

## Late-Breaking Science Oral Abstracts

Friday, February 24, 2017, 10:30am – 12:30pm

*LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2017:*

*For late-breaking science being presented at ISC 2017, the embargo lifts when the first presentation begins in the scientific session in which the abstract is being presented: either 11:20 am CST on Wednesday, Feb. 22; 6:15 pm CST on Wednesday, Feb. 22; 11:00 am CST on Thursday, Feb. 23; 1:30 pm CST on Thursday, Feb. 23; or 11:53 am CST on Friday, Feb. 24. News media activities promoting late-breaking science are under embargo until the times noted above.*

**Presentation Number:** LB16

**Presentation Title:** Randomized Trial of Hemostatic Therapy for 'Spot Sign' Positive Intracerebral Hemorrhage: Primary Results From the SPOTLIGHT/STOP-IT Study Collaboration

**Author Block:** David J. Gladstone, Richard I. Aviv, Univ of Toronto, Toronto, ON, Canada; Andrew M. Demchuk, Michael D. Hill, Univ of Calgary, Calgary, AB, Canada; Kevin E. Thorpe, Univ of Toronto, Toronto, ON, Canada; Jane C. Khoury, Heidi J. Sucharew, Univ of Cincinnati, Cincinnati, OH; Stephanie De Masi, Val Panzov, Judith Hall, Applied Health Res Inst, Li Ka Shing Knowledge Inst, Toronto, ON, Canada; Muhammad Mamdani, Univ of Toronto, Toronto, ON, Canada; Fahad Al-Ajlan, Univ of Calgary, Calgary, AB, Canada; Janice Carrozzella, Univ of Cincinnati, Cincinnati, OH; Edward C. Jauch, Medical Univ of South Carolina, Charleston, SC; Joseph P. Broderick, Matthew L. Flaherty, Univ of Cincinnati, Cincinnati, OH; for the SPOTLIGHT and STOP-IT Study Steering Committee and Investigators

**Abstract Body: Background**--Intracerebral hemorrhage (ICH) lacks an effective emergency treatment. We tested the hypothesis that the CT angiography defined 'spot sign' could identify a subgroup of patients at increased risk for ICH expansion who may benefit from hemostatic therapy with recombinant factor VIIa (rFVIIa). **Methods**--We conducted parallel investigator-initiated multicenter RCTs in Canada (SPOTLIGHT) and USA (STOP-IT) with harmonized protocols and preplanned pooled analysis. Eligible non-anticoagulated spot-positive ICH patients were randomly assigned to intravenous rFVIIa 80µg/kg or placebo within 6h of onset. Spot-negative patients were prospectively observed. The primary outcome was blinded measurement of 24h ICH volume, assessed in an ITT analysis by linear regression adjusting for trial, baseline ICH volume, and onset-to-needle (OTN) time. Secondary outcomes included total (ICH+IVH) volume; proportion with 90-day mRS 5-6; ischemic stroke/MI/PE within 4 days; and comparison of spot-positive vs. spot-negative outcomes. **Results**--We enrolled 69 spot-positive and 73 spot-negative ICH patients at 26 sites (2010-2016). Median (IQR) times (min) were: onset-to-CT 86 (70,161); CT-to-needle 71 (57,96); OTN 178 (138,197). Median (IQR) ICH volume (ml) increased from baseline to follow-up in both groups: 16 (10,39) to 22 (10,53) [rFVIIa] vs. 20 (9,33) to 29 (14,52) [placebo]. Median total volume increased from baseline to follow-up: 24 (15,40) to 26 (18,56) [rFVIIa] vs. 25 (9,45) to 31 (16,60) [placebo]. No treatment effect was observed on log<sub>e</sub> ICH volume (p=0.9), total

volume ( $p=0.9$ ), or 90-day mRS 5-6 ( $p=0.6$ ). There was 1 ischemic stroke (post-op) in the rFVIIa group. The spot sign was highly predictive of ICH expansion and death/disability; ICH volumes did not increase meaningfully from baseline to follow-up among spot-negative patients. **Conclusions**--These data affirm the value of emergency CT angiography for prognostication in acute ICH. For spot-positive ICH patients, rFVIIa treatment did not significantly alter final ICH volume or clinical outcomes in this trial, although nearly all were treated more than 2h post-onset. [Funded by peer-reviewed grants from CIHR, NINDS, OSN, OMRI; ClinicalTrials.gov NCT01359202 & NCT00810888]

**Author Disclosure Block:** **D.J. Gladstone:** None. **R.I. Aviv:** Research Grant; Significant; PI of a peer-reviewed grant on intracerebral hemorrhage from the Canadian Institutes of Health Research. **A.M. Demchuk:** None. **M.D. Hill:** None. **K.E. Thorpe:** None. **J.C. Houry:** None. **H.J. Sucharew:** None. **S. De Masi:** None. **V. Panzov:** None. **J. Hall:** None. **M. Mamdani:** None. **F. Al-Ajlan:** None. **J. Carrozzella:** None. **E.C. Jauch:** None. **J.P. Broderick:** Consultant/Advisory Board; Modest; Consultant fees from Pfizer paid to his Department. **M.L. Flaherty:** Other Research Support; Significant; Study drug provided by Novo Nordisk for the STOP-IT Study. Speakers' Bureau; Significant; CSL Behring. Expert Witness; Significant; Expert witness in medico-legal cases.

