

Late-Breaking Science Oral Abstracts

Wednesday, February 17, 2016, 10:30am – 12:00 noon

LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2016:

For late-breaking science being presented at ISC 2016, 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, Feb. 17; 3:30 pm PST on Wednesday, Feb. 17; 6:15 pm PST on Wednesday, Feb. 17; 11:00 am PST on Thursday, Feb. 18; 1:30 pm PST on Thursday, Feb. 18; or 11:53 am PST on Friday, Feb. 19. News media activities promoting late-breaking science are under embargo until the times noted above.

Presentation Number: LB1

Publication Title: Main Results of the Insulin Resistance Intervention After Stroke (IRIS) Trial

Author Block: **Walter N Kernan**, Catherine M Viscoli, Yale Sch of Med, New Haven, CT; Harold P Adams Jr, Univ of Iowa, Iowa City, IA; Lawrence M Brass, Yale Sch of Med, New Haven, CT; Antonio Carolei, Univ of L'Aquila, L'Aquila, Italy; Wayne Clark, Oregon Health Sciences Univeristy, Portland, OR; Robin Conwit, Natl Insts of Neurological Disorders and Stroke, Bethesda, MD; Bruce M Coull, Univ of Arizona, Tucson, AZ; Gary A Ford, Oxford Univ, Oxford, United Kingdom; Karen L Furie, Alpert Sch of Med at Brown Univ, Providence, RI; Mark Gorman, Univ of Vermont, Burlington, VT; Peter D Guarino, Fred Hutchinson Cancer Res Ctr, Seattle, WA; Silvio E Inzucchi, Anne M Lovejoy, Yale Sch of Med, New Haven, CT; Mark W Parsons, Univ of Newcastle, New South Wales, Australia; Peter N Peduzzi, Yale Sch of Med, New Haven, CT; Peter A Ringleb, Univ of Heidelberg, Heidelberg, Germany; Gregory G Schwartz, Univ of Colorado Sch of Med, Denver, CO; J D Spence, Univ of Western Ontario, London, ON, Canada; David Tanne, Tel Aviv Univ, Tel Aviv, Israel; Lawrence H Young, Yale Sch of Med, New Haven, CT; for the IRIS Trial Investigators

Abstract Body: **OBJECTIVE.** To test the effectiveness of the PPAR- γ agonist and insulin sensitizing drug, pioglitazone, for reducing the risk of stroke and myocardial infarction among insulin resistant, non-diabetic patients with a recent ischemic stroke or transient ischemic attack (TIA).

METHODS. IRIS is a double blind, placebo-controlled, randomized clinical trial. Eligible patients were age 40 years of age or older, within 6 months of a qualifying ischemic stroke or TIA, and insulin resistant as defined by a Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) score greater than 3.0. Patients were excluded for diabetes, heart failure, bladder cancer, active liver disease, or moderate-severe peripheral edema. Pioglitazone (or matching placebo) was initiated at 15 mg and titrated to 45mg/day over 12 weeks. The primary outcome is time to fatal/non-fatal stroke or fatal/non-fatal myocardial infarction. Secondary outcomes include all-cause mortality, diabetes onset, and cognitive decline.

RESULTS. During 2005-2013, a total of 3876 participants were enrolled from 179 sites in seven countries. The overall study group had a mean age of 63.5 years and was comprised of 66% men, 11% Black, and 4% Hispanic participants. The mean body mass index was 30.0 kg/m² and the mean National Institutes of Health Stroke Scale score was 1.1 (range 0-18). Participant follow-up ended in July, 2015. Average follow-up duration was 4.1 years. The analysis for the main study outcomes is expected to be completed in late 2015.

CONCLUSION. The IRIS trial is exploring a novel approach to secondary stroke prevention based on the hypothesis that modification of insulin resistance with pioglitazone will reduce risk for vascular complications in the brain and heart. The main results will be available for presentation in February, 2016.

Author Disclosure Block: **W.N. Kernan:** Research Grant; Significant; Takeda Pharmaceuticals provides Yale with drug to support a trial Dr. Kernan is conducting and funds for blood storage. **C.M. Viscoli:** None. **H.P. Adams:** None. **L.M. Brass:** None. **A. Carolei:** None. **W. Clark:** None. **R. Conwit:** None. **B.M. Coull:** None. **G.A. Ford:** None. **K.L. Furie:** None. **M.**

Gorman: None. **P.D. Guarino:** None. **S.E. Inzucchi:** Expert Witness; Modest; Served as an expert witness on behalf of Takeda Pharmaceuticals in patent litigation. **A.M. Lovejoy:** None. **M.W. Parsons:** None. **P.N. Peduzzi:** None. **P.A. Ringleb:** None. **G.G. Schwartz:** None. **J.D. Spence:** None. **D. Tanne:** None. **L.H. Young:** None.

