved patient selection outweighs the disadvantages of additional resource utilisation, radiation and contrast exposure, and treatment delay associated the use of additional multimodal CT imaging. This study aims to evaluate the effect of additional CT imaging on the number of acute stroke patients treated with IV rtPA and their outcomes. **Methods** PRACTISE is a prospective, multicentre randomised controlled trial (RCT) comparing current evidence based imaging (NCCT alone, control arm) with additional multimodal CT imaging (CT+CTA+CTP, experimental arm). Patients with acute ischaemic stroke, ≥ 18 years, and clinically eligible for IV rtPA treatment are randomised in the ratio of 1:1 into each arm. Primary endpoint is the proportion treated with rtPA. Secondary endpoints evaluate times to decision making, comparison of different image processing software and clinical outcomes at 3 months. Randomisation of a maximum of 400 patients is planned. **Results:** By the end of October 2016 , nine sites were open for recruitment with 86 patients recruited. . **Conclusions:** Understanding the role of CTA and CTP in thrombolysis decision would guide their use in clinical practise. If additional diagnostic testing identifies a subgroup of patients that are more or less likely to respond to treatment and hence influences treatment decisions favourably, then these could be adopted as standard practice.

Author Disclosure Block: **S. El Tawil:** None. **A. Murray:** None. **J. Wardlaw:** None. **L. Kalra:** None. **I. Ford:** None. **T. Robinson:** None. **E. Warburton:** None. **J. Freeman:** None. **K. Muir:** None.

Presentation Number: CTP4

Publishing Title: Rapid Intervention With Glyceryl Trinitrate in Hypertensive Stroke Trial-2 (RIGHT-2): Safety and Efficacy of Transdermal Glyceryl Trinitrate, a Nitric Oxide Donor

Author Block: **Mark Dixon**, Jason P Appleton, Timothy England, Diane Havard, Harriet Howard, Malcolm Jarvis, Alan Montgomery, Univ of Nottingham, Nottingham, United Kingdom; Stuart Pocock, London Sch of Hygiene and Tropical Med, Dept of Statistics, London, United Kingdom; John Potter, Univ of East Anglia, Norwich Medical Sch, Norwich, United Kingdom; Christopher Price, Univ of Newcastle, The Medical Sch, Newcastle, United Kingdom; Tom Robinson, Univ of Leicester, Dept of Cardiovascular Sciences, Leicester, United Kingdom; Christine Roffe, Keele Univ, Inst of Science and Technology in Med, Keele, United Kingdom; Niro Siriwardena, Univ of Lincoln, Sch of Health and Social Care, Lincoln, United Kingdom; Nikola Sprigg, Univ of Nottingham, Nottingham, United Kingdom; Joanna Wardlaw, Univ of Edinburgh, Ctr for Clinical Brain Sciences, Edinburgh, United Kingdom; 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 ambulance-based stroke trials in the UK. In both RIGHT and 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 is testing the safety and efficacy of transdermal GTN in the pre-hospital setting. **Methods** Paramedics from 5 UK ambulance services serving over 40 comprehensive or primary stroke care centres are screening, consenting, randomising and treating 850 patients presenting within 4 hours of FAST-positive stroke and with systolic BP >120 mmHg. Treatment comprises GTN or similar sham patch, and is continued in hospital for 3 days. The primary outcome is the modified Rankin Scale at day 90. Secondary outcomes include vascular events, disability, quality of life, mood and cognition. Neuroimaging and biomarkers are examining potential mechanisms of action. **Status** Recruitment commenced in October 2015. Challenges with the trial and baseline characteristics of the first recruited patients will be presented. As of Monday 7th November 2016, 265 patients have been recruited from five ambulance trusts conveying patients into 28 active stroke centres. Further ambulance services and hospitals are welcome to join. **Funding:** British Heart Foundation **Contact Information: Website:** www.right-2.ac.uk **E-mail:** right-2@nottingham.ac.uk or philip.bath@nottingham.ac.uk **Telephone:** +44 115 823 1672

Author Disclosure Block: **M. Dixon:** None. **J.P. Appleton:** None. **T. England:** None. **D. Havard:** None. **H. Howard:** 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. **P.M.W. Bath:** None.

Presentation Number: CTP5

Publishing Title: Alteplase-Tenecteplase Trial Evaluation for Stroke Thrombolysis (ATTEST 2)

Author Block: Alicia Murray, Keith Muir, Ian Ford, Univ of Glasgow, Glasgow, United Kingdom; **Gary Ford**, Oxford Univ Hosp NHS Trust, Oxford, United Kingdom; Joanna Wardlaw, Univ of Edinburgh, Edinburgh, United Kingdom

Abstract Body:

Background

IV thrombolysis with alteplase, the only medical treatment currently approved for acute ischaemic stroke, significantly increases the probability of excellent recovery. Data from small randomised trials suggest that the modified tissue plasminogen activator tenecteplase is potentially superior to IV alteplase, with respect to both safety and efficacy in stroke, in addition to having simpler administration. More data are required to establish the true risk-benefit profile compared with alteplase.

Objectives & Methods

ATTEST-2 will establish whether tenecteplase is superior to alteplase by undertaking a prospective randomised open blinded end-point (PROBE) trial in patients eligible for IV thrombolysis based on non-contrast CT imaging. 60 UK centres will recruit 1870 patients, beginning Q4 2016.

Outcome

Primary outcome is the distribution of modified Rankin Scale (mRS) outcomes at day 90, determined by the Rankin Focused Assessment method, analysed by ordinal distribution ("shift") analysis of the of scores in intervention and control groups.

Conclusion

An agent with superior risk:benefit ratio to alteplase would potentially extend thrombolytic treatment to a greater proportion of patients than at present and reduce the need for mechanical thrombectomy. This trial will contribute to the optimisation of reperfusion strategies.

Author Disclosure Block: **A. Murray:** None. **K. Muir:** None. **I. Ford:** None. **G. Ford:** None. **J. Wardlaw:** None.

Presentation Number: CTP6

Publishing Title: Remote Ischemic Conditioning Prevents Ischemic Cerebrovascular Events in Children With Moyamoya Disease: A Randomized Controlled Trial

Author Block: Sijie Li, Wenbo Zhao, Xuanwu Hosp, Capital Medical Univ, Beijing, China; Shuling Shang, Tangshan Union Medical Coll Hosp, Tangshan, China; Ran Meng, Xuanwu Hosp, Capital Medical Univ, Beijing, China; Yuchuan Ding, Wayne State Univ, Detroit, MI; Xunming Ji, Xuanwu Hosp, Capital Medical Univ, Beijing, China

Abstract Body: Introduction: Moyamoya disease is a common reason of transient ischemic attack (TIA) and stroke in children. Remote ischemic conditioning (RIC) has been shown to prevent recurrent stroke in intracranial arterial stenosis, but it is unclear whether RIC can prevent TIA or stroke in children with moyamoya disease. This study aims to evaluate the effect of RIC on TIA/stroke in children with moyamoya disease. **Methods:** A total of 25 moyamoya disease patients (aged 7.8 ± 3.2), diagnosed by DSA and presenting as TIA or stroke, were allocated randomly to the RIC group ($n=13$) and the control group ($n=12$). All subjects received standard background therapies. Subjects in the RIC group underwent RIC twice daily for 12 months. RIC was performed by an electric autocontrol device with cuffs placed on bilateral arms and inflated to 200 mmHg for 5-min followed by deflation for 5-min, repeated 5 times. TIA and stroke were collected and compared between groups. Status of cerebral flow and perfusion were detected by SPECT at Month 0, 6 and 12, and presented as regional radionuclide uptake index (R_f and R_m respectively) which are ratios compared to cerebellum. Chinese Wechsler Intelligence Scale for Children was used to evaluate the intelligence at Month 0, 6 and 12. The primary outcome was the reduction of TIA and stroke. **Results:** 12 subjects in the RIC group and 10 subjects in the control group completed clinical and SPECT evaluations of this study. Kaplan-Meier survival analysis shows that TIA was significantly reduced in the RIC group ($p<0.05$). At Month 0, 6 and 12, the average of R_f were 0.82 ± 0.06 , 0.86 ± 0.04 and 0.91 ± 0.04 in RIC group versus 0.81 ± 0.05 , 0.82 ± 0.05 and 0.85 ± 0.04 in the control group ($p_0>0.05$, $p_6<0.05$ and $p_{12}<0.01$), and the average of R_m were 1.24 ± 0.11 , 1.20 ± 0.05 and 1.14 ± 0.06 in RIC group versus 1.28 ± 0.08 , 1.25 ± 0.06 and 1.25 ± 0.05 in control group ($p_0>0.05$, $p_6<0.05$, and $p_{12}<0.01$). Intelligence of subjects shows no significant difference between groups ($p>0.05$). **Conclusions:** RIC might be an effective way to improve cerebral flow and perfusion and reduce TIA in children with moyamoya disease. Future larger studies should be sufficiently powered to examine the effect of RIC on these populations in the long term.

Author Disclosure Block: S. Li: None. W. Zhao: None. S. Shang: None. R. Meng: None. Y. Ding: None. X. Ji: None.

Presentation Number: CTP7

Publishing Title: General or Local anesthesia in Intra Arterial Therapy (“GOLIATH”)

Author Block: **Claus Z Simonsen**, Leif H Sørensen, Aarhus Univ Hosp, Aarhus, Denmark; Albert J Yoo, Texas Stroke Inst, Plano, TX; Mads Rasmussen, Aarhus Univ Hosp, Aarhus, Denmark

Abstract Body: Background: There is equipoise as to what kind of anesthesia patients should receive during Endovascular Therapy (EVT) for acute ischemic stroke. Observational studies suggest that general anesthesia (GA) is associated with worse outcomes compared to conscious sedation (CS). The objective of GOLIATH is to examine whether the choice of anesthetic regime during EVT influence patient outcome. Our hypothesis is that CS is associated with less infarct growth and better functional outcome. Methods: GOLIATH is an investigator-initiated, single-center, randomized study. Patients with anterior circulation stroke, scheduled for EVT, are randomized to receive either GA or CS. Inclusion criteria are: NIHSS ≥ 10 , mRS 0-2 before randomization, groin puncture <6 hours from symptom onset/last seen well, clot in anterior circulation and infarct volume <70 ml before randomization. Exclusion criteria are: MRI contraindication, GCS <9/intubated on arrival, allergy to anesthetic drugs. The primary outcome measure is infarct growth after 48-72 hours (determined by serial diffusion-weighted MRI). Secondary outcomes include 90 day modified Rankin Scale score, time parameters, blood pressure variables, use of vasopressors, procedural and anesthetic complications, success of revascularization, radiation dose and amount of contrast media. Preliminary results: The study began March 9th 2015. Per November 1st 2016 we have included 103 patients, resulting in one included patient per 5.9 days. Planning for 128 patients, the study will likely end in March 2017. We have had 93 screenfailures. (22 presented with NIHSS <10, 19 had stroke in posterior circulation, 16 had groin puncture >6 hours, 5 intubated at arrival, 5 had a stroke volume >70 ml at presentation, 2 had mRS >2, 2 were under 18 years old, 2 were included in another study and 1 withdrew consent. 17 received a CT scan due to MRI contraindications. 2 patients were excluded due to concern from anesthesia. Fifty-three has been treated under CS and 50 under GA. No difference was found so far in age (74 vs. 71, $p=0.20$), NIHSS (17 vs. 17, $p=0.91$) or time to groin puncture (177 min vs. 182 min, $p=0.24$) comparing CS vs. GA. Discussion: The results from this study may guide future decisions regarding the optimal anesthetic regime for EVT.

