The Transatlantic Asymptomatic Carotid Intervention Trial

A first-of-its-kind trial looks at treating asymptomatic carotid patients.

BY BARRY T. KATZEN, MD, FOR THE TACIT INVESTIGATORS*

Of the 600,000 strokes that occur each year in the US, 400,000 are in asymptomatic patients. With unparalleled scope, content, and magnitude, the Transatlantic Asymptomatic Carotid Intervention Trial (TACIT) will study all-risk patients who have asymptomatic carotid artery stenosis of greater than 70% by duplex ultrasonography, and will assign these patients to one of three treatment arms. The first arm will provide optimal medical therapy alone, consisting of antiplatelet, antilipidemic, and antihypertensive therapy, as well as tight glycemic control and tobacco cessation efforts. The second arm will provide optimal medical therapy plus carotid endarterectomy. The third arm will provide optimal medical therapy plus carotid artery stenting, with embolic protection using commercially available devices at the time of trial initiation.

Although 75% of the at-risk stroke population has asymptomatic carotid artery obstruction—by far the largest population—the TACIT study is the first to compare contemporary medical therapy alone in this population. TACIT's randomization into three arms of the trial will provide much needed and unbiased information regarding the added therapeutic benefit of revascularization strategies in an era of sophisticated medical management. No previous trial has specifically examined this question.

THE TACIT TRIAL

TACIT will comprise 100 sites, equally divided between the US and Europe, and will enroll at least 2,400 evaluable patients in the study: 850 patients in each of the revascularization arms, and 700 patients in the medical treatment arm alone. The primary endpoint is the 3-year rate of all strokes and death. Secondary endpoints include transient ischemic attack, myocardial infarction, economic cost and quality-of-life analysis, neurocognitive function, and duplex stenosis progression. Anticipated initiation of enrollment is early 2007. Major findings of the study will be reported after completion of 3-year follow-up in all patients.

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The TACIT investigators seek answers to unresolved and potentially paradigm-changing questions such as "Are we too aggressive in this modern era of best medical therapy?" and "Should physicians intervene in asymptomatic patients with severe carotid artery stenosis?" If interventionists are being too aggressive, the risk of intervention on these patients may be greater than the risk of events with medical therapy alone, and/or the number of patients who will need to be treated to actually see benefit will be prohibitive. Because carotid revascularization is one of the most frequently practiced procedures in the US and Europe, the ramifications of TACIT on clinical practice are protean.

Anticipated Secondary Data

TACIT will provide additional key observations. In addition to the primary endpoint, secondary analysis will parse out rates of transient ischemic attack, ipsilateral

stroke, disabling stroke, fatal stroke, myocardial infarction, and progression of carotid stenosis both after revascularization and as part of natural history in individuals treated with medical therapy alone. TACIT will also consider parameters that have never been looked at before, such as outcomes of intense neurocognitive evaluation. Rodney Raabe, MD, and his colleagues from Spokane, Washington, conducted a prospective study looking at cognitive function before and after stenting. Cognitive function was rigorously assessed using a standardized battery of computer-based psychological and cognitive tests, with preliminary data suggesting that patients with "asymptomatic carotid artery stenosis" have greater levels of measurable cognitive decline if they are treated medically than if they undergo revascularization. A substudy of duplex plaque characteristics will also be included within TACIT because there are data that occlusive plaque, as well as other characteristics, predispose people to both procedural and *de novo* risk of having subsequent clinical events. The duplex clinical evaluation and neuropsychology will be at 3 months, 6 months, and annually after 3 years.

COMPARABLE TRIALS

CREST

CREST (Carotid Revascularization: Endarterectomy versus Stent Trial) is a US-based, multicenter, randomized study funded by the National Institutes of Health and Guidant Corporation. CREST is currently enrolling asymptomatic patients, but unlike TACIT, does not have a medical treatment arm and does not consider mechanistic or intermediary endpoints.

ACT I

ACT I is a randomized, open-label, multicenter study that will consider endartectomy versus stenting. Unlike TACIT, ACT I does not contain a medical arm. Started in March of 2005, it includes patients who have severe carotid artery disease, have not had symptoms related to their carotid artery disease in the last 180 days, and are able to undergo either an interventional stenting or surgical procedure. The purpose of ACT I is to demonstrate the equivalence in asymptomatic extracranial carotid stenotic diseased patient outcomes between carotid artery stenting and the surgical procedure of carotid endarterectomy for the prevention of strokes.

LOCATION, FUNDING, AND PARTICIPATION

TACIT is sponsored by the Society of Interventional Radiology Foundation Cooperative Alliance for Interventional Radiology Research (CAIRR) Clinical Trials Network, along with the CIRSE Foundation of Europe.

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Initiated in 2004, CAIRR is charged with identifying and executing collaborative and pivotal research studies addressing high-priority public health problems. Because TACIT is an extensive and detailed study that will require funding from multiple sources, industry, pharmaceuticals, the NIH, and European funding mechanisms are being explored. The site selection committee in the US is chaired by Kenneth Rosenfield, MD, and by Marc Sapoval, MD, in Europe. Specific sites have not yet been determined. For more information on TACIT, contact SIR Foundation Executive Director Keith Hume at hume@sirweb.org. ■

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