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Presentation Number: LB2

Publication Title: Finding Atrial Fibrillation In Stroke Patients - A Multicenter Randomised Evaluation Of Enhanced And Prolonged Holter Monitoring (Find-AFRandomised- Trial)

Author Block: Rolf Wachter, Univ of Goettingen, Göttingen, Germany; Klaus Gröschel, Univ Med Mainz, Mainz, Germany; Götz Gelbrich, Univ of Würzburg, Würzburg, Germany; Gerhard F Hamann, Bezirkskrankenhaus Günzburg, Günzburg, Germany; Pawel Kermer, Krankenhaus Sanderbusch, Sande, Germany; Jan Liman, Univ of Goettingen, Göttingen, Germany; Joachim Seegers, Univ of Regensburg, Regensburg, Germany; Katrin Wasser, Anna Schulte, Falko Jürries, Anna Messerschmid, Nico Behnke, Univ of Goettingen, Göttingen, Germany; Sonja Gröschel, Timo Uphaus, Anne Grings, Tugba Ibis, Univ Med Mainz, Mainz, Germany; Sven Klimpe, Practice for Neurology, Nierstein, Germany; Michaela Wagner-Heck, Horst-Schmidt-Kliniken, Wiesbaden, Germany; Magdalena Arnold, Evgeny Protsenko, Krankenhaus Sanderbusch, Sande, Germany; Peter U Heuschmann, Univ of Würzburg, Würzburg, Germany; David Conen, Univ Hosp Basel, Basel, Switzerland; Mark Weber-Krüger, Univ of Goettingen, Göttingen, Germany

Abstract Body: Background

Atrial fibrillation (AF) is a known risk factor for recurrent ischemic stroke, but often remains undiagnosed in acute stroke patients presenting in sinus rhythm. If AF is detected, oral anticoagulation can effectively prevent recurrent ischemic events. Enhanced and prolonged Holter-ECG-monitoring initiated early after stroke may increase AF detection rates.

Methods

We performed a multicenter, randomized, controlled study in patients ≥ 60 years with ischemic stroke ≤ 7 days after symptom onset, irrespective of stroke etiology, presenting with sinus rhythm at admission and without history of AF. We investigated whether intensified and enhanced rhythm monitoring (IEM) by means of repeated 10-day Holter-ECG-monitoring after 0, 3 and 6 months was superior to standard-of-care AF-detection according to current stroke guidelines (≥ 24 -hour ECG Monitoring). The primary endpoint was newly detected AF (≥ 30 seconds) within 6 months and before stroke recurrence. Major secondary endpoints included the detection of AF within 12 months and stroke recurrence within 12 months. All data were analyzed following the intention-to-treat principle.

Results

398 patients were prospectively enrolled and randomised in a 1:1 ratio. The study population had a mean (\pm SD) age of 73 ± 7 years, 40.2 % (160 patients) were female. The median time from symptom onset to randomization was 3 days (IQR 2;5). After 6 months, AF was detected in 13.5 % of patients in the IEM group (27 patients) as compared to 4.5 % (9 patients) in the control group (absolute difference 9.0 %, 95% confidence interval (CI) 3.5;14.6 %, $p=0.002$, number needed to screen = 11). Between 6 and 12 months no further case was revealed in the IEM group whereas 4 patients were newly diagnosed in the control group, resulting in an absolute difference of 6.9 % (CI 1.0;12.8 %) after 12 months between the groups (13.5 % vs. 6.6 %, $p=0.018$). Data on stroke recurrence by 12 months are still undergoing independent adjudication and will be presented at ISC 2016.

Conclusions

Repeated 10-day Holter-ECG monitoring initiated early after ischemic stroke was superior to standard of care for the detection of atrial fibrillation within 6 months in stroke patients ≥ 60 years. (Funded by Boehringer Ingelheim; ClinicalTrials.gov NCT01855035).

Author Disclosure Block: **R. Wachter:** Research Grant; Significant; Boehringer Ingelheim. Speakers' Bureau; Modest; Bayer, Boehringer Ingelheim, BMS/Pfizer, Daiichi. **K. Gröschel:** Speakers' Bureau; Modest; Bayer, Boehringer Ingelheim, Bristol Myers-Squibb, Pfizer. Honoraria; Modest; Bayer, Boehringer Ingelheim, Bristol Myers-Squibb, Daiichi Sankyo, Pfizer, . **G. Gelbrich:** None. **G.F. Hamann:** None. **P. Kermer:** Speakers' Bureau; Modest; Boehringer Ingelheim. Consultant/Advisory Board; Modest; Boehringer Ingelheim. Other; Modest; Travel Grant, Boehringer Ingelheim. **J. Liman:** None. **J. Seegers:** None. **K. Wasser:** None. **A. Schulte:** None. **F. Jürries:** None. **A. Messerschmid:** None. **N. Behnke:** None. **S. Gröschel:** None. **T. Uphaus:** None. **A. Grings:** None. **T. Ibis:** None. **S. Klimpe:** None. **M. Wagner-Heck:** None. **M. Arnold:** None. **E. Protsenko:** None. **P.U. Heuschmann:** Research Grant; Modest; From University Göttingen during study conduct (within FIND-AF randomized, from German Ministry of Research and Education, EU, Charité, Berlin Chamber of Physicians, German Parkinson Society, University Hospital Würzburg, Robert-Koch-Institute, Charité–Universitätsmedizin Berlin (within MonDAFIS; MonDAFIS is supported by an unrestricted research grant to the Charité from Bayer), University Hospital Heidelberg (within RASUNOA-prime; RASUNOA-prime is supported by an unrestricted research grant to the University Hospital Heidelberg from Bayer, BMS, Boehringer-Ingelheim). **D. Conen:** None. **M. Weber-Krüger:** None.

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Presentation Number: LB25

Publication Title: Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis: Initial and Five-year Results of the ACT 1 Trial

Author Block: Kenneth Rosenfield (Shared Senior Author), Massachusetts General Hosp, Boston, MA; Jon S Matsumura (Shared Senior Author), Univ of Wisconsin, Madison, WI; Seemant Chaturvedi, Univ of Miami, Miami, FL; Tom Riles, NYU Langone Sch of Med, New York, NY; Gary M Ansel, Ohio Health System, Columbus, OH; D. Chris Metzger, Wellmont Cardiovascular Associates Heart Inst, Kingsport, TN; **Lawrence R Wechsler**, Univ of Pittsburgh Sch of Med, Pittsburgh, PA; Michael R Jaff, Massachusetts General Hosp, Boston, MA; William Gray, MaineLine Health System, Philadelphia, PA; on behalf of the ACT I Investigators

Abstract Body: Background: Previous clinical trials have suggested that carotid artery stenting with embolic protection (CAS) is an effective alternative to carotid endarterectomy (CEA) in patients at average and high risk for surgical complications.

Methods: The Asymptomatic Carotid Trial (ACT I) compared CAS and CEA in asymptomatic (absence of stroke or transient ischemic attack 180 days prior to the procedure) patients age < 80 years with severe carotid stenosis, who were not considered to be at high risk for surgical complications ACT I was designed to enroll 1658 patients, but was halted early due to slow enrollment after 1453 subjects were randomized. Patients were followed for up to five years. The primary composite outcome was tested at a non-inferiority margin of 3%.

Results: The primary composite outcome of death, stroke, and myocardial infarction within 30 days plus ipsilateral stroke within one year was non-inferior between CAS and CEA (3.8% v 3.4%, P=0.011 for non-inferiority). Thirty day stroke and death rate was 2.9% with CAS compared to 1.7% with CEA (P=0.33). From 30 days to five years, the rate of freedom from any stroke was 97.8% for CAS and 97.3% for CEA (P=0.51), and overall survival 87.1% and 89.4% (P=0.21). Cumulative five year stroke free survival was 93.1% v 94.7% (P=0.44).

Conclusion: In this trial of asymptomatic patients with severe carotid artery stenosis who were not at high risk for surgical complications, CAS was non-inferior to CEA for the primary one year composite outcome. In analyses including up to five years of follow-up, there were no significant differences in nonprocedural stroke, all stroke, and survival.

Author Disclosure Block: **K. Rosenfield (Shared Senior Author):** Research Grant; Significant; Atrium/Maquet, Lutronix/Bard. Ownership Interest; Modest; Cruzar Systems, Valcare, Eximo, Capture Vascular, Shockwave, Micell, Endospan, Silk Road Vascular, Embolitech. Ownership Interest; Significant; Contego, Access Vascular, MD Insider, Vortex, PQ Bypass, Primacea, Janacare. Consultant/Advisory Board; Modest; Cardinal Health, Surmodics, Inari Medical, Volcano/Philips, Proteon, Cruzar Systems, Valcare, Eximo, Contego, Access Vascular, MD Insider, Capture Vascular, Shockwave, Micell, Endospan, Silk Road Vascular. **J.S. Matsumura (Shared Senior Author):** Research Grant; Significant; Gore, Endologix, Covidien/Medtronic, Cook Medical. **S. Chaturvedi:** None. **T. Riles:** None. **G.M. Ansel:** Consultant/Advisory Board; Modest; Abbott Vascular, Cordis, Gore. **D. Metzger:** Honoraria; Modest; Abbott Vascular, Cordis. **L.R. Wechsler:** Ownership Interest; Modest; Silk Rod Medical. Consultant/Advisory Board; Modest; Abbott Vascular, Silk Road Medical. **M.R. Jaff:** Ownership Interest; Significant; Primacea. Consultant/Advisory Board; Modest; Boston Scientific, Cordis, Medtronic Vascular, Cardinal Health. **W. Gray:** Consultant/Advisory Board; Modest; Abbott Vascular.