**Presentation Number:** LB17

**Presentation Title:** Randomized Controlled Trial of Early versus Delayed Statin Therapy in Patients With Acute Ischemic Stroke

**Author Block:** **Shinichi Yoshimura**, Kazutaka Uchida, Takashi Daimon, Hyogo Coll of Med, Nisinomiya City, Japan; Ryuzou Takashima, Kazuhiro Kimura, Shionogi & Co., Ltd, Osaka City, Japan; Takeshi Morimoto, Hyogo Coll of Med, Nisinomiya City, Japan

**Abstract Body:** Introduction: Physical disability is frequently observed after acute stroke even after thrombolysis or endovascular therapy. Among the medications attempted to alleviate the disabilities, statin is known to have a potential preferable effect on neurological function. We investigated whether immediate statin therapy after acute ischemic stroke improved the 90-day neurological function compared to the delayed therapy. Methods: We conducted a multicenter, open-label, randomized controlled trial (RCT) in patients with acute ischemic strokes in 13 institutes. Patients who had diagnosed dyslipidemia before or LDL-C  $\geq$  100 mg/dl and hospitalized within 24-hour after the onset of cerebral infarction were enrolled. Patients diagnosed as transient ischemic attack or cardio-embolic stroke were excluded. The patients randomly received early (within 24-hour after admission) or delayed (7th day after admission) administration of atorvastatin 20 mg/day, pitavastatin 4 mg/day, or rosuvastatin 5 mg/day. The primary endpoint was the modified Rankin Scale at 90 days. The secondary endpoints included National Institute of Health Stroke Scale on day 7, changes in laboratory test, occurrence of major adverse cardiac and cerebrovascular event and safety at 90 days. We estimated the 270 patients needed to attest the superiority of early statin therapy with 80% of power and two-tailed 0.05 of alpha. Results: A total of 270 patients were enrolled in the study, and 14 patients were excluded. Baseline characteristics of patients were not significantly different between the early (n=131) and delayed group (n=125). Conclusions: The primary endpoint and other secondary endpoints will be presented in the conference. This is the first RCT of early versus delayed statin therapy after acute ischemic stroke, and may provide a new treatment option for the patients with dyslipidemia after acute ischemic stroke. (This study was supported by Shionogi Co., Ltd. and the representative of Shionogi participated into the design and the drafting the manuscript, but the operation, data collection, and statistical analyses were solely conducted by the academic authors.)

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**Presentation Number: LB18**

**Presentation Title:** A Randomized Double-Blind Pilot Study Assessing Vagus Nerve Stimulation (VNS) During Rehabilitation for Improved Upper Limb Motor Function After Stroke

**Author Block:** **Jesse Dawson**, Univ of Glasgow, Glasgow, United Kingdom; **Gerard Francisco**, Nuray Yozbatiran, Univ of Texas, Health Science Ctr, Houston, TX; **Steve Cramer**, Univ of California, Irvine, Orange, CA; **Steve Wolf**, Emory Univ, Atlanta, GA; **Navzer Engineer**, **David Pierce**, **Wilson Brent Tarver**, MicroTransponder Inc, Dallas, TX; **Patricia Smith**, **Wiggington Jane**, Univ of Texas Southwestern, Dallas, TX; **Teresa Kimberley**, Univ of Minnesota, Minneapolis, MN

**Abstract Body: Introduction:** VNS paired with rehabilitation improves forelimb function in rodent models of stroke. A first-in-human PROBE study (n=20) showed VNS paired with upper limb rehabilitation was safe and feasible in patients with arm weakness up to 5 years after stroke. The per-protocol analysis showed greater improvement in upper-limb Fugl-Meyer (UEFM) scores in VNS treated patients compared to controls. This double blind study with control sham stimulation was performed to further assess use of VNS paired with upper limb rehabilitation. **METHODS:** Patients with chronic moderate to severe UE hemiparesis after ischemic stroke were enrolled (3 US, 1 UK site). All participants were implanted with a VNS device and randomised to either paired-VNS with rehabilitation (0.8 mA) or control VNS with rehabilitation (0.0 mA). All received 6-weeks of intensive and task-specific rehabilitation (3 sessions per week, 2 hour duration, ~50 repetitions per task and 300-400 movements per session). Outcomes were assessed on days 1 & 30 after completion of therapy. The primary efficacy outcome was change in UEFM score. A  $\geq 6$  point increase from baseline was considered clinically meaningful (CM). **RESULTS:** Seventeen patients (8 female) were implanted (8 VNS, 9 control). Mean age (SD) was 59.8 (10.4) years. The mean (SD) time from stroke was 1.5 (1.0) years. Study related serious adverse events included a wound infection (resolved with antibiotics), dysphagia (resolved within a week after implant surgery), and two vocal cord paralyses (1 recovered, 1 ongoing). In the per-protocol analysis 75% of VNS+rehab subjects had a CM improvement in UEFM compared to 25% in the rehab-only group. The mean UEFM improvement in the VNS group was  $7.6 \pm 4.8$  (mean $\pm$ std) points and  $4.9 \pm 3.1$  in the control groups. Full final statistical results will be presented. **CONCLUSIONS:** VNS appears feasible and safe in adults with chronic stroke. This pilot study confirms the first feasibility study results. A pivotal study will be undertaken for US commercial (PMA) approval.

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