From the groundbreaking CREST-2 trial indicate the value and positive results of intensive medical therapy, whether patients also received revascularization as well, said Dr. Brajesh K. Lal, principal investigator.

In providing an update on the study that seeks to determine how best to prevent strokes, he added that while overall enrollment is on target, enrollment in the surgery arm of the trial is lagging. “We would definitely like more surgeons to be more active in enrolling patients,” said Dr. Lal. The trial is in no danger of being shut down, but if the surgical arm lags too far behind, credibility suffers, he explained.

CREST-2 – Carotid Revascularization and Medical Management for Asymptomatic Carotid Stent Trial – began enrolling patients 18 months ago. The study aims to enroll 2,450 patients in 120 centers across North America, with patients evaluated as to whether they are better cared for with medical therapy alone, or with medical therapy plus carotid endarterectomy or carotid artery stenting.

Patients are randomly assigned to one of the two procedures plus intensive medical management or medical management alone. The intensive medical management includes not only regular checks of cholesterol, hemoglobin, blood pressure and other indicators, with medication where needed, but also smoking cessation and exercise.
programs and third-party coaches phoning biweekly to discuss progress on all activities pertaining to vascular risk-factor control.

“We’re doing very well with intensive medical therapy,” said Dr. Lal. The data show efforts in controlling cholesterol and blood pressure, for example, “have been phenomenal.” These results are being seen in the entire group of patients enrolled in the study, so even patients undergoing surgery or stenting are benefiting from the intensive medical therapy.

Local doctors, a central group of risk-factor management specialists and the lifestyle coaches form the three levels of care involved with the medical management portion of the study. The key results are still blinded, he added, because enrollment is ongoing.

The study also is on target thus far in terms of women and minority enrollment. Total mix is 41 percent women and 11 percent minorities, slightly exceeding the targets of 40 and 10 percent, respectively. “Studying if there are differences by sex and various racial and ethnic backgrounds is one of our secondary endpoints,” said Dr. Lal.

In addition, four additional, related studies are in the works:

- **CREST-T (Transcarotid artery revascularization):** A trial comparing traditional stenting vs. the new TCAR (transcarotid artery revascularization) procedure, which involves a cut-down at the bottom of the neck. “It’s never been tested in a head-to-head comparison,” said Dr. Lal. “This randomized controlled trial will help us learn which procedure has a higher rate of complications.”
- **CREST-P (Plaque):** Studying the structure of the plaque and the forces acting on the plaque, to try to identify those patients at higher risk for stroke.
- **CREST-B (Bio-banking):** Plaque from surgical patients will be collected and evaluated chemically, biochemically and histologically, to try to determine what mechanisms cause the plaque to rupture and cause a stroke. Since all enrolled patients’ blood is also being collected, the team will do genetic testing to look for stroke risk factors.
- **CREST-H (Hemodynamics):** looking for how brain perfusion is impacted by carotid stenosis and how brain function also is affected by the reduced perfusion. A total of 150 CREST-2 patients will undergo a perfusion MRI scan both before and after surgery so doctors can view blood flowing to the brain; brain function also will be tested.

Dr. Lal likens CREST-2 to a “solar system of studies,” with the new studies orbiting CREST-2. Most are being funded by the National Institute of Neurological Disorders of the NIH through their StrokeNet Program.

“There are close to 10 million people walking around with plaque in their carotid arteries,” Dr. Lal said. “Because we’re not going to operate on all of them, we need a better way to identify which ones should be treated more aggressively. These additional studies will provide important information on risk factors and identifying higher-risk patients at a fraction of the cost.”

Much time, effort and money are required to mount a study like CREST 2, said Dr. Lal. “It happens once in a generation. Because patients are already being enrolled and information collected, it’s possible to conduct the secondary studies for little additional expense but vastly more insights and answers,” he said.

CREST-2 is supported by $40 million in funding from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health, with an extended eight years of support instead of the usual NIH maximum funding term of five years.

The NIH, through its National Heart, Lung and Blood Institute, also helps funds two major SVS Foundation mentored research awards, the Mentored Clinical Scientist Research Career Development Award and the Mentored Patient-Oriented Research Career Development Award. Those two are among several research awards available to SVS members, and funded through the SVS Foundation. The Foundation’s annual appeal is underway now. Click here for more information on how to contribute.

For more information, visit crest2trial.org.
(For more news from SVS in the December 2016 Specialist, please click here.)

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