Author Disclosure Block: **C.Z. Simonsen:** None. **L.H. Sørensen:** None. **A.J. Yoo:** Research Grant; Significant; Penumbra, Neuravi. **M. Rasmussen:** None.

Presentation Number: CTP8

Publishing Title: Rationale, Design, and Progress of the Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit Trial

Author Block: **Jose-Miguel Yamal**, Suja S Rajan, UTHealth Sch of Public Health, Houston, TX; Stephanie A Parker, Ritvij Bowry, Tzu-Ching Wu, Nicole R Gonzales, UTHealth, Houston, TX; David Persse, Houston Fire Dept Emergency Medical Services, Houston, TX; Asha P Jacob, UTHealth Sch of Public Health, Houston, TX; Andrew D Barreto, UTHealth, Houston, TX; Andrei V Alexandrov, Univ Clinical Health, Univ of Tennessee, Memphis, TN; William Jones, Univ of Colorado, Denver, CO; James C Grotta, Memorial Hermann Hosp, Houston, TX

Abstract Body: Background Earlier tPA treatment for acute ischemic stroke (AIS) increases chance of better outcome. Mobile Stroke Units (MSU) substantially speed evaluation, triage, and initiation of tPA, thereby possibly improving long-term outcomes.

Objective We aim to determine if, compared to Standard Management (SM), MSU management results in better patient-centered clinical outcomes, reduced healthcare utilization, and higher Quality of Life (QoL) in tPA-eligible AIS patients calling 911.

Design Phase III, multicenter, prospective cluster-randomized (MSU vs SM weeks) comparative effectiveness study. With 693 tPA-eligible patients (446 MSU and 247 SM), the study will have 80% power with a 0.05 Type I error rate to detect a clinically-meaningful difference of 0.09 in the mean utility-weighted modified Rankin scale (uw-mRS) between groups.

Population Studied AIS patients who call 911 within 4hr 30 min of last seen normal. Both MSU and SM patients will be identified and enrolled based on their pre-hospital status. The population analyzed will be the subset that are tPA-eligible based on blinded review.

Intervention Management of AIS patients on an MSU versus SM.

Outcome Measures Primary outcome is the 90 day mean uw-mRS in MSU vs SM patients. Co-primary outcomes are QoL and healthcare utilization serially measured using EQ5Ds and patient self-report, respectively, up to one year after the stroke. Secondary outcomes include ordinal analysis of mRS, number and timing of tPA and endovascular procedures, symptomatic ICH, and number of stroke mimics treated.

Analysis Mean uw-mRS will be compared between groups using a two-sample t-test or Wilcoxon rank sum test if the assumption of normality does not hold and using linear regression adjusted for baseline uw-mRS, any baseline covariates significantly different between the two groups, and covariates known to be associated with mRS.

Trial Status As of November 2016, 231 patients have been enrolled with 146 in the MSU arm and 85 in the SM arm. Two new centers in Denver and Memphis will start in late 2016 with target end of recruitment September 2019.

Conclusions Management of AIS patients by MSU could result in faster tPA treatment, lower disability, and improved QoL.

Author Disclosure Block: **J. Yamal:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **S.S. Rajan:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **S.A. Parker:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. Consultant/Advisory Board; Modest; Consultant for Frazer Limited, Consultant for Stryker Corporation. **R. Bowry:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **T. Wu:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **N.R. Gonzales:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **D. Persse:** None. **A.P. Jacob:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **A.D. Barreto:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. **A.V. Alexandrov:** Research Grant; Modest; PCORI, tPA was supplied by Genentech. **W. Jones:** Research Grant; Modest; PCORI, tPA was supplied by Genentech. **J.C. Grotta:** Research Grant; Modest; AHA, PCORI, tPA was supplied by Genentech. Consultant/Advisory Board; Modest; Consultant for Frazer Limited, Consultant for Stryker Corporation.

Presentation Number: CTP9

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

Author Block: Heather M Haughey, Karen C Johnston, Univ of Virginia, Charlottesville, VA

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 >110 mg/dL or glucose of \geq 150mg/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 60 sites including Neurological Emergencies Treatment Trials (NETT) sites and StrokeNet sites.

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.

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 nearly 45 sites. As of November 1, 2016, 890 subjects have been enrolled.

Sponsor: NIH-NINDS U01NS069498, U01NS056975, U01NS059041

Author Disclosure Block: H.M. Haughey: Research Grant; Significant; NIH-NINDS U01 NS069498.

K.C. Johnston: Research Grant; Modest; NIH-NINDS U01 NS079077, NIH-NINDS 1K12NS098482, NIH-NHLBI/NINDS UM1 HL088925. Research Grant; Significant; NIH-NINDS U01 NS069498. Honoraria; Modest; John Hopkins, Albert Einstein, NINDS/ANA Career Development Symposium, UCSF. Consultant/Advisory Board; Modest; Diffusion Pharmaceuticals, Roche/Genentech, NIH-NHLBI SPRINT DSMB.

Presentation Number: CTP10

Publishing Title: Platelet Oriented Inhibition in New TIA and Minor Ischemic Stroke

Author Block: Mary Farrant, UCSF, San Francisco, CA; Clay Johnston, The Univ of Texas at Austin, Austin, TX; J. Donald Easton, Anthony S. Kim, UCSF, San Francisco, CA; Jordan Elm, Medical Coll of South Carolina MUSC, Charleston, SC

Abstract Body: The Platelet-Oriented Inhibition in New TIA and minor ischemic stroke (POINT) Trial, is a prospective, randomized, double-blind, multicenter international 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 (NIHSS \leq 3). A total of 5,840 patients will be recruited; each subject is followed for 90 days from randomization. The first subject was enrolled on May 28, 2010. International sites joined the trial in August of 2013.

Principal Investigator: S. Claiborne Johnston, MD, PhD, The University of Texas at Austin

Co-Principal Investigators: J. Donald Easton, MD, University of California, San Francisco
Anthony S. Kim, MD, MAS, University of California, San Francisco

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Director, POINT Trial—UCSF Clinical Coordinating Center (CCC), San Francisco, California, 94158;
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Planned Number of Centers: 325; Present Number: 292

Planned Number of Subjects: 5,840; Present Number: 3,982 (October 2016)

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 - June 2016 (pending extension)

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. A. Kim: None. J. Elm: None.

Presentation Number: CTP11

Publishing Title: Crest-2 Registry (c2r) Ensures Carotid Stenting Quality While Supporting Trial

Author Block: Brajesh K Lal, Univ of Maryland Medical Ctr, Baltimore, MD; Kenneth Rosenfield, Massachusetts General Hosp, Boston, MA; Donald Heck, Mayo Clinic Jacksonville, Jacksonville, FL; Seemant Chaturvedi, Univ of Miami Miller Sch of Med, Miami, FL; Gary Roubin, Cardiovascular Associates of the Southeast, Birmingham, AL; Kimberlly Nordstrom, Heather Morris, Univ of Maryland, Baltimore, MD; **James Meschia**, Thomas G Brott, Mayo Clinic Jacksonville, Jacksonville, FL

Abstract Body:

Objectives:

C2R (clinicaltrials.gov NCT02240862) commenced enrollment of carotid artery stent (CAS) procedures on February 1, 2015. The objectives are to promote rapid enrollment in the NINDS-NIH funded CREST-2 randomized trial and provide a pathway for CREST-2 interventionists to maintain case-volumes to optimize procedural safety.

Methods:

Patients eligible for C2R, and for CMS reimbursement if enrolled in C2R, include patients with severe asymptomatic or symptomatic carotid stenosis who are at standard or high risk for carotid endarterectomy (CEA). Operators are credentialed by a multi-specialty committee. For enrolled patients, sites submit data through the Society for Vascular Surgery's Vascular Quality Initiative or the American College of Cardiology's National Cardiovascular Data Registry; and additional data to C2R. The information is reviewed centrally. Safety and outcome results are assessed to ensure high quality CAS procedures nation-wide, and to guide selection of operators for CREST-2. C2R is a collaboration with CMS, FDA, NIH and industry partners.

Results:

Data are available through 10/31/2016. 117 interventionists from 66 sites across the US enrolled 1549 patients and 1610 procedures (57 bilateral and 4 restenosis). The mean age was 68.0 years (± 7.7 , range 40-80) and 32.5% were women. Cardiovascular comorbidities included smoking 76.3%, hypertension 89.7%, diabetes 39.5% and coronary disease 45.2%. Ratio of symptomatic to asymptomatic was 64%/36%; the most common indications were primary atherosclerosis 56.7% or restenosis 32.7%. All FDA-approved stents and embolic protection devices were represented including filter-protection in 89.6%. Thirty-day stroke and death rate was 1.7%. Other complications included congestive heart failure (0.4%), dysrhythmia (0.9%), and access site complications (3.9%).

Conclusions:

C2R is the first national registry for CAS co-sponsored by federal and industry partnerships. It ensures that CAS is performed for a wide range of indications by appropriately credentialed interventionists. Periprocedural stroke and death rates have been low. C2R has been instrumental in transitioning 89 conditionally approved interventionists to full approval to enroll patients into CREST-2.

Author Disclosure Block: **B.K. Lal:** None. **K. Rosenfield:** None. **D. Heck:** None. **S. Chaturvedi:** None. **G. Roubin:** None. **K. Nordstrom:** None. **H. Morris:** None. **J. Meschia:** None. **T.G. Brott:** None.

