Carotid Artery Stenting for Standard-Surgical-Risk Patients

Implications of the new FDA approval in the United States.

BY CHUCK SIMONTON, MD, AND PATRICK VERTA, MD

On January 26, 2011, the Circulatory System Devices Advisory Panel was convened by the US Food and Drug Administration (FDA) to review and discuss new data from the pivotal, National Institutes of Health–sponsored, prospective, randomized clinical trial, CREST (Carotid Revascularization Endarterectomy Versus Stenting Trial), which compared surgical carotid endarterectomy (CEA) to carotid artery stenting (CAS) in standard-surgical-risk patients.[1] The panel's task was to make a recommendation to the FDA concerning the safety, effectiveness, and benefit-risk profile of CAS with the RX Acculink carotid stent system (Abbott Vascular, Santa Clara, CA) compared to CEA. Presentations were made by Abbott Vascular and the FDA followed by panel deliberation and a final vote at the end of the day. The multidisciplinary panel voted by a strong majority that the data from CREST showed sufficient evidence for the effectiveness, safety, and a favorable benefit-risk profile of CAS with the Acculink stent system, thus in effect recommending that the FDA move forward with the expanded indication.[2]

On May 6, 2011, the FDA approved CAS as a therapeutic option for standard-surgical-risk patients with an approved and updated product indications for use label for the Acculink stent and the RX Accunet embolic protection system (Abbott Vascular) (see *RX Acculink Carotid Stent System* sidebar). The approval was linked to the condition that a postapproval, single-arm, prospective study would be conducted by Abbott Vascular to further confirm the effectiveness and safety in the broader real-world setting and that Abbott Vascular would be committed to its ongoing program of physician training and education.

THE NEW INDICATION

The new indication represents an expansion of the previously approved indication of CAS for high-surgical-risk patients to include symptomatic or asymptomatic patients who are at standard surgical risk. The duplex ultrasound and angiographic eligibility criteria for CAS are somewhat different for patients with previous symptoms of transient ischemic attack, amaurosis fugax, or stroke (symptomatic) and patients who are asymptomatic. For symptomatic patients, there must be at least 70% stenosis by duplex ultrasound or at least 50% stenosis by angiography, whereas for asymptomatic patients, the criteria are at least 70% by duplex ultrasound and at least 60% by angiography.

These eligibility criteria for the product label were recommended by the FDA because they are consistent with the inclusion criteria for patients who were enrolled in CREST. Patients must also have anatomic suitability for embolic protection with the Accunet system because the approval is restricted to use of the Acculink stent in conjunction with the Accunet embolic protection filter. It is also assumed that physicians will follow the guidelines developed by professional societies for appropriate patient selection based on anatomic and clinical patient characteristics.

IMPLICATIONS OF THE NEW INDICATION

Following the FDA's announcement of the new indication for CAS for standard-surgical-risk patients and their communication to Abbott Vascular of the approval and conditions, the company was then able to begin formally promoting this indication to physicians and other appro-

priate health care providers. Given the robust nature of the supporting clinical data from CREST, which represents the expected patient outcomes for CAS relative to CEA in this patient population, clinicians now have the option of either revascularization procedure for their patients with obstructive carotid artery disease who meet the appropriate clinical, anatomic, and duplex ultrasound and angiographic eligibility criteria.

Although CAS was shown to be noninferior to CEA in CREST for the primary composite endpoint of death, any stroke, or myocardial infarction (MI) at 30 days plus ipsilateral stroke to 1 year, there was a difference in the directionality for two of the components of the primary endpoint: stroke and MI. The risk of minor stroke was significantly higher for CAS, whereas the risk of MI was significantly higher for CEA, resulting in a relative clinical balance of risk between the two therapies in the judgment of the advisory panel and the FDA. Of interest, the vast majority of minor strokes after CAS had resolved by the National Institutes of Health Stroke Scale and modified Rankin scale score evaluations at 6 months postprocedure, whereas the impact of MI on long-term mortality was fixed and significant. Importantly, however, these differences were small between CAS and CEA and were overall very low for both procedures compared to previous trials.

The importance of the difference in minor stroke and MI risk observed in CREST should be taken into consideration when assessing a patient's risk for CAS or CEA. In addition, the incidence of cranial nerve injuries and of other access site complications requiring treatment was significantly higher after CEA than after CAS. Consultations by physicians with their patients should include a fair and balanced discussion of these different risks, including other clinical and vascular anatomic features of the patient, who may favor one procedure over the other due to the experience of the physician. The key to the proper impact of the new expanded indication for CAS in the United States is that the new indication does not imply that one procedure is superior to the other based on the available clinical trial evidence but that now CAS can be considered as an option for standard-surgical-risk patients.

The implications of the new approval from a regulatory perspective include Abbott Vascular's obligation to complete a postapproval study in a large, single-arm study to confirm effectiveness and safety in the broader, real-world population of operators and patients. In addition, Abbott Vascular must show documentation of the continued physician education and training that is required before the product is introduced into a hospital. As with all products, the company must continue to track, review, and follow-up on all product complaints according to the guidance published in the Federal Register.

Finally, after FDA approval, Abbott Vascular has presented the FDA's review and the evidence from CREST to the Centers for Medicare & Medicaid Services (CMS) to open a new national coverage determination for consideration to establish CMS reimbursement for CAS for standard-surgical-risk patients. This request has been filed with CMS, and the process is currently ongoing, with the next steps for CMS to decide whether to proceed with the national coverage determination and then triggering a period of open public comments before a final decision is reached. Clearly, for patients who are Medicare or Medicaid beneficiaries and who are standard-surgical-risk candidates for CAS, the addition of expanded reimbursement for CAS by CMS will be essential for them to have full access to the procedure. For younger, non-Medicare or Medicaid patients who have private insurance, many private carriers are now approv-

RX ACCULINK CAROTID STENT SYSTEM

Acculink Carotid Stent

- Self-expanding nitinol (nickel titanium, super-elastic at body temperature) stent
- Straight configuration
  Diameters: 5, 6, 7, 8, 9, 10 mm
  Lengths: 20, 30, 40 mm
- Tapered configuration
  Diameters: 6–8, 7–10 mm
  Lengths: 30, 40 mm

Acculink Stent Delivery System

- Single-use device that uses a sheath to mechanically constrain the Acculink carotid stent at a small diameter for delivery to the treatment site

Accunet Embolic Protection System

- Fixed-wire filter for carotid stenting interventions
- Flexible filter basket to conform to tortuosity
- Captures high volume; allows adequate blood flow

ing reimbursement either through preapproval processes or, in some cases, by broader changes to include routine reimbursement for these patients.

THE FUTURE

Given the convincing evidence from CREST that shows that in well-trained hands in the United States, CAS can be performed at very acceptable levels of risk compared to CEA, particularly in the latter half of the CREST trial when the risk of stroke with CAS improved with each year of enrollment.[1] The future is bright for CAS as a less-invasive approach to carotid revascularization in properly selected patients. Alongside CREST are the large completed and ongoing CAS postmarket studies in high-surgical-risk patients, which also show this continued decline in 30-day stroke rates during the