

## Late-Breaking Science Oral Abstracts

Wednesday, January 24, 2018, 10:30am – 12:00 noon

*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: LB1**

**Presentation Title: Results of the DEFUSE 3 Study**

**Author Block: Gregory W Albers**, STANFORD UNIVERSITY MEDICAL CTR, Stanford, CA; on behalf of the DEFUSE 3 Investigators

### **Abstract Body:**

**Background:** Endovascular reperfusion in acute ischemic stroke is effective in patients with large vessel occlusion who can be treated within 6 hours from symptom onset. The aim of DEFUSE 3 is to demonstrate that, among patients with large vessel anterior circulation occlusion who have a favorable imaging profile on computed tomography perfusion or magnetic resonance diffusion/perfusion imaging, endovascular therapy with a mechanical thrombectomy device reduces disability in patents treated in the 6-16 hour time window.

**Methodology:** The study was a prospective, randomized, multicenter, phase III, blinded endpoint, controlled trial. Patients underwent imaging with computed tomography perfusion or magnetic resonance diffusion/perfusion, and automated software (RAPID) determined if the Target Mismatch Profile was present. Patients who met both clinical and imaging selection criteria were randomized 1:1 to endovascular therapy plus medical management or medical management alone. The individual endovascular therapist chose the specific FDA-cleared device (or devices) employed. The primary endpoint was the distribution of scores on the modified Rankin Scale at day 90. The secondary endpoint was the proportion of patients with modified Rankin Scale 0-2 at day 90. The primary safety endpoints were death and symptomatic intracranial hemorrhage.

**Results:** 182 patients were enrolled and randomized between 6 and 16 hours of symptom onset when the DSMB terminated the study because of a high likelihood of benefit in the endovascular group. The final results of the study are currently under embargo but will be presented at the International Stroke Conference.

**Author Disclosure Block: G.W. Albers:** Ownership Interest; Significant; iSchemaView. Consultant/Advisory Board; Significant; iSchemaView, Medtronic.

**Presentation Number: LB2**

**Presentation Title: Tenecteplase Versus Alteplase Before Endovascular Thrombectomy (EXTEND-IA TNK): A Multicenter, Randomized, Controlled Trial**

**Author Block:** Bruce C Campbell, Peter J Mitchell, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; Leonid Churilov, The Florey Inst of Neuroscience and Mental Health, Univ of Melbourne, Parkville, Australia; Nawaf Yassi, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; Timothy J Kleinig, Royal Adelaide Hosp, Adelaide, Australia; Richard J Dowling, Bernard Yan, Steven J Bush, Helen M Dewey, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; Vincent Thijs, Austin Hosp, Univ of Melbourne, Heidelberg, Australia; Rebecca Scroop, Royal Adelaide Hosp, Adelaide, Australia; Marion Simpson, Mark Brooks, Hamed Asadi, Austin Hosp, Univ of Melbourne, Heidelberg, Australia; Teddy Y Wu, Christchurch Hosp, Christchurch, New Zealand; Darshan G Shah, Princess Alexandra Hosp, Brisbane, Australia; Tissa Wijeratne, Sunshine Hosp, Univ of Melbourne, St Albans, Australia; Ferdinand Miteff, Christopher R Levi, Priority Res Ctr for Brain and Mental Health Res, John Hunter Hosp, Univ of Newcastle, Newcastle, Australia; Peter Bailey, Henry Rice, Laetitia de Villiers, Gold Coast Univ Hosp, Southport, Australia; Helen Brown, Kendal Redmond, David Leggett, Princess Alexandra Hosp, Brisbane, Australia; Wayne Collecutt, Christchurch Hosp, Christchurch, New Zealand; Andrew A Wong, Alan Coulthard, Royal Brisbane and Womens Hosp, Brisbane, Australia; Deborah Field, Lyell McEwin Hosp, Adelaide, Australia; Henry Ma, Ronil V Chandra, Monash Medical Ctr, Monash Univ, Clayton, Australia; Mark W Parsons, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; Geoffrey A Donnan, The Florey Inst of Neuroscience and Mental Health, Univ of Melbourne, Parkville, Australia; Stephen M Davis, Royal Melbourne Hosp, Univ of Melbourne, Parkville, Australia; for the EXTEND-IA TNK Investigators

**Abstract Body:**

**Background** Alteplase remains standard before endovascular thrombectomy in eligible patients. We hypothesized that tenecteplase would increase reperfusion at initial angiogram compared to alteplase.