Presentation Number: CTP12

Publishing Title: Extension of Stroke Care by Added Neuroprotection to Endovascular Treatment - Escape-na1 Trial

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Abstract Body: Introduction. The evolution of endovascular therapy has resulted in an ischemia-reperfusion model in the human that mimics the pre-clinical models. Even with endovascular treatment, 40-50% of patients continue to have a poor outcome and therefore adjuvant therapy is needed. NA-1 is a novel peptide molecule that has proven neuroprotective effect in rodents and large, old-world primates (cynomolgous macaques). Efficacy and safety has been shown in a human model of small volume ischemia in the ENACT trial. We propose a phase 3 randomized clinical trial in community-onset ischemic stroke patients who will undergo concomitant reperfusion treatment with endovascular thrombectomy. Methods. Up to 40 sites internationally will recruit adult acute ischemic stroke patients with good pre-morbid status (Barthel Index > 90), and a proven proximal large artery occlusion (ICA and M1-MCA only), within a 12-hour treatment window for enrolment. All patients or their legally authorized surrogate will provide written informed consent. Patients with poor ASPECTS (0-4) or poor collaterals on multiphase CTA (Tan score 0-1), or distal occlusions will be excluded. The principle of imaging selection is: small core, large occlusion, favourable collaterals. Patients will be randomized to NA-1 or saline placebo using a randomized minimization algorithm to preserve balance on important prognostic factors, and with dynamic allocation to conceal group assignment. NA-1 or saline placebo will be delivered by a 10-minute intravenous infusion immediately after baseline CT imaging. All patients will be treated with endovascular thrombectomy. Concurrent treatment with intravenous alteplase (tPA) will be expected according to routine standard of care. The primary efficacy outcome will be the modified Rankin Scale assessed at 90 days, dichotomized at mRS 0-2 vs. 3-6, and analysed using a multivariable model adjusting for baseline minimization variables. Secondary outcomes are hierarchical and will next include the 'shift' along the mRS using a proportional odds model. Safety outcomes include hypotension and intracerebral hemorrhage. Progress. The first patients enrolled are expected in the late 4th quarter 2016 / 1st quarter 2017. The study is expected to take 3 years to complete.

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Presentation Number: CTP13

Publishing Title: NAVIGATE ESUS Trial: Geographic Variations in Ineligibility Rates and Causes

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Abstract Body: Background: NAVIGATE ESUS is an international, double-blind, randomized trial of rivaroxaban 15 mg versus aspirin 100 mg in patients with recent embolic stroke of undetermined source (ESUS).^{*} The study aims to enroll approximately 7000 participants at 480 sites in 31 countries. We sought to identify geographic variations in ineligibility rates and their causes. **Methods:** Screening logs were collected from 34 NAVIGATE ESUS sites, that were not achieving the recruitment target, in 14 countries between April 1 and August 1, 2016. Countries were categorized into four regions; Australasia (AU), Europe (EU), North/South America (AM) and South Africa (SA). We compared ineligibility rates and causes between the geographic regions. A $p \leq 0.001$ was statistically significant (Bonferroni correction). **Results:** In total 1120 patients were screened (AM:464; AU:33; EU:566; SA:29). Ineligibility rates were relatively constant across regions (AM:91%, AU:82%, EU:89%, SA:91%; $p=0.3$), however causes varied. Considering all sites the most frequent causes for ineligibility were the presence of atrial fibrillation (17%), non-visualization of the qualifying infarct (16%), and lacunar stroke (9%). Patient refusal rates were highest in AU (18%) and SA (17%) followed by EU (8%) and AM (3%; $p<0.001$). The most frequent reason for refusal was not wanting to be a research participant (36/72 refusals). Concerns regarding randomization to anticoagulation therapy ($n=10$) or blinded treatment (4) were less frequent. Lacunar strokes were more frequent in AU(18%) and SA (22%) than AM (9%) and EU (8%; $p=0.001$). Not visualizing the qualifying stroke on neuroimaging was more common in EU (23%) than the other regions (AM:10%, AU:6%, SA:2%; $p<0.001$), while implantable cardiac rhythm monitoring devices were more frequent in AU (3%, AM:0.2%, EU:0%, SA:0%; $p=0.001$). Patients being evaluated >6 months from their qualifying event were more frequent in AM (6%) and AU (3%), than EU (0.2%) and SA (0%; $p<0.001$). **Conclusions:** Analysis of screening log data from a global stroke trial found regional differences in ineligibility causes and highlight region-specific modifiable factors that could potentially improve study recruitment. ^{*}European Stroke Journal. 2016;1(3):146-154.

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Presentation Number: CTP14

Publishing Title: TEMPO-2: TNK-tPA for Minor Stroke With Proven Acute Symptomatic Occlusion Trial-2

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Abstract Body: Background: Minor stroke and TIA with an intracranial occlusion are associated with a 20-30% risk of deterioration and disability. Tenecteplase (TNK-tPA) compared to alteplase is easier to administer, has a longer half-life, higher fibrin specificity and possibly less intracerebral hemorrhage (ICH). It may be an ideal thrombolytic agent in this population. A pilot study, TEMPO-1, showed feasibility and safety. TEMPO-2 (NCT02398656) examines tenecteplase for the treatment of minor stroke with imaging defined intracranial occlusion.

Methods: Multi-center, prospective, open-label, randomized controlled trial comparing tenecteplase to best standard of care. Patients with an NIHSS < 6, intracranial arterial occlusion on CTA, and within a 12h treatment window will be enrolled (expected sample size of 1274 patients). Patients will be randomized 1:1 to receive 0.25mg/kg intravenous tenecteplase or control, defined as the best standard of care and minimally must include immediate treatment with ASA. The primary outcome will be a responder analysis defined by the modified Rankin Scale score at 90 days. Safety will be assessed by the rate of symptomatic ICH. Secondary outcomes include complete neurological (NIHSS 0-1) and functional (mRS 0-1) recovery at 90 days, recanalization at 4-8h on CTA and minor bleeding.

Trial status: The study has received regulatory approval and is registered. The trial is currently running in Canada. Sites in Europe and Australia are expected to start enrolment in 2017. The first 66 patients have been enrolled. This study is in the site activation phase and is expected to continue for up to 5 years.

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Sponsor: The Governors of the University of Calgary

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Presentation Number: CTP15

Publishing Title: The Bleeding With Antithrombotic Therapy Study 2 (BAT2)

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Abstract Body: Background—In accordance with increase in the use of oral antiplatelets and anticoagulants for prevention of stroke and cardiovascular diseases, bleeding complications including intracranial hemorrhage have become serious concerns for health professionals. However, limited evidence exists over the risk factors for bleeding among broad range of patients on oral antithrombotic therapy.

Aims—To determine the incidence and details of bleeding complications in patients with cerebro- or cardiovascular diseases treated with oral antithrombotic therapy and to develop bleeding risk prediction models including laboratory and imaging biomarkers.

Methods—The BAT2 is an investigator initiated, prospective, multicenter, observational study. Patients with cerebro- or cardiovascular diseases who start or continue oral antiplatelets or anticoagulants (including vitamin K antagonists and direct oral anticoagulants) will have laboratory tests and multimodal magnetic resonance imaging of brain. Six thousand patients will be enrolled in this study across the Network for Clinical Stroke Trials (NeCST; 50+ sites in Japan) and be followed-up every 6 months for 2 years. The primary outcome is major bleeding defined by the International Society on Thrombosis and Haemostasis (ISTH). The secondary outcomes are clinically relevant non-major bleeding, hemorrhagic event details, and ischemic events and those details. Funding is from the Japan Agency for Medical Research and Development (AMED) which is Japanese governmental research fund.

Results—Since October, 2016, site set-up in the study is ongoing with 22 of 50+ hospitals actively recruiting patients. The study is ongoing through 2020.

Conclusions—The results of this trial will not only provide data regarding bleeding events in patients taking oral antithrombotics for prevention of cerebro- and cardiovascular diseases, but also provide novel models to stratify bleeding risk for those.

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Presentation Number: CTP16

Publishing Title: Intracerebral Hemorrhage Deferoxamine (iDEF) Trial

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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 192 subjects have been enrolled as of 10/31/2016.

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Presentation Number: CTP17

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

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Abstract Body: **BACKGROUND:** The balance of risk versus benefit of thrombolysis for acute ischemic stroke patients with mild deficits (persistent or rapidly improving to mild) 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 (NCT02072226) is a double-blind, multicenter, randomized, phase 3b trial of alteplase for 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” (ie, inability to return to work or perform basic activities of daily living based on current deficits). Patients meeting eligibility criteria will be randomly (1:1) assigned to receive either (1) IV alteplase 0.9 mg/kg (maximum 90 mg) with oral aspirin placebo or (2) IV alteplase placebo with oral aspirin 325 mg. **SAMPLE SIZE:** Approximately 948 patients will be enrolled across the United States. **PRIMARY EFFICACY OUTCOME MEASURE:** Difference in proportion of a favorable functional outcome (modified Rankin Scale score of 0 or 1) between the two treatment groups at 90 days after randomization. **STATISTICAL ANALYSIS:** The primary efficacy outcome will be analyzed via a Cochran-Mantel-Haenszel test, stratified by pretreatment 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:** First patient in (FPI) was May 1, 2014. As of November 1, 2016, 295 patients have been enrolled.

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Presentation Number: CTP18

Publishing Title: Design of ACTION II: A Multicenter, Double-Blind, Placebo-Controlled, Randomized, Parallel-Group, Dose-Ranging Study to Evaluate the Efficacy and Safety of Intravenous (IV) Natalizumab on Functional Independence and Activities of Daily Life in Patients With Acute Ischemic Stroke (AIS)

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Abstract Body: Introduction: Clinical and preclinical data suggest that peri-infarct inflammation can contribute to secondary injury and worsen outcomes 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 parenchymal tissue. This is the basis of natalizumab's efficacy in its approved indications of multiple sclerosis and Crohn's disease; a single IV infusion achieves rapid and nearly complete saturation of $\alpha 4\beta 1$ integrin that lasts approximately 3 weeks. Results from the ACTION I study suggested preliminary evidence of a benefit on functional outcomes with natalizumab treatment in patients with AIS; no safety concerns were identified. **Objective:** To assess the effects of natalizumab (primary objective) and to explore dose and exposure response (secondary objective) on clinical measures of independence and activities of daily life in patients with AIS. **Design:** ACTION II is a multicenter, double-blind, placebo-controlled, randomized, parallel-group, dose-ranging phase 2 study to evaluate the efficacy and safety of natalizumab over a 90-day period in patients with AIS. **Population:** A total of 240 patients (80 per treatment arm) aged 18-80 years with AIS (with last known normal ≤ 9 hours prior to study drug initiation) and a National Institutes of Health Stroke Score (NIHSS) of 5-23 will be enrolled. **Intervention:** Eligible patients are randomized 1:1:1 to receive one dose of IV natalizumab 600 mg or 300 mg or placebo. Randomization is stratified by tissue plasminogen activator (tPA) use (yes vs no), baseline NIHSS category (5-15 vs 16-23), and region. All patients will receive standard of care for stroke. **Outcome Measures:** The primary endpoint is a composite global measure of functional disability based on a score of 0 or 1 on the modified Rankin Scale (mRS) and a score of ≥ 95 on the Barthel Index (BI) at day 90. Secondary endpoints will include mRS, BI, Stroke Impact Scale-16, Montreal Cognitive Assessment, and NIHSS at 90 days, and safety at 24 hours and 5, 30, and 90 days. **Trial Status:** ACTION II is currently enrolling patients in Germany, Spain, the United Kingdom, and the United States.

