Late-Breaking Science Oral Abstracts

Friday, January 26, 2018, 10:30am – 12:30pm

LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2018:

For late-breaking science being presented at ISC 2018, the embargo lifts when the first presentation begins in the scientific session in which the abstract is being presented: either 11:20 am PST on Wednesday, Jan. 24; 6:30 pm PST on Wednesday, Jan. 24; 11:00 am PST on Thursday, Jan. 25; 3:33 pm PST on Thursday, Jan. 25; or 11:53 am PST on Friday, Jan. 26. News media activities promoting late-breaking science are under embargo until the times noted above.

Presentation Number: LB16

Presentation Title: Pharyngeal Electrical Stimulation for Early Decannulation in Tracheotomised Stroke Patients with Dysphagia (PHAST-TRAC): A Randomised, Single-blind, Pivotal, Superiority Trial

Author Block: Rainer Dziewas, Stroke, Univ of Munster, Munster, Germany; Inge van der Tweel, Biostatistics, Univ Medical Ctr, Utrecht, Netherlands; Shaheen Hamdy, GI Sciences, Univ of Manchester, Manchester, United Kingdom; **Philip M Bath**, Univ of Nottingham, Nottingham, United Kingdom

Abstract Body:
Background Dysphagia after stroke is common, especially in ventilated patients in intensive care. Pharyngeal electrical stimulation (PES) has been shown to reduce aspiration and dysphagia in pilot trials, including in ventilated stroke patients.
Methods Patients with recent stroke who required ventilation and tracheotomy were randomised in this phase III trial to receive three days of PES or sham. The primary outcome was readiness for decannulation at 24-72 hours post treatment, assessed using fibreoptic endoscopic evaluation of swallowing (FEES) and based on the absence of massive saliva, and presence of spontaneous swallows and laryngeal sensibility. Patients in both groups who failed were treated with a (further) course of PES. Secondary outcomes included need for recannulation, and serious adverse events. Data are number (%), median [interquartile range] or mean (standard deviation).
Results The Data & Safety Monitoring Committee recommended that the trial should stop early. 81 patients were screened from 8 centres in Germany, Austria and Italy. 69 participants (PES 35, sham 34) were randomised: age 64 (12) years; female 25 (36.2%); haemorrhagic stroke 20 (29%); National Institutes of Health Stroke Scale 17.5 (4.6); dysphagia severity rating scale 12 (0); percutaneous endoscopic gastrostomy feeding tube 9 (13.0); onset to randomisation 27 [19, 41] days.
Conclusion Pharyngeal electrical stimulation is a novel potential treatment for post stroke dysphagia. The on-treatment results are being analysed and will be presented in 2018.

Author Disclosure Block: R. Dziewas: Speakers' Bureau; Modest; Phagenesis Ltd. Honoraria; Modest; Phagenesis Ltd. Consultant/Advisory Board; Modest; Chief Investigator PHAST-TRAC, Phagenesis Ltd. **I. van der Tweel:** Honoraria; Modest; Phagenesis Ltd. **S. Hamdy:** Employment; Modest; Phagenesis Ltd. Ownership Interest; Modest; Phagenesis Ltd. **P.M. Bath:** Speakers' Bureau; Modest; Phagenesis Ltd. Honoraria; Modest; Phagenesis Ltd. Consultant/Advisory Board; Modest; Chair of PHAST-TRAC Trial Steering Committee and Consultant to Phagenesis Ltd..

Presentation Number: LB17

Presentation Title: DEFUSE 3 Angiographic Results Correlated with Clinical and Imaging Outcomes

Author Block: **Michael P Marks**, STANFORD HOSPITAL, Stanford, CA; for the DEFUSE 3 Investigators