**Methods** EXTEND-IA TNK was an investigator-initiated, multicenter, prospective, randomized, open-label, blinded-endpoint (PROBE) study in large vessel occlusion (internal carotid, basilar or middle cerebral artery) ischemic stroke patients with stroke onset 0-4.5h, pre-stroke modified Rankin Scale (mRS)  $\leq 3$  (no upper age limit) and no contraindications to IV thrombolysis. Patients were randomized to IV tenecteplase (0.25mg/kg, max 25mg) or alteplase (0.9mg/kg, max 90mg) prior to thrombectomy. The primary outcome measure was substantial reperfusion on the initial catheter angiogram, assessed by blinded core lab as modified Treatment In Cerebral Infarction (mTICI) 2b/3 or the absence of retrievable thrombus (sequential testing of non-inferiority, followed by superiority if non-inferiority was demonstrated). Secondary outcomes included day 90 mRS and favorable clinical response [ $\geq 8$  point reduction in NIHSS or 0-1] at day 3. Safety outcomes were death and symptomatic intracerebral hemorrhage (SICH).

**Results** Of 202 patients randomized, 101 received tenecteplase and 101 alteplase. Baseline characteristics were well matched: mean (SD) age 71(14) tenecteplase vs 72(13) alteplase, median (IQR) NIHSS 17 (13-22) vs 17 (12-22), median (IQR) thrombolysis to initial angiogram time 58 (37-72) vs 61 (41-80) min. Substantial pre-thrombectomy reperfusion occurred in 22/101 (22%) tenecteplase vs 10/101 (10%) alteplase patients, risk difference 0.12 (0.02-0.21), OR 2.6 (1.1-5.9),  $p(\text{non-inferiority})=0.002$ ,  $p(\text{superiority})=0.02$ . Favorable clinical response occurred in 72% tenecteplase vs 69% alteplase patients ( $p=0.66$ ). Symptomatic intracerebral hemorrhage occurred in 1% tenecteplase vs 1% alteplase patients

( $p=0.99$ ). Day 90 mRS will be available for ISC.

**Conclusions** Tenecteplase was superior to alteplase, doubling the incidence of pre-thrombectomy reperfusion and has convenient bolus delivery. Symptomatic hemorrhage was rare and did not differ between lytics. Tenecteplase is a more effective option for pre-thrombectomy thrombolysis.

**Author Disclosure Block:** **B.C. Campbell:** None. **P.J. Mitchell:** None. **L. Churilov:** None. **N. Yassi:** None. **T.J. Kleinig:** None. **R.J. Dowling:** None. **B. Yan:** None. **S.J. Bush:** None. **H.M. Dewey:** None. **V. Thijs:** None. **R. Scroop:** None. **M. Simpson:** None. **M. Brooks:** None. **H. Asadi:** None. **T.Y. Wu:** None. **D.G. Shah:** None. **T. Wijeratne:** None. **F. Miteff:** None. **C.R. Levi:** None. **P. Bailey:** None. **H. Rice:** None. **L. de Villiers:** None. **H. Brown:** None. **K. Redmond:** None. **D. Leggett:** None. **W. Collicutt:** None. **A.A. Wong:** None. **A. Coulthard:** None. **D. Field:** None. **H. Ma:** None. **R.V. Chandra:** None. **M.W. Parsons:** None. **G.A. Donnan:** None. **S.M. Davis:** None.

**Presentation Number: LB3**

**Presentation Title: Magnitude of Benefit of Endovascular Thrombectomy 6-24 Hours After Onset in Acute Ischemic Stroke Patients with Clinical-Core Mismatch**

**Author Block:** Jeffrey L Saver, Geffen Sch of Med at UCLA, Los Angeles, CA; Raul G Nogueira, The Marcus Stroke and Neuroscience Ctr, Grady Memorial Hosp, Dept of Neurology, Emory Univ Sch of Med, Atlanta, GA; Ashutosh P Jadhav, UPMC, Pittsburgh, PA; Diogo C Haussen, the Marcus Stroke and Neuroscience Ctr, Grady Memorial Hosp, Dept of Neurology, Emory Univ Sch of Med, Atlanta, GA; Ronald F Budzik, Riverside Hosp/Ohio Health Res Inst, Columbus, OH; Alain Bonafe, Montpellier, Montpellier, France; Parita Bhuva, Texas Stroke Inst, Plano, TX; Dileep R Yavagal, Jackson Memorial Hosp, Miami, FL; Ricardo A Hanel, Lyrly Neurosurgery/Baptist Jacksonville, Jacksonville, FL; Marc Ribo, Vall d' Hebron, Barcelona, Spain; Christophe Cognard, Toulouse, Toulouse, France; Cathy A Sila, Univ Hosp Medical Ctr of Cleveland, Cleveland, OH; Ameer E Hassan, Valley Baptist, Harlingen, TX; David S Liebeskind, Geffen Sch of Med at UCLA, Los Angeles, CA; Wade S Smith, UCSF, Parramus, CA; Tudor G Jovin, UPMC, Pittsburgh, PA; for the DAWN Trial Investigators

**Abstract Body:**

**Background:** The DAWN trial recently established that endovascular thrombectomy improves outcomes among late-presenting acute ischemic stroke patients, 6-24h after last known well, with clinical-core mismatch evidence of persisting salvageable tissue. Number needed to treat (NNT) and benefit per hundred (BPH) indices of effect magnitude would be useful to patients, physicians, and policy-makers.