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Presentation Number: CTP19

Publishing Title: Eraser: A Study Using Predictive Analytics to Assess Mechanical Thrombectomy

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Abstract Body: Aim and hypothesis: Using a new study design, we investigate whether next-generation thrombectomy devices improve clinical outcomes in ischemic stroke patients. We hypothesize that mechanical thrombectomy (MT) is superior to intravenous tPA therapy alone. Methods and design: ERASER is an investigator-initiated prospective single-arm, multi-center, controlled, open label study to compare the safety and effectiveness of a new recanalization device and distal access catheter in acute ischemic stroke patients and vessel occlusion of the internal cerebral artery or middle cerebral artery. Study outcome: The primary effectiveness endpoint is the volume of saved tissue (VOST). VOST is defined as difference of brain volume that is predicted to develop infarction and actual infarct volume by using an optimized high-level machine-learning model that is trained on data from a historical cohort treated with IV tPA. Secondary endpoints include recanalization rate and modified Ranking scale score at 90 days. Sample size estimates: Based on own preliminary data, 45 patients fulfilling all inclusion criteria need to complete the study to show an efficacy > 38% with a power of 80% and a one-sided alpha error risk of 0.05 (based on a one sample t-test). Current status: 63 patients have been included from nine centers in Germany and Switzerland without safety concerns. Currently, a pre-defined interim analysis of the primary endpoint is being conducted. The results will be presented during the ISC 2017. Based on the results, a decision about the continuation of the study will be made. Discussion: ERASER is the first prospective study in interventional stroke therapy to use predictive analytics as primary endpoint. The results can be easily compared to previous trials by analyzing the secondary endpoints. Such trial design cannot replace RCTs with clinical endpoints but serve as exemplary trial design for evaluating non-pivotal neurovascular interventions.

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Presentation Number: CTP20

Publishing Title: Minimally Invasive Surgery plus rt-PA for Intracerebral Hemorrhage Evacuation (MISTIE) Phase III

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Abstract Body: Intracerebral hemorrhage (ICH) impacts 100,000 Americans each year; a substantial public health problem that will only grow with our aging population. MISTIE III (NCT01827046; NINDS funded; actively recruiting) is a randomized, open-label, multicenter evaluation of the efficacy and safety of minimally invasive surgery (MIS) plus 1 mg of rt-PA administered every eight hours for up to nine doses as compared to subjects treated with conventional medical management. Trial personnel across approximately 100 study centers have adaptively randomized (1:1) 400 of the targeted 500 subjects with supratentorial ICH without suspected underlying structural etiology (tumor, vascular malformation or aneurysm). Subjects are identified and recruited through the Emergency Department, clinical stroke service, and direct admissions to the Neurocritical Care Unit at each study center. All subjects are followed daily for six days post randomization. Subjects randomized to receive the surgical intervention undergo aspiration of clot followed by up to nine drug administrations. All subjects are required to attend follow-up clinic visits at 30, 180, and 365 days after onset of ICH, with a telephone follow-up at 90 and 270 days. Central functional outcome endpoint (modified Rankin Scale 0-3 at 180 days) adjudication is performed by blinded investigators at the University of Glasgow. Subjects enrolling in this study may also consent to participate in an ancillary study titled *Mechanisms of Tissue Injury in MISTIE III (MTI-M3)*. Clinically and biologically, MISTIE III is a robust pathway applicable to other multiple molecular strategies that might further mitigate injury to brain tissue. Indications point to greater local cellular survival and improved long-term recovery corresponding to the well-established tissue and animal models. MISTIE III will test the critical hypotheses regarding the generalizability and effectiveness of the MIS+rtPA procedure to improve outcome after ICH. Coordinating center contact information may be found at www.braininjuryoutcomes.com.

Author Disclosure Block: **N. McBee:** Research Grant; Modest; NINDS. **K. Lane:** Research Grant; Modest; NINDS. **W. Mould:** Research Grant; Modest; NINDS. **S. Mayo:** Other Research Support; Modest; Subcontract. **K. Vermillion:** Research Grant; Modest; NINDS. **T. Hartmann:** Research Grant; Modest; NINDS. **A. Bistran-Hall:** Research Grant; Modest; NINDS. **A. Stadnik:** Other Research Support; Modest; Subcontract. **P. Money:** Other Research Support; Modest; Subcontract. **P. Camarata:** None. **W. Ziai:** Research Grant; Modest; NINDS. **K.R. Lees:** Other Research Support; Modest; Subcontract. **J. Dawson:** Other Research Support; Modest; Subcontract. **A. Mendelow:** Other Research Support; Modest; Subcontract. **B. Gregson:** Other Research Support; Modest; Subcontract. **C. Anderson:** Other Research Support; Modest; Subcontract. **R.E. Thompson:** Research Grant; Modest; NINDS. **I. Awad:** Other Research Support; Modest; Subcontract. **M. Zuccarello:** Other Research Support; Modest; Subcontract. **D.F. Hanley:** Research Grant; Modest; NINDS.

Presentation Number: CTP21

Publishing Title: STROKE-AF: A Randomized Trial of Atrial Fibrillation Detection in Patients With Ischemic Stroke of Presumed Known Origin

Author Block: Lee H Schwamm, Massachusetts General Hosp, Boston, MA; Hooman Kamel, Weill Cornell Med, New York, NY; Christopher B Granger, Duke Clinical Res Inst, Durham, NC; Robert Kowal, Baylor Heart and Vascular Hosp, Baylor Univ Medical Ctr., Dallas, TX; Paul D Ziegler, Dept of Res, Medtronic plc., Minneapolis, MN; Richard A Bernstein, Davee Dept of Neurology, Feinberg Sch of Med of Northwestern Univ., Chicago, IL

Abstract Body: Background: The presence of atrial fibrillation (AF) in patients with ischemic stroke confers an increased risk for stroke recurrence, regardless of the duration of AF episodes. Therefore, detection of AF in any patient with ischemic stroke usually leads to chronic oral anticoagulation. Detection of AF can be difficult when it occurs in brief asymptomatic episodes. Long-term continuous cardiac monitoring is highly effective in detecting this type of AF, however, its utility in patients with strokes presumed due to large vessel atherosclerosis or small vessel disease is unclear. Objective: To provide a description of the STROKE-AF trial design and the status of enrollment. Methods: STROKE-AF (ClinicalTrials.gov ID: NCT02700945) is a prospective, randomized, controlled, open-label trial enrolling patients who have had an ischemic stroke within the past 10 days attributed to large artery atherosclerosis in the cervical or intracranial vessels, or to small vessel disease. Patients must be ≥ 60 years of age, or 50-59 with ≥ 1 additional stroke risk factor. Approximately 500 patients at 40 centers in the US will be enrolled to compare AF detection rates through 12 months with an insertable cardiac monitor versus standard of care monitoring, with a 1:1 randomization and 85% power to show a statistically significant difference ($p < 0.05$). The number of patients with small vessel disease will be limited in order to ensure a robust dataset for subgroup analysis for stroke types. The primary outcome of AF will be defined as an AF event lasting at least 30 seconds, adjudicated by the endpoint adjudication committee. Enrollment is ongoing at 21 sites, and as of November 9 2016, 56 subjects have been enrolled. The trial is sponsored by Medtronic, plc. The PIs are Dr. Richard Bernstein (Northwestern University, IL) and Dr. Lee Schwamm (Massachusetts General Hospital, MA). Contact information: Jennifer Heim, Medtronic, plc. jennifer.l.heim@medtronic.com, Tel: 763-526-3553. Conclusion: STROKE-AF will provide information on the incidence of AF in patients with an ischemic stroke of presumed known origin and on the utility of long-term continuous monitoring in this population.

Author Disclosure Block: L.H. Schwamm: Research Grant; Modest; PCORI PROSPER. Consultant/Advisory Board; Significant; Medtronic. H. Kamel: Research Grant; Significant; U01NS095869 for the ARCADIA trial (AIFA). C.B. Granger: Research Grant; Significant; AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Daiichi Sankyo, FDA, Janssen, Novartis, GSK, Medtronic, Medtronic Foundation, NIH, Pfizer;. Consultant/Advisory Board; Modest; Daiichi Sankyo, Janssen, Gilead, GSK, Lilly, Medtronic, Novartis, Verseon;. Consultant/Advisory Board; Significant; BMS, Boehringer Ingelheim, Pfizer. R. Kowal: Consultant/Advisory Board; Significant; Medtronic. P.D. Ziegler: Employment; Significant; Medtronic. Ownership Interest; Significant; Medtronic. R.A. Bernstein: Consultant/Advisory Board; Significant; Medtronic, Boehringer Ingelheim.

Presentation Number: CTP22

Publishing Title: A Phase III Trial of Bun/Cr-based Hydration Therapy to Reduce Stroke-in-evolution and Improve Short-term Functional Outcomes for Dehydrated Patients With Acute Ischemic Stroke

Author Block: Leng Chieh Lin, Chang Gung Memorial Hosp, Chiayi, Taiwan; **Lee Meng**, Chang Gung Memorial Hosp, Puzi, Taiwan

Abstract Body: Objective: Our preliminary findings suggest that providing patients with acute ischemic stroke hydration therapy on the basis of their presenting BUN/Cr ratio may help reduce the occurrence of stroke-in-evolution and therefore improve prognosis. **Design:** randomized double-blind control trial.

Patients: Inclusion criteria: 1) Acute ischemic stroke diagnosed by a stroke care specialist, 2) has a measurable neurologic deficit according to the National Institutes of Health Stroke Scale, 3) the time between the onset of neurological symptoms and starting therapy are less than 12 hours, 4) admission BUN/Cr \geq 15 Exclusion criteria: 1) no informed consent obtained, 2) initial NIHSS >15, 3) prepared for or received fibrinolytic therapy, 4) prepared for or received surgical intervention with 14 days, 5) congestive heart failure 6) history of liver cirrhosis or severe liver dysfunction (ALT or AST > x 3 upper normal limit), 7) admission blood Cr >2 mg/dl, 8) initial blood pressure SBP<90 mmHg, 9) core temperature \geq 38°C, 10) indication of diuretics, 11) any conditions needed more aggressive hydration or blood transfusion, 12)cancer under treatment, 13) life expectancy or any reasons for follow-up < 3 months **Interventions:**

Patients of control group will receive intravenous normal saline 60 cc per hour, and patients of study group will receive intravenous normal saline 20cc per kilogram of body weight, one third of which will be given as a bolus followed by delivery of the remaining two third as a constant infusion over a period of 8 hours. **Measurements:** The trial will be carried out in two parts. Part 1 assesses the rate of SIE which is defined as a deterioration from baseline in the score on the NIHSS by 4 or more points 72 hours after the onset of stroke. Part 2, We use two outcome measures, including Barthel index, and modified Rankin scale for neurological evaluation to assess whether BUN/Cr ratio based hydration therapy results in sustained clinical benefit at three months. **Statistical Analysis :** Sample size calculation is performed using two sample proportion test to achieving an 80% power at the 5% level of significance. By assuming that the missing rate is set 10%, the sample size with equal allocation can be determined by 244 per arm.