Abstract Body:
Background: DEFUSE 3 is a prospective randomized Phase III multicenter controlled trial evaluating endovascular therapy for patients with acute ischemic anterior circulation strokes due to large artery occlusion treated between 6-16 hours of stroke onset. The study hypothesized that endovascular therapy improves functional outcome and imaging outcomes in this patient population. The aim of this abstract is to correlate the angiographic findings in the endovascular therapy group with clinical and radiologic outcomes.
Methods: Endovascular therapy was performed with FDA approved thrombectomy devices and suction thrombectomy catheters used alone or in combination. If tandem lesions were present cervical angioplasty with or without stent placement could be performed. Patients undergoing endovascular therapy had core lab adjudication of the primary arterial occlusive lesion (AOL), and pre- and post-treatment Thrombolysis in Cerebral Infarction (TICI) score. The modified TICI scoring system was used (TICI 2B = 50-99% reperfusion and TICI 3 = 100% reperfusion). These angiographic results were correlated with functional outcome (assessed with 90-day modified Rankin Score) and baseline vessel imaging and perfusion data from CTA/CTP or MRA/MRP as well with 24 hour follow-up MR DWI/PWI/MRA assessed for infarct volume and growth as well as degree of reperfusion.
Results: 182 patients were enrolled in the DEFUSE 3 study and 92 were randomized to endovascular therapy. Patients arrived 9.28 $\pm$ 2. 63 hours (mean $\pm$ SD) after stroke onset. The endovascular group had femoral access at 11.26 $\pm$ 2.63 hours after stroke onset and reperfusion was obtained 46 $\pm$ 25 minutes after femoral access. The results of the study are currently under embargo but will be presented at the International Stroke Conference.

Author Disclosure Block: M.P. Marks: Ownership Interest; Significant; ThrombX Medical Inc..

Presentation Number: LB18

Presentation Title: Final Results of the RHAPSODY Trial

Author Block: Patrick Lyden, Cedars-Sinai Medical Ctr, Los Angeles, CA; Christopher S. Coffey, Univ of Iowa, Iowa City, IA; Merit Cudkowicz, Massachusetts General Hosp, Boston, MA; Robin A Conwit, NINDS, Bethesda, MD; Kent E. Pryor, ZZ Biotech, LLC, Houston, TX; on behalf of the RHAPSODY Investigators

Abstract Body:
Background and Purpose. Agents acting on the protease activated receptor (PAR) protect brain and blood brain barrier (BBB) in models of stroke, spinal cord injury, amyloid deposition, and other neurodegenerative disorders. We studied 3K3A-APC, a PAR1 active recombinant variant of activated protein C (APC) that protects brain, BBB, and reduces thrombolysis-associated hemorrhage in animals. We conducted a dose-finding safety trial in acute ischemic stroke (AIS) patients treated with IV rt-PA, thrombectomy or both. We also sought evidence of BBB stabilization by quantifying hemorrhage.
Methods. The NeuroNEXT trial NN104 (RHAPSODY) was designed to establish a maximally tolerated dose (MTD) of 3K3A-APC in AIS patients treated with recanalization therapy. Inclusion/exclusion criteria were broad. We adapted a continuous reassessment method (CRM) designed to escalate quickly through dose tiers (120, 240, 360, and 540μg/kg) based on the incidence of dose limiting toxicities (DLTs) until finally reaching a MTD. Participants were assigned to one tier or placebo and received 5 infusions separated by 12 hours, beginning within 2 hours of recanalization therapy. Cerebral magnetic resonance, including susceptibility-weighted, images were obtained at 7, 30 and 90 days after stroke.
Results. Between January 2015 and July 2017 we consented 130 participants and dosed 110; 20 were excluded prior to first administered dose. Demographics resembled those expected for a stroke population. Of the 110 participants, 54% received rt-PA alone, 5% thrombectomy alone, and 45% both. The CRM filled all cohorts as planned: participants received placebo (n=44) or 3K3A-APC (n=66): 120μg/kg (n=15); 240μg/kg (n=24); 360μg/kg (n=12); and 540μg/kg (n=15). There were 7 DLTs (4 placebo, 3 treatment) resulting in an MTD of 540μg/kg with a 7% estimated DLT rate. Hemorrhage quantification after placebo or 3K3A-APC is ongoing.
Conclusions. RHAPSODY successfully studied a neuroprotectant for AIS using a novel trial design allowing thrombectomy, thrombolysis or both, and successfully used a new CRM for dose finding. PAR1 targeted therapy may reduce ischemia/reperfusion-associated hemorrhage. A Phase 2B trial is planned to confirm these findings. Unique identifier: NCT02222714.

Author Disclosure Block: P. Lyden: None. **C.S. Coffey:** None. **M. Cudkowicz:** None. **R.A. Conwit:** None. **K.E. Pryor:** Employment; Significant; yes.