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Clinical Alert

Angioplasty Combined with Stenting Plus Aggressive Medical Therapy vs. Aggressive Medical Therapy Alone for Intracranial Arterial Stenosis: NINDS Stops Trial Enrollment Due to a Higher Risk of Stroke and Death in the Stented Group.

The National Institute of Neurological Disorders and Stroke (NINDS) has stopped enrollment in a clinical trial that is evaluating whether intracranial angioplasty combined with stenting adds benefit to aggressive medical therapy alone for preventing stroke in patients with symptomatic intracranial arterial stenosis. The Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) study is the first prospective randomized multicenter trial to compare aggressive medical management alone versus aggressive medical management plus angioplasty combined with stenting in patients with symptomatic high-grade (70-99%) stenosis of a major intracranial artery (intracranial carotid, middle cerebral artery, intracranial vertebral artery, and basilar artery). All patients were enrolled within 30 days after a TIA or non-disabling stroke that was attributed to the intracranial arterial stenosis. Aggressive medical management in both arms consists of aspirin 325 mg / day for the entire follow-up, clopidogrel 75mg / day for 90 days after enrollment, intensive management of vascular risk factors (primarily targeting systolic blood pressure < 140 mm Hg (< 130 mm Hg if diabetic) and LDL < 70 mg / dl), and provision of a lifestyle modification program to all study patients. Recruitment began in November of 2008 and was halted on April 5, 2011 after 451 (59%) of the planned 764 patients had been enrolled at 50 participating sites in the US. The angioplasty and stenting system used in the trial is the Gateway-Wingspan system.

The NINDS acted on the recommendation of the study's Data Safety Monitoring Board (DSMB). At the time of the most recent DSMB review, 14% of patients treated with angioplasty combined with stenting experienced a stroke or died within the first 30 days after enrollment compared with 5.8% of patients treated with medical therapy alone, a highly significant difference. The 30-day rate of stroke or death in the intensive medical treatment arm is substantially lower than the estimated rate of 10.7% based on historical controls, most of whom received standard medical care. In addition the 30-day rate in the stented patients is substantially higher than the estimated rate of 5.2% – 9.6% based on registry data. There were 5 stroke-related deaths within 30 days after enrollment, all in the stenting arm. There was one non stroke-related death in the medical arm within 30 days after enrollment. Beyond 30 days, the rates of stroke in the territory of the stenotic artery are similar in the two groups, but fewer than half the patients have been

followed for one year. As such, follow-up of currently enrolled patients and comprehensive analysis of the total trial data set will be important in the final interpretation of this study.

The SAMMPRIS Executive Committee [1] is in agreement with NINDS and the DSMB that enrollment in the study should be stopped and that the trial data currently available indicate that aggressive medical management alone is superior to angioplasty combined with stenting in patients with recent symptoms and high grade intracranial arterial stenosis. All are indebted to the patients who contributed to this important study.

Further information about this trial (NCT00576693) can be found at www.clinicaltrials.gov.

[1] SAMMPRIS Executive Committee: Marc Chimowitz MBChB (Neurology PI), Colin Derdeyn MD (Interventional Co-PI), David Fiorella MD (Interventional Co-PI), Michael Lynn M.S. (Statistical PI), Tanya Turan MD (Director Risk Factor Management), Bethany Lane RN (Project Manager), Janice Malloy MBA (Study Administrator), Scott Janis PhD (NINDS Representative),

The trial is sponsored by NINDS, the Clinical Coordinating Center is based at the Medical University of South Carolina, the Statistical Coordinating Center is based at Emory University, and the Imaging Coordinating Center is based at Washington University.

NINDS (www.ninds.nih.gov) is the nation's leading funder of research on the brain and nervous system. The NINDS mission is to reduce the burden of neurological disease – a burden borne by every age group, by every segment of society, by people all over the world.

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