Author Disclosure Block: L. Lin: None.

Presentation Number: CTP23

Publishing Title: Xanthine Oxidase Inhibition for Improvement of Long Term Outcomes Following Ischaemic Stroke and Transient Ischaemic Attack

Author Block: **Jesse Dawson**, Univ of Glasgow, Glasgow, United Kingdom; **Niall Broomfield**, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom; **Krishna Dani**, Univ of Glasgow, Glasgow, United Kingdom; **Alexander Doney**, Univ of Dundee, Dundee, United Kingdom; **Kirsten Forbes**, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom; **Graeme Houston**, Univ of Dundee, Dundee, United Kingdom; **Kennedy Lees**, Terence Quinn, Keith Muir, Univ of Glasgow, Glasgow, United Kingdom; **Allan Struthers**, Univ of Dundee, Dundee, United Kingdom; **Matthew Walters**, Univ of Glasgow, Glasgow, United Kingdom

Abstract Body: XILO-FIST is a randomised double-blind placebo controlled clinical trial. It is evaluating the effect of allopurinol 300-mg twice daily on white matter hyper-intensity (WMH) progression and arterial blood pressure (BP) in patients with recent ischaemic stroke. The trial is funded by the British Heart Foundation and the Stroke Association via a joint programme grant. Allopurinol, a xanthine oxidase inhibitor, lowers serum uric acid and reduces oxidative stress in the vasculature. It reduced progression of carotid-intima media thickness and lowered blood pressure in a small clinical trial of patients with previous ischaemic stroke. XILO-FIST aims to assess benefit of a longer course of treatment on robust surrogate markers of risk and to establish whether it helps control BP after stroke. XILO-FIST will include 464 participants aged greater than 50-years with ischaemic stroke within the past month. Participants are randomised on a 1:1 basis to 2-years treatment with allopurinol or placebo. Participants will undergo brain MRI, detailed cognitive assessment, ambulatory blood pressure monitoring and blood sampling at baseline and after 2-years treatment. The primary endpoint is WMH progression, measured using the Rotterdam Progression Scale. Secondary endpoints include change in WMH volume, mean day-time systolic BP and measures of cognitive function. Up to 100 participants with left ventricular hypertrophy will undergo additional cardiac MRI. The trial has been adopted by the Scottish Stroke Research Network and the UK Clinical Research Network. The first participant first visit was in May 2015. By 7th November 2016 the trial was open in 13 sites in the UK. 213 participants were enrolled and 159 were randomised (with most of remainder in the trial run-in phase). On average 12 participants per month are being randomised. 23 participants have completed 1-year follow up. We aim to finish recruitment by end of 2017.

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Presentation Number: CTP24

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

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Abstract Body: Background: Cooling is a promising neuroprotective intervention in experimental ischaemic stroke; cooling to 35°C reduced infarct size by about one third. Cooling awake ischaemic stroke patients to 35°C has been shown feasible and safe, but has not been tested in a large clinical trial.² **Aims:** To determine whether systemic cooling to target temperature of 34 to 35°C, improves functional outcome at 3 months in patients with acute ischaemic stroke. **Methods:** Open, randomised, phase III, multicentre, international clinical trial with masked outcome assessment testing the safety and efficacy of therapeutic cooling in 800 awake adult patients with acute ischaemic stroke. Cooling will be initiated within 6 hours of symptom onset with an intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 to 60 minutes, followed by either surface or endovascular cooling to 34 to 35°C, maintained for 12 hours. Shivering and discomfort will be prevented and treated with anti-shivering drugs. All patients will receive best medical treatment, including alteplase, if indicated. The primary outcome is centrally adjudicated modified Rankin Scale at 90 days (shift analysis). A trial with 400 patients per arm has 80% power to detect a 7% absolute improvement in the mRS at the 5% significance level. As of 7th November 2016, 75 patients have been recruited across 18 sites in 5 countries. 26 UK patients have been enrolled in the UK, at Northwick Park, UCLH, Nottingham, Liverpool, Royal London, Surrey, and Newcastle. **Conclusion:** EuroHYP-1 is ongoing, funded by the European Commission 7th Framework Programme (FP7/2007-2013-278709).

Author Disclosure Block: **P.M.W. Bath:** None. **H. Gregory:** None. **K. Lees:** None. **M. Macleod:** None. **B. van der Worp:** None. **D. Krieger:** None. **J. Petersson:** None. **D. Staykov:** None. **S. Schwab:** None. **B. Colam:** None. **N. Sprigg:** None.

Presentation Number: CTP25

Publishing Title: Short Term Outcomes After Intracranial Stenting and Angioplasty in Patients With Symptomatic Intracranial Arterial Stenosis: Analysis of Clinical Registry in China

Author Block: Yabing Wang, Liqun Jiao, Feng Ling, Capital Medical Univ, Beijing, China

Abstract Body: *Background and Purpose*—Intracranial arterial stenting and angioplasty is performed in a limited capacity after Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial. There is significantly higher incidence of intracranial arterial stenosis (IAS) in Asian population. It is important to study IAS in this large patient population. We evaluated the safety and efficacy of angioplasty and stenting for IAS in Chinese population with multicenter prospective clinical registry.

Methods—Patients with symptomatic IAS (50-99%) were enrolled in 27 high volume medical centers in China from Dec 2013 through Dec 2015. The patients were treated with angioplasty alone or angioplasty with stenting (either balloon-expandable stent [BES] or self-expandable stent [SES]) as determined by the operators. Primary outcomes within 30 days - stroke, transient ischemic attack, and death were recorded.

Results—1124 consecutive patients were recruited (60.3±9.8 years, 27% female and 73% male), including 1070 patients treated with angioplasty and stenting and 54 patients with balloon angioplasty alone. IAS distribution was as follows: middle cerebral artery - 306, basilar artery - 280, vertebral artery - 345, and internal carotid artery -193. Overall perioperative morbidity was seen in 106 patients (9.4%) including perforator occlusion (41 patients, 3.6%), subarachnoid hemorrhage(28 patients, 2.4%), symptomatic intracerebral hemorrhage (30 patients, 2.6%) and in-stent thrombosis(7 patients, 0.6%).The mortality within 30 days was 1.6%. Patients treated with BES were likely to have lower degree of residual stenosis than patients treated with SES (3.2% v/s 4.1%), but more likely to have perforator occlusion (7.9% v/s 1.9%).

Conclusions—There is better short-term safety and efficacy with angioplasty and stenting treatment for symptomatic IAS in Chinese population compared to SAMMPRIS trial stenting cohort. Further prospective randomized controlled trials in Asian population are needed.

ClinicalTrials ID:NCT01994161

Author Disclosure Block: Y. Wang: None. L. Jiao: None. F. Ling: None.

Presentation Number: CTP26

Publishing Title: The Analysis of Revascularization in Ischemic Stroke With EmboTrap - ARISE II Trial

Author Block: **Osama Zaidat**, Mercy Health, St.Vincent's Hosp, Toledo, OH; Jeffrey L. Saver, UCLA Comprehensive Stroke Ctr, Los Angeles, CA; Tommy Andersson, Karolinska Univ Hosp, Stockholm, Sweden; Heinrich P Mattle, Inselspital, Univsspital Bern, 3010 Bern, Switzerland

Abstract Body: Objectives: Recent studies have demonstrated the clinical effectiveness of stent-retrievers in treating Large Vessel Occlusive stroke. A next generation stent-retriever, the EmboTrap® Revascularization Device, may provide clinicians in the United States with a new tool to treat these patients. The EmboTrap device, which has been used extensively in Europe, is engineered to retain and retrieve clot with a proprietary dual-layer stent-like structure and an integrated distal protection zone.

Methods: The ARISE II trial is an international multi-center single-arm study evaluating the effectiveness of the EmboTrap device in delivering TIC1 2b-3 revascularization in 3 passes or less. (NCT02488915) Key inclusion criteria are patients between the ages of 18-85 presenting with an acute ischemic stroke with NIHSS score of 8-25 within 8 hours of symptom onset and an angiographically confirmed occlusion in the ICA, MCA M1 or M2, VA or BA. Both patients ineligible for IV-tPA and patients treated with IV-tPA may be included. Exclusion criteria are consistent with other acute ischemic stroke interventional trials. Up to 228 patients at 30 centers in the US and Europe will be enrolled. The primary efficacy endpoint of the study is mTICI 2b-3 revascularization in the target vessel after 3 or fewer passes of the EmboTrap device. The primary safety endpoint is symptomatic intracerebral hemorrhage (sICH) within 24 hours, together with any other serious adverse events. Secondary endpoints include good clinical outcome as measured by mRS score of 0-2 at 90 days, time to treat, and mortality. **Trial Status:** Enrollment began in November 2015. As of November 2016, 179 patients (including roll-in and evaluable subjects) have been enrolled at 18 sites (10 US, 8 Europe). A total of 22 sites in the US and EU have been opened. **Conclusion:** Study enrollment completion is expected in Q1 2017.

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Presentation Number: CTP27

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

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

Abstract Body: Background Markers of blood coagulation activation rise immediately after stroke; and, persistent elevations in these levels are associated with poorer clinical outcomes in patients treated and not treated with IV tPA. Blood coagulation markers are particularly high in diabetic patients with hyperglycemia. We hypothesize that the decrease in levels of markers of blood coagulation will be greater in patients treated with IV insulin to reduce BG than in patients treated with SQ Insulin as the standard fashion. **Objectives** To determine the relationships between levels of blood coagulation markers and hyperglycemia control and functional neurological outcome in Stroke Hyperglycemia Insulin Network Effort (SHINE) treatment and control patients. **Design** I-SPOT is designed to accompany SHINE clinical trial. Excluded are patients with known coagulation disorder and patients receiving endovascular treatment. **Population** SHINE enrolled subjects (adult AIS patients with hyperglycemia) who have not received anticoagulants, have no severe liver disease nor hypercoagulable disorders are eligible for I-SPOT. **Sample Size** 315 Subjects will be enrolled in the I-SPOT trial. 195 who have not received fibrinolytics and 120 who have received fibrinolytics. **Intervention/Outcome Measures** Blood coagulation marker levels will be measured at baseline and 48 hours after randomization. Outcome Measures: Baseline stroke-severity adjusted 90-day modified Rankin Scale Questionnaire for Verifying Stroke Free Symptoms (QVSFS) **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. **Results** Samples for both time points have been drawn from 129 of the 141 subjects. **Trial Status** Enrollment is ongoing at 39 of the approximately 50 SHINE sites. 143 subjects have been enrolled.

Author Disclosure Block: **N.T. Gentile:** Research Grant; Significant; NIH-NINDS 1U01NS079077. **A.K. Rao:** Research Grant; Significant; NIH-NINDS 1U01NS079077. **H. Reimer:** Research Grant; Significant; NIH-NINDS 1U01NS079077. **A. Bruno:** Research Grant; Modest; NIH-NINDS 1U01NS079077. **V. Ramakrishnan:** Research Grant; Modest; NIH-NINDS 1U01NS079077. **W. Barsan:** None.

Presentation Number: CTP28

Publishing Title: New Generation Hydrogel Endovascular Aneurysm Treatment Trial

Author Block: Rami J Aoun, Mayo Clinic, Phoenix, AZ; **Jennifer D Ward**, Byron K Yip, Jason F Kniss, Northwestern Univ, Chicago, IL; Bernard R Bendok, Mayo Clinic, Phoenix, AZ

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

Hypothesis: The 2nd Generation HydroCoil Embolic System allows for a higher packing density, higher initial occlusion, lower recanalization, and lower retreatment rates compared to bare platinum coils.

Objective: To compare clinical and angiographic outcomes (initial complete occlusion, recanalization, retreatment, and adverse event rates) in patients receiving the 2nd Generation HydroCoil Embolic System versus patients receiving bare platinum coils.

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

Results: As of January 15, 2016, a total of 600 patients have been enrolled. The study is now closed to accrual and follow-up data is currently being collected.

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

Author Disclosure Block: **R.J. Aoun:** None. **J.D. Ward:** None. **B.K. Yip:** None. **J.F. Kniss:** None. **B.R. Bendok:** None.

Presentation Number: CTP29

Publishing Title: Newton 2: Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Efficacy and Safety Study Comparing Eg-1962 to Standard of Care Oral Nimodipine in Adults With Aneurysmal Subarachnoid Hemorrhage

Author Block: **Daniel Hänggi M.D.**, Nima Etminan, Univ Hosp Mannheim, Mannheim, Germany; Stephan Mayer, Mount Sinai Hosp, New York, NY; Francois Aldrich, Univ of Maryland Medical Ctr, Baltimore, MD; Michael Diringer, Washington Univ Sch of Med, St. Louis, MO; Andrew Carlson, Univ of New Mexico Sch of Med, Albuquerque, NM; George Wong, Prince of Wales Hosp, Hong Kong, China; Erich Schmutzhard, Medical Univ Innsbruck, Innsbruck, Austria; Herbert Faleck, Edge Therapeutics, Berkeley Heights, NJ; R. Loch Macdonald, St. Michael's Hosp, Toronto, ON, Canada; NEWTON-2 Investigators

Abstract Body: Background and Objective: Aneurysmal subarachnoid hemorrhage (aSAH) is associated with high morbidity and mortality. EG-1962 is a sustained release microparticle formulation of nimodipine that is administered through an external ventricular drain (EVD) as a single injection in patients with aSAH following repair of the ruptured aneurysm by clipping or coiling. EG-1962 was studied in a randomized, open-label, phase 1/2a, dose-escalation study to determine safety, tolerability, pharmacokinetics and clinical effects (NEWTON) in World Federation of Neurological Surgeons (WFNS) grade 2 to 4 patients. EG-1962 was generally safe and well-tolerated, reduced the incidence of DCI and rescue therapy and improved clinical outcome. EG-1962 is therefore being evaluated in a phase 3 study. **Design:** NEWTON-2 is a randomized, double-blind, placebo-controlled study to evaluate efficacy and safety of a single 600 mg dose of EG-1962 administered through an EVD to patients with aSAH, compared to standard of care oral nimodipine. Subjects will be WFNS grades 2 to 4, modified Fisher grades 2 to 4 on computed tomography and have an EVD inserted as part of standard of care. The ruptured aneurysm can be repaired by clipping or coiling. Intraventricular study drug must be given within 48 hours of the onset of aSAH. Up to 374 subjects will be randomized. The primary endpoint is clinical outcome 90 days after aSAH as measured on the extended Glasgow outcome scale. The secondary endpoint is the 90 day Montreal cognitive assessment. Safety data as well as proportion of subjects with delayed cerebral ischemia and infarction, need for rescue therapy and health economic outcomes will be evaluated. **Study Status:** The study is currently recruiting. **Principle Investigator:** Univ.-Prof. Dr. med. Daniel Hänggi, Department of Neurosurgery, University Medical Center Mannheim, Ruprecht-Karls-University Heidelberg, Mannheim, Germany. **Study Sponsor and Registration:** Edge Therapeutics (contact: R. Loch Macdonald, M.D., Edge Therapeutics, Ph: 908 315-5936, Email: rlmacdonald@edgetherapeutics.com). www.clinicaltrials.gov Identifier: NCT02790632

Author Disclosure Block: **D. Hänggi:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **N. Etminan:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **S. Mayer:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **F. Aldrich:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **M. Diringer:** Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **A. Carlson:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **G. Wong:** Research Grant; Modest; Edge Therapeutics, Inc.. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **E. Schmutzhard:** Research Grant; Modest; Edge Therapeutics, Inc. Consultant/Advisory Board; Modest; Edge Therapeutics, Inc. **H. Faleck:** Employment; Significant; Edge Therapeutics, Inc. **R. Macdonald:** Employment; Significant; Edge Therapeutics, Inc..

Presentation Number: CTP30

Publishing Title: Secondary Stroke Prevention by Uniting Community and Chronic Care Model Teams Early to End Disparities: The SUCCEED Trial

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Abstract Body: Registry Trial Number: NCT01763203

Background: Recurrent stroke risk can be mitigated by controlling vascular risk factors, yet risk factors are suboptimally controlled in most stroke survivors, particularly among indigent populations with barriers to accessing healthcare.

Objective: To develop and test the impact of an outpatient team intervention on risk factor control among adults with recent stroke/TIA, enrolled from the largest US safety-net healthcare system.

Design: Randomized-controlled trial.

Population: 516 adults, recruited from 4 Los Angeles County-Department of Health Services hospitals and 1 comprehensive stroke center serving low income zip codes. Inclusion criteria: recent (<90 days) TIA, ischemic stroke or intracerebral hemorrhage and either systolic BP (SBP) ≥ 130 mm Hg, or SBP 120-130 mm Hg with history of hypertension or on antihypertensive medications prior to index event. Exclusion criteria: <40 years old, unable to give informed consent, or not fluent in English, Spanish, Korean, Mandarin or Cantonese.

Intervention: Participants randomized to the intervention arm are managed by a team consisting of an advanced practice clinician (Nurse Practitioner or Physician Assistant) and a community health worker (CHW). Participants receive self-management tools (including goal cards and BP monitors), ≥ 3 clinic visits, ≥ 3 home visits, and the opportunity to participate in CHW-facilitated Chronic Disease Self-Management workshops. Evidence-based protocols guide the team's management of vascular risk factors, lifestyle factors, stroke literacy, healthcare system navigation, and depression. The team uses a web-based application to communicate, manage patient panels, access protocols/scripts, receive decision support, and track tasks. Participants randomized to the control arm receive usual care and stroke risk factor handouts.

Outcomes: Primary: SBP control. Secondary: Control of other vascular risk factors, medication adherence, cost-effectiveness.

Analyses: Intention-to-treat analysis to determine effectiveness of intervention at 12 months, cost analysis, and sustainability plan.

Trial Status: Enrolled 376 of 516 participants as of 11/8/16.

Author Disclosure Block: **A. Towfighi:** None. **M. Ayala-Rivera:** None. **T. Sivers-Teixeira:** None. **E. Mojarro-Huang:** None. **M. Ramirez:** None. **H. McCreath:** None. **J. Wacksman:** None. **E.M. Cheng:** None. **J. Tran:** None. **C. Ediss:** None. **A. Montoya:** None. **M. Castro:** None. **N. Sanossian:** None. **A. Razmara:** None. **T. Dutta:** None. **B. Mehta:** None. **S. Song:** None. **R. Bryg:** None. **N. Rao:** None. **S. Wu:** None. **P. Willis:** None. **L. Moreno:** None. **M. Fernandez:** None. **D. Martinez:** None. **A. Richards:** None. **F. Barry:** None. **V. Hill:** None. **B. Mittman:** None. **W. Cunningham:** None. **H.H. Liu:** None. **D. Ganz:** None. **D. Factor:** None. **N. Ibrahim:** None. **B.G. Vickrey:** None.

Presentation Number: CTP31

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

Author Block: Latisha K Sharma, David S Liebeskind, Ivie Tokunboh, Johanna L Avelar, Jeffrey L Saver, UCLA Stroke Ctr, Los Angeles, CA

Abstract Body:

Background and Objective: Remote ischemic preconditioning (RPreC) activates multiple endogenous cellular and molecular mechanisms that protect brain (and myocardial) 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. The study will have a randomized phase and a follow-up phase. 60 enrolled patients will be randomized 2:1 to best standard medical care plus active RPreC for 1 year and then follow-up for 1 year versus best standard medical care alone for 1 year and then active RPreC for 1 year.

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

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 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.

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

Author Disclosure Block:

L.K. Sharma: None. **D.S. Liebeskind:** None. **I. Tokunboh:** None. **J.L. Avelar:** None. **J.L. Saver:** None.

Presentation Number: CTP32

Publishing Title: The Intracerebral Hemorrhage Acutely Decreasing Blood Pressure Trial II (ICHADAPTII): Impact of Antihypertensive Therapy on Ischemic Lesion Development in Hemorrhagic Stroke Patients

Author Block: Ana Klahr, Univ of Alberta, Edmonton, AB, Canada; Dariush Dowlatshahi, Univ of Ottawa, Ottawa, ON, Canada; Hely Shah, Brian Buck, Alejandro Manosalva, Hayrapet Kalashyan, Alan Wilman, Thomas Jeerakathil, Kenneth Butcher, Univ of Alberta, Edmonton, AB, Canada

Abstract Body: Background: Aggressive blood pressure (BP) reduction in acute intracerebral hemorrhage (ICH) patients may improve outcome. Magnetic resonance imaging (MRI) studies demonstrated sub-acute ischemic lesions in 14-41% of ICH patients.

Objective and Hypothesis: The aim is to assess ischemic lesion development in ICH patients randomized to different BP treatment targets. It is hypothesized that aggressive BP reduction is not associated with ischemic injury.

Design: The Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial II (ICH-ADAPT II NCT02281838) is a randomized open-label, blinded-endpoint trial.

Population: Male and female patients (270) ≥ 18 years of age, with acute ICH confirmed by CT scan within 6 hours of symptom onset are randomized 1:1 to an aggressive treatment of BP to <140 versus <180 mmHg. All patients must have two systolic BP measurements ≥ 180 mmHg recorded >2 mins apart and hematoma volume <90 mL to qualify for enrolment.

Intervention: Patients randomized to the aggressive therapy group are treated with a protocol based on repeated intravenous labetalol and/or hydralazine boluses to lower systolic BP to <140 mmHg within 1 hour of randomization and maintain this pressure for a minimum of 24 hours. Patients randomized to the conservative group receive parenteral antihypertensive therapy if systolic BP is ≥ 180 mmHg. Patients are assessed with serial MRI, including diffusion-weighted imaging (DWI) at 48 hours, 7 and 30 days.

Analysis: DWI sequences will be assessed for the presence, number and total volume of regions with diffusion restriction.

Primary Outcome Measure: DWI lesion frequency in the first 48 hours.

Secondary Outcome Measures: DWI lesion frequency within 30 days, hematoma expansion at 24 hours, 30-day mortality rate and 90-day modified Rankin Scores.

Trial Status: Ongoing. 75 patients enrolled (November 2016)

Contact: Dr. Ken Butcher M.D.(ken.butcher@ualberta.ca), University of Alberta, Canada. Sponsored by University of Alberta. <https://clinicaltrials.gov/show/NCT02281838>. Funded by the Heart and Stroke Foundation of Canada (GIA G-14-0006004).

Author Disclosure Block: A. Klahr: None. D. Dowlatshahi: None. H. Shah: None. B. Buck: None. A. Manosalva: None. H. Kalashyan: None. A. Wilman: None. T. Jeerakathil: None. K. Butcher: None.

Presentation Number: CTP33

Publishing Title: Treatment Evaluation of Acute Stroke for Using in Regenerative Cell Elements (TREASURE): A Randomized Controlled Phase II/III Trial of MultiStem (HLCM051)

Author Block: Kiyohiro Houkin, Hokkaido Univ Hosp, Sapporo, Japan; Shinichiro Uchiyama, Clinical Res Ctr for Med, Intl Univ of Health and Welfare, Ctr for Brain and Cerebral Vessels, Sanno Hosp and Sanno Medical Ctr, Tokyo, Japan; Kazuo Minematsu, Dept of Cerebrovascular Med, Natl Cerebral and Cardiovascular Ctr, Suita, Japan; Akihiko Taguchi, Dept of Regenerative Med Res, Inst of Biomedical Res and Innovation, Kobe, Japan

Abstract Body: Background: Cell therapy is a promising neuro-restorative approach which suppresses inflammatory responses after acute stroke. MultiStem (HLCM051), a bone marrow-derived, allogenic, clinical-grade product that has shown safety and tolerability with stroke patients. In post hoc analyses, it also has suggested favorable clinical outcome within a 36-hour treatment window (NCT01436487). **Study Design:** TREASURE is a multicenter (approximately 30 sites in Japan), randomized, double-blind, placebo-controlled, phase II/III study. Patients with a persistent neurologic deficit with the National Institute of Health Stroke Scale (NIHSS) of 8-20 will be randomized 1:1 to receive a single intravenous infusion of MultiStem (1200 million cells per patients) or placebo within 18-36 hours of stroke onset. Estimated sample size is 220 (110 patients per arm), which has 90% power at the 5% significance level. Protocol stopping rules will be in place with an independent Data Safety Monitoring Board assembled if serious safety events, including infusion reactions, occur related to investigational product. **Outcome Measures:** Primary outcome is the proportion of subjects achieving an excellent outcome at day 90 defined by all the following criteria: modified Rankin Scale (mRS) 0-1; NIHSS score 0-1; and Barthel Index score ≥ 95 . The key secondary outcomes will be defined including excellent outcome at day 365, categorical shift in mRS at day 90 and day 365. Biomarkers (inflammatory cytokine and T cell levels in serum) will be measured to examine potential mechanisms of action. **Statistical Analysis:** The primary efficacy outcome will be analyzed via a Cochran-Mantel-Haenszel test. **Trial Status:** Recruitment is ongoing. Study is expected to be completed in October 2018. **Conclusion:** TREASURE is the first study to verify the treatment efficacy and safety of cell therapy for acute ischemic stroke. It can provide a new treatment option and expand the therapeutic window for stroke when we successfully develop this cell product.

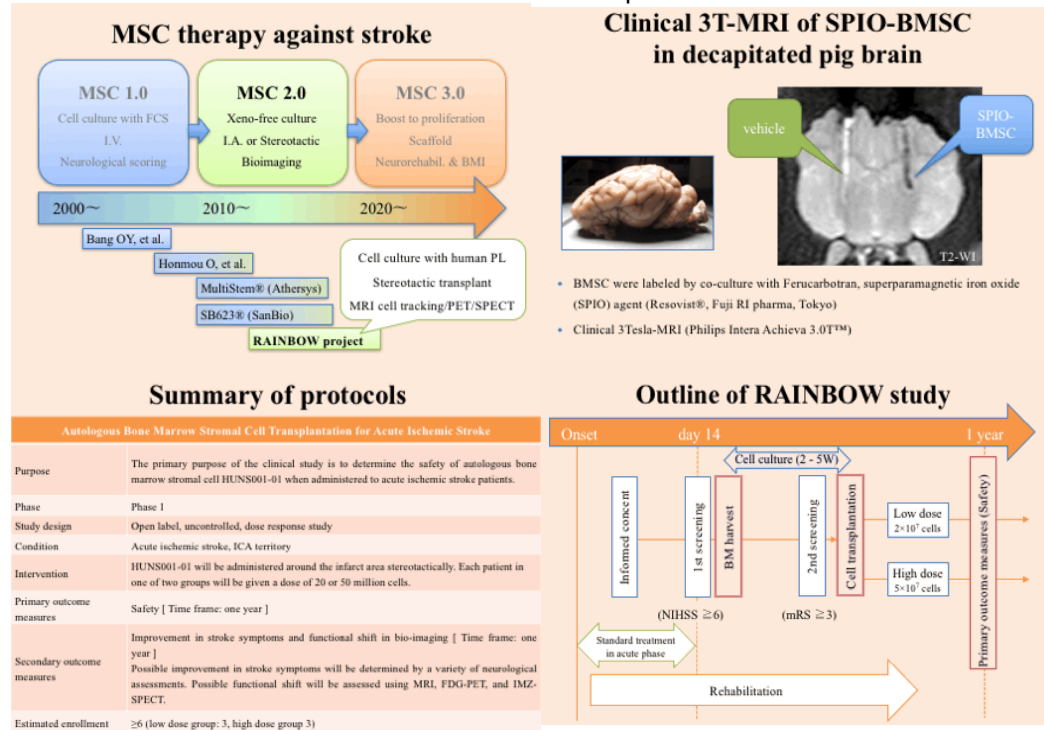
Author Disclosure Block: **K. Houkin:** Honoraria; Modest; Otsuka Pharmaceutical, Eisai Co., T-PEC, Sanwa Kagaku Kenkyusho, Kyowa Hakko Kirin Pharma, Inc, SanBio, Dai-ichi Sankyo, Mitsubishi Tanabe Pharma Cooperation, Boehringer-Ingelheim, Japan Medi-Physics, Novartis Pharma K.K., Bayer Healthcare, Pfizer, Mochida Pharmaceutical, Leica Microsystems. Consultant/Advisory Board; Modest; HEALIOS K.K. **S. Uchiyama:** Honoraria; Modest; DaiichiSankyo, Dainihon Sumitomo, Takeda, Shinogi, Mitsubishi Tanabe, Astellas, AstraZeneca. Honoraria; Significant; Bayer, Boehringer-Ingelheim, Sanofi. **K. Minematsu:** Honoraria; Modest; Bayer Healthcare, Otsuka Pharmaceutical, Boehringer-Ingelheim, AstraZeneca, Pfizer, Mitsubishi Tanabe Pharma Cooperation, Japan Stryker, Kowa, Nihon Medi-Physics Co, BMS, Sawai Pharmaceutical Co., Sumitomo Dainippon Pharma Co Ltd, Medico's Hirata, Dai-ichi Sankyo, Asteras Pharma, Kyowa Hakko Kirin Pharma, Inc, Sanofi S.A., MSD, Eisai Co., Towa Pharmaceutical Co. **A. Taguchi:** Honoraria; Modest; HEALIOS K.K..

Presentation Number: CTP34

Publishing Title: Autologous Bone Marrow Stromal Cell Transplantation Against Stroke; RAINBOW Study

Author Block: Hideo Shichinohe, Masahito Kawabori, Chengbo Tan, Zifeng Wang, Takeo Abumiya, Naoki Nakayama, Ken Kazumata, Kiyohiro Houkin, Hokkaido Univ, Sapporo, Japan

Abstract Body: Recent studies have elucidated that the bone marrow stromal cells (BMSCs) have therapeutic potential against stroke. Now we prepare the novel clinical trials, Research on advanced intervention using novel bone marrow stem cell (RAINBOW) study. It is a phase 1, open label, uncontrolled, dose response study. The primary purpose is to determine the safety of autologous BMSC product, HUNS001-01, when administered to acute ischemic stroke patients. After 2 weeks pass from the onset, about 50 mL of bone marrow is extracted from the iliac bone of the patient. The BMSCs are cultured with human platelet lysate (hPL) instead of fetal calf serum (FCS). They are labeled with superparamagnetic iron oxide (SPIO). HUNS001-01 is administered around the infarct area stereotactically. Each patient will be given a dose of 20 or 50 million cells. Neurological scoring, MRI for cell tracking, 18F-FDG PET, and 123I-Iomazenil SPECT were performed for 1 year after the administration. Estimated enrollment is more than 6 patients. The trials will start in this winter.



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Presentation Number: CTP35

Publishing Title: Critical Periods After Stroke Study

Author Block: Alexander W Dromerick, MedStar Natl Rehabilitation Network, Washington, DC; Dorothy F Edwards, Univ of Wisconsin - Madison, Madison, WI; Matthew A Edwardson, Georgetown Univ, Washington, DC; **Margot L Giannetti**, Jessica Barth, Kathaleen P Brady, Claire P Wilson, MedStar Natl Rehabilitation Network, Washington, DC; Evan Chan, MedStar Health Res Inst, Hyattsville, MD; Shashwati Geed, MedStar Natl Rehabilitation Network, Washington, DC; Ming T Tan, Georgetown Univ, Washington, DC; Massimo S Fiandaca, Howard J Federoff, Univ of California - Irvine, Irvine, CA; Elissa L Newport, Georgetown Univ, Washington, DC

Abstract Body: Background: Better treatment of stroke, whether to reduce impairment or target the goals and preferences of individuals, can enable independence and increase participation. We are investigating the optimal time after stroke for intensive upper extremity motor training.

