The CREST Trial Update

A report on the progress made in the CREST Trial during 2004 and how it will impact 2005.

BY SUSAN HUGHES, BSN; JAMIE ROBERTS, LPN, CRC; THOMAS G. BROTT, MD; ROBERT W. HOBSON II, MD; AND ALICE SHEFFET, PHD, FOR THE CREST INVESTIGATORS

CREST is the only NIH/NINDS-sponsored clinical trial comparing carotid artery stenting (CAS) to carotid endarterectomy (CEA) for the treatment of carotid stenosis. With an anticipated enrollment of 2,500 patients, it is also the largest currently enrolling randomized trial in North America comparing the use of these two modalities in preventing stroke, myocardial infarction, and death within the symptomatic (transient ischemic attack or nondisabling stroke) patient population. The dedicated efforts of everyone involved have resulted in significant progress during the past 8 months.

2004 PROGRESS

So far in 2004, the number of randomizing centers has increased from 35 to 48, for a 27% improvement. Principal Investigator specialties within these additional sites include three cardiologists, three neurologists, two interventional (neuro) radiologists, and five vascular surgeons. The representation and distribution of North American centers has been strengthened, with randomizing sites located within 23 states and one Canadian province (Figure 1). CREST also has a total of 14 lead-in centers and 25 start-up centers, including several throughout Canada that are poised to start enrolling within the next few months. The trial has enrolled nearly 1,000 lead-in patients this year, making CREST the largest database of CAS available. The number of subjects randomized into CREST since December 31, 2003, has doubled, resulting in a current enrollment that is meeting NIH requirements. Three abstracts based on lead-in data were presented at the 29th International Stroke Conference in February of this year.

MOVING FORWARD

Spring of 2004 was very important for carotid revascularization. The results of the Asymptomatic Carotid Surgery Trial (ACST) were published in *The Lancet* (2004;363:1491-1502). These results were nearly identical to those previously reported in North America in the Asymptomatic Carotid Atherosclerosis Study (ACAS). Specifically, the risk of perioperative stroke or death and subsequent ipsilateral stroke was about half in the surgical group compared to the medical group. Perhaps more important, the ACST results showed benefit for CEA in the prevention of disabling stroke, fatal stroke, and stroke in women. These results in asymptomatic patients led the CREST executive committee to propose to the NINDS Data Safety Monitoring Board that the eligibility criteria be widened to include asymptomatic patients. Not only will this make the trial results more applicable to general practice, but including asymptomatic patients will also speed up patient enrollment. Additional trial enhancements are also just around the corner and will be part of the proposed amendment to the protocol, which will allow CREST to reach out to an even larger population.

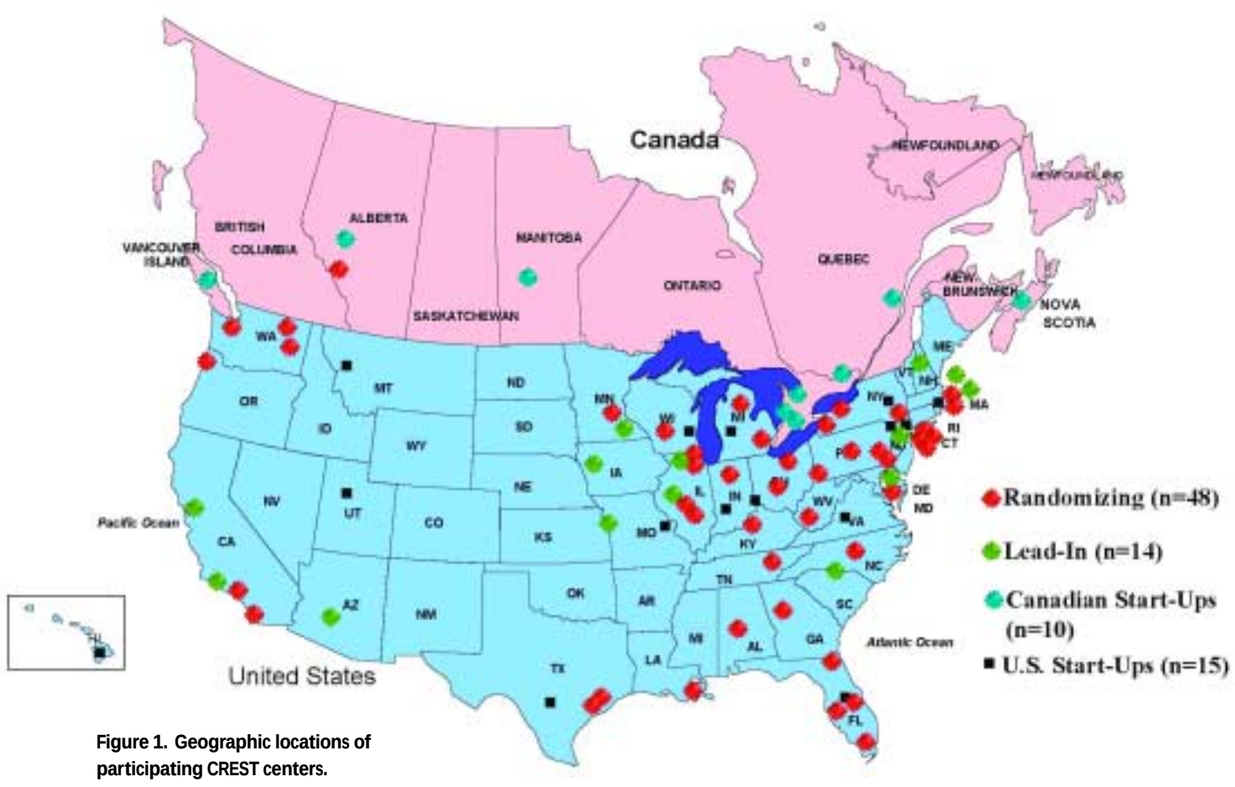

Figure 1. Geographic locations of participating CREST centers.

The following are proposed additions to the CREST protocol, which are designed to (1) widen the generalizability of the results to clinical practice, and (2) improve the rate of enrollment:

- Expansion of the number of clinical sites in North America.
- Inclusion of asymptomatic subjects with no recent (within 180 days) neurological events and carotid stenosis >60% by angiography or >70% by ultrasound.
- Inclusion of subjects with a history of an isolated episode of atrial fibrillation if their physician does not consider them to be at risk of experiencing cardiogenic emboli.
- Inclusion of subjects who may be sensitive to antiplatelet therapy, but who are able to tolerate a reduced daily dose of 81 mg of aspirin. Currently, subjects are required to tolerate a daily dosage of 325 mg to 650 mg of aspirin after the procedure.

2004 has been a breakthrough year for CREST. Besides experiencing marked increases in site participation and subject enrollment, the trial is in a position to achieve greater enrollment with the approval of asymptomatic participants. ■