**Methods:** From core-adjusted 90 day modified Rankins Scale (mRS, global disability) outcome distributions in the DAWN thrombectomy and medical control groups, NNT and BPH values were derived for all dichotomized cutpoints of the mRS by calculating the inverse of the absolute risk difference; and for improvements by 1 level or more across all steps of the 6 level mRS, and utility-weighted mRS, using automated joint outcome table resampling.

**Results:** For individual cutpoints of the mRS, numbers needed to treat for 1 additional good outcome at 90d were: normal (mRS 0)-19.2; nondisabled (mRS 0-1)-4.4; functionally independent (mRS 0-2)-2.8; ambulatory (mRS 0-3)-3.0; not requiring continuous caregiver (mRS 0-4)-10.2; alive (mRS 0-5)-not different. For reduced disability by 1 mRS level or more on the 6 level mRS, and by any patient-valued improvement in disability-related quality of life on the UW-mRS, the NNT was 2.0 (95% CI 1.7-2.3). Per BPH values, for every 100 patients treated, thrombectomy yields improved disability-related quality of life in 50, including functional independence in 35. NNT values for thrombectomy was similar in the 6-12h window vs 12-24h window for both 6 level shift NNT (2.2 vs 1.8) and mRS 0-2 NNT (3.0 vs 2.8), but independent (mRS 0-2) outcomes were achieved more frequently in thrombectomy patients in the 6-12h than 12-24h window (54% vs 44%).

**Conclusions:** Endovascular thrombectomy at 6-24h in patients with clinical-core mismatch confers benefit of substantial magnitude, improving 90 day disability levels in one-half of patients, including conferring functional independence in one-third.

**Author Disclosure Block:** J.L. Saver: Other; Modest; University of California. R.G. Nogueira: Other; Modest; Travel only reimbursement from Stryker. A.P. Jadhav: None. D.C. Haussen: None. R.F. Budzik: None. A. Bonafe: None. P. Bhuva: None. D.R. Yavagal: Consultant/Advisory Board; Modest; Medtronic consultant and steering committee member of SWIFT-Prime clinical trial (Medtronic). Other; Modest; Neuralanlytics. R.A. Hanel: Research Grant; Modest; Medtronic unrestricted research grant, consultant. Ownership Interest; Modest; Neurvana stockholder, Three Rivers stockholder, inneuroCo

stockholder. Consultant/Advisory Board; Modest; Stryker Consultant, microvention consultant, codman consultant. **M. Ribo:** None. **C. Cognard:** Consultant/Advisory Board; Modest; Consultant for Stryker, Microvention, Medtronic. **C.A. Sila:** Honoraria; Modest; Medtronic honorarium. Other; Modest; administrative analysis of our stroke center activities. **A.E. Hassan:** Honoraria; Modest; Medtronic speaking, proctoring fees, Penumbra speaking fees, Microvention speaking fees, GE healthcare speaking fees. Consultant/Advisory Board; Modest; Stryker Consultant, Medtronic consulting fees, Penumbra consulting fees, Microvention consulting fees, GE healthcare consulting fees. **D.S. Liebeskind:** Research Grant; Modest; NIH Grant. Consultant/Advisory Board; Modest; Stryker consultant as imaging core lab, Medtronic consultant as imaging core lab. **W.S. Smith:** Consultant/Advisory Board; Modest; Stryker DSMB Chair. **T.G. Jovin:** Ownership Interest; Modest; Silk Road Stock, Anaconda Biomed Stock, Route 92 Stock, Blockade Medical Stock, FreeOx Biotech Stock. Consultant/Advisory Board; Modest; PI DAWN, Silk Road consultant, Anaconda Biomed Scientific Advisory Board, Route 92 Scientific Advisory Board, Blockade Medical Scientific Advisory Board, FreeOx Biotech Scientific Advisory Board, Codman Neurovascular Consultant, Data Safety Monitoring Board, Neuravi Consultant, Steering Committee Member. Other; Modest; DAWN travel related expenses only.