There is evidence for timing effects in rehabilitation; motor training delivered at certain times may be more effective. It is hypothesized that the periods of greatest responsiveness after a stroke are analogous to the sensitive periods in normal human development. We expect that individuals receiving early intensive motor training will show greater upper extremity motor improvement measured at one year post stroke compared to individuals receiving therapy at later time points.

Methods and Analysis: 64 participants will be adaptively randomized to receive an additional bolus of 20 hours of upper extremity therapy either within 30 days post-stroke, 2-3 months post-stroke, 6-9 months post-stroke, or to a control group. The primary outcome is the Action Research Arm Test at one year. Blood will be drawn at up to 3 time points for biomarker studies.

Results: We have enrolled two run-in subjects and randomized forty-one participants to date; the study will be completed in 2 years. Results from this study will help to plan a Phase III clinical trial.

Conclusion: If sensitive periods exist in rehabilitation and can be identified after stroke, then current resources can be better targeted to promote recovery. Inclusion of biomarker determination opens up the possibility of understanding the biological mechanisms of recovery and supports future drug development.

Author Disclosure Block: **A.W. Dromerick:** None. **D.F. Edwards:** None. **M.A. Edwardson:** None. **M.L. Giannetti:** None. **J. Barth:** None. **K.P. Brady:** None. **C.P. Wilson:** None. **E. Chan:** None. **S. Geed:** None. **M.T. Tan:** None. **M.S. Fiandaca:** None. **H.J. Federoff:** None. **E.L. Newport:** None.

Presentation Number: CTP36

Publishing Title: NIH StrokeNet Evolving Trial Proposal Process

Author Block: **Joseph P Broderick**, Univ of Cincinnati, Cincinnati, OH; **Yuko Y Palesch**, Wenle Zhao, Medical Univ of South Carolina, Charleston, SC; **Scott Janis**, **Claudia S Moy**, Natl Inst of Neurological Disorders & Stroke, Bethesda, MD

Abstract Body: Introduction: 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, recovery & rehabilitation. The NIH StrokeNet was fully funded in April 2014, with a National Coordinating Center (NCC), a National Data Management Center (NDMC), and 25 Regional Coordinating Centers. Three working groups (prevention, treatment, and recovery & rehabilitation) were established to assist in the development of protocols.

Methods: Protocol Principal Investigators (PPIs) with potential NIH StrokeNet applications submit their concepts to the NINDS scientific representative as well as to the relevant working group for initial discussion. If the project is deemed to be potentially appropriate for NIH StrokeNet, a formal concept proposal is submitted to the NINDS Extramural Science Committee (ESC) for official approval to submit an NIH grant application. If approved, the proposed study is referred to the appropriate working group to assess feasibility and to the NIH StrokeNet NCC and NDMC to assist in developing a final budget. The expected time from approval of concept proposal by the NINDS ESC to grant submission by the PPI is 3 months.

Results: Since May 2014 there have been 23 concept proposals vetted by the working groups. NINDS ESC has approved 17 grant submissions. Three trials that have been funded are TeleRehabilitation, DEFUSE 3, and ARCADIA. Currently, there are 11 trials under NIH review and 3 trials are being revised for resubmission.

Conclusion: The NIH StrokeNet trial proposal process facilitates submission of high quality stroke trial applications to the NIH.

Author Disclosure Block: **J.P. Broderick:** Consultant/Advisory Board; Modest; PRISMS Trial Steering Committee, Pfizer consulting fees, AstraZeneca SOCRATES Trial Advisory Board. Other; Modest; Consulting fees and honoraria are placed in an educational/research stroke fund at the University of Cincinnati Department of Neurology and Rehabilitation Medicine. **Y.Y. Palesch:** Other; Modest; Member of DSMB for a Brainsgate Ltd Trial. **W. Zhao:** None. **S. Janis:** None. **C.S. Moy:** None.

Presentation Number: CTP37

Publishing Title: 30 Day Results of Revascularization of Extracranial Carotid Artery Stenosis (RECAS) Trial in Mainland China

Author Block: Yang Bin, Chen Yanfei, Wang Yabing, Gao Peng, Ma Yan, Jiao Liqun, Xuanwu hospital, Beijing, China

Abstract Body:

Background

Carotid endarterectomy is more effective than medical management in the prevention of stroke in patients with severe symptomatic or asymptomatic atherosclerotic carotid artery stenosis. Stents are an alternative treatment to carotid endarterectomy for symptomatic carotid stenosis, ICSS trial has established equivalent safety and efficacy. Many hospitals have developed CEA and CAS in mainland China, but the data of safety and efficacy is rare.

Methods

The revascularization of extracranial carotid artery stenosis (RECAS) study is a multicentre, prospective cohort trial. Patients with symptomatic carotid artery stenosis in 38 centers were continuously assigned to receive carotid artery stenting or carotid endarterectomy. Patients were followed up by independent clinicians not directly involved in the treatment. The primary end point of the study was the cumulative incidence of a major cardiovascular event at 1 year — a composite of death, stroke, or myocardial infarction within 30 days after the intervention or death or ipsilateral stroke between 31 days and 1 year. This study is registered, number NCT01994187.

Results

The trial enrolled 2743 patients (CAS group, n=1504; CEA group, n=1196; CEA+CAS group, n=43). The primary end point was achieved in 4.72% (71/1504) in patients treated with carotid artery stents, and 5.02% (60/1196) in patients treated with carotid endarterectomy, an absolute difference of 0.30%. Risks of any stroke (3.68% vs 3.51%) was higher in the stenting group than in the endarterectomy group, but the risks of any death (0.75% vs 0.77%) was lower in the stenting group than in the endarterectomy group. Five procedural myocardial infarctions were recorded in the stenting group, compared with nine in the endarterectomy group.

Interpretation

Completion of long-term follow-up is needed to establish the efficacy of carotid artery stenting compared with endarterectomy.

Author Disclosure Block: Y. Bin: None. C. Yanfei: None. W. Yabing: None. G. Peng: None. M. Yan: None. J. Liqun: None.

Presentation Number: CTP39

Publishing Title: Telerehabilitation in the Home Versus Therapy In-Clinic for Patients With Stroke

Author Block: Steven C Cramer, Univ of California, Irvine, Orange, CA; Telerehabilitation in the Home Versus Therapy In-Clinic for Patients With Stroke Investigators

Abstract Body: The current study will test the effectiveness of a novel home-based telehealth system designed to improve motor recovery and patient education after stroke. A minimum of 124 subjects with arm motor deficits 4-36 weeks after a stroke due to ischemia or to intracerebral hemorrhage will be randomized to receive 6 weeks of intensive arm motor therapy (a) in a traditional in-clinic setting or (b) via in-home telerehabilitation (rehabilitation services delivered to the subject's home via an internet-connected computer). The intensity, duration, and frequency of this therapy will be identical across the two groups, with subjects in both treatment arms receiving 36 sessions (18 supervised and 18 unsupervised), 80 minutes each (including a 10 minute break), over 6 weeks. The primary endpoint is within-subject change in the arm motor Fugl-Meyer (FM) score from the Baseline Visit to 30 Day Follow-Up Visit. Arm motor status is the focus here because it is commonly affected by stroke, is of central importance to many human functions, and is strongly linked to disability and well being after stroke. Additional study aims pertain to comparing methods for providing stroke education, and to understanding motivation in relation to patient compliance.

Author Disclosure Block: S.C. Cramer: Consultant/Advisory Board; Modest; MicroTransponder, Toyama. Consultant/Advisory Board; Significant; Dart Neuroscience.

Presentation Number: CTP40

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

Author Block: James F. Meschia, Mayo Clinic, Jacksonville, FL; Brajesh K Lal, Univ of Maryland, Baltimore, MD; George Howard, University of Alabama at Birmingham, Birmingham, AL; Gary S. Roubin, Cardiovascular Associates of the Southeast, Birmingham, AL; **Robert D. Brown Jr**, Mayo Clinic, Rochester, MN; Kevin M. Barrett, Mayo Clinic, Jacksonville, FL; Seemant Chaturvedi, Univ of Miami Miller Sch of Med, Miami, FL; Marc I Chimowitz, Medical Univ of South Carolina, Charleston, SC; Bart M. Demaerschalk, Mayo Clinic, Phoenix, AZ; Virginia J. Howard, Univ of Alabama at Birmingham, Birmingham, AL; John Huston III, Mayo Clinic, Rochester, MN; Ronald M. Lazar, Columbia Univ Medical Ctr, New York City, NY; Wesley S. Moore, Univ of California Los Angeles, Los Angeles, CA; Claudia S. Moy, Natl Inst of Neurological Disorders and Stroke, Bethesda, MD; Tanya N. Turan, Jenifer H. Voeks, Medical Univ of South Carolina, Charleston, SC; Thomas G Brott, Thomas G. Brott, Mayo Clinic, Jacksonville, FL

Abstract Body: Despite a dramatic decline in carotid revascularization procedures, they remain one of the most common vascular procedures. 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, guidelines based on the results of prior randomized trials in asymptomatic carotid stenosis are outdated. The NINDS-funded CREST-2 is a pair of parallel randomized trials, each with a planned sample size of 1240 patients, will compare (1) CEA and intensive medical therapy (IMT) versus IMT alone, and (2) CAS and IMT versus IMT alone. 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 is assessed on a regular schedule through computer-assisted telephone interview. IMT is directed centrally and includes 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 7, 2016, 381 patients have been randomized. 112 centers have been approved to randomize by the CREST-2 Site Selection Committee, and site selection is ongoing for a total of 120 sites (including collaboration with NIH-StrokeNet). The Surgical and Interventional Management Committees have credentialed 295 surgeons and 131 interventionists. An additional 121 interventionists have been approved to submit additional cases via the CREST-2 Companion Registry which provides a CMS-reimbursed pathway for full credentialing in CREST-2. An update regarding the numbers of centers certified, surgeons and interventionists 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:** None. **K.M. Barrett:** None. **S. Chaturvedi:** None. **M.I. Chimowitz:** None. **B.M. Demaerschalk:** None. **V.J. Howard:** None. **J. Huston:** None. **R.M. Lazar:** None. **W.S. Moore:** None. **C.S. Moy:** None. **T.N. Turan:** None. **J.H. Voeks:** None. **T.G. Brott:** None. **T.G. Brott:** None.