



October 9, 2007

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Center for Devices and Radiological Health
Food and Drug Administration
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Re: Trial Designs for Carotid Artery Stenting

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Catherine M. Rydell, CAE
Saint Paul, Minnesota

Dear Sir/Madam:

On behalf of the American Academy of Neurology (AAN), an association of more than 20,000 neurologists and neuroscience professionals, we appreciate the opportunity to submit comments to the Food and Drug Administration (FDA) on clinical trial designs for carotid artery stenting (CAS) in patients not at high risk for adverse events from surgical revascularization.

The AAN fully supports the American Heart Association's (AHA) position as communicated in their September 26, 2007 letter to the FDA. We further emphasize the following:

- The negative results of two recent randomized trials in conventional risk patients underscores the need the completion of well-designed randomized controlled trials (RCTs)
- The AAN supports the ongoing, controlled trials to evaluate use of CAS in conventional risk patients
- Alternative designs to (RCTs) should not interfere with recruitment of current trials: CREST and ACT-1 (i.e., they should only include subjects that would not be included in ongoing RCTs)
- Alternative designs to RCTs would be reasonable after the ongoing RCTs are completed
- Off label use of devices impedes enrollment and negatively affects trial completion in a timely and cost efficient manner and should continue to be restricted

Stenting news in 2006 was dismal with two trials failing to demonstrate the efficacy of CAS. The SPACE trial failed to demonstrate the periprocedural noninferiority of carotid-artery stenting to carotid endarterectomy (CEA). The EVA-3S trial was stopped for both safety and futility reasons. The trial did not demonstrate noninferiority of stenting versus the surgical procedure. For now, carotid stenting outside of a randomized trial seems prudent only for symptomatic patients with high surgical risk.

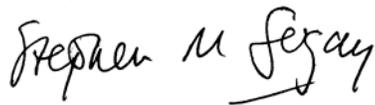
We support trial methodology to consider conventional risk patients for carotid endarterectomy to include:

- both symptomatic and asymptomatic subjects with atherosclerotic extracranial internal carotid stenoses, determined to be $\geq 70\%$ and $\leq 99\%$ stenoses
- patients under and over 80 years of age
- patients eligible and at reasonable risk for carotid endarterectomy and CAS
- endpoints: total stroke, ipsilateral stroke, myocardial infarction, all-cause mortality, and event severity
- Follow-up:
 - 30-day and 1-year
 - longer times for trials that include medical management
 - 2-year follow-up for those involving symptomatic CAS
 - 5-year follow-up for those involving asymptomatic disease

In summary, the AAN feels that the FDA needs to avoid endorsement of trial designs that interfere with recruitment of current trials, in particular, the CREST and ACT-1 trials. To gather results in a timely and cost efficient manner, alternatives may be halting coverage of off label use and linking reimbursement with clinical trials to enable gathering the additional evidence regarding the efficacy of CAS.

Thank you for your careful attention to our concerns. Should you have questions regarding our comments or require anything further, please contact Sarah Tonn, MPH, AAN Staff, at stonn@aan.com or 651.695.2819.

Sincerely,

A handwritten signature in black ink that reads "Stephen M. Sergay". The signature is written in a cursive, flowing style with a prominent underline at the end.

Stephen Sergay, MB BCh, FAAN
President, American Academy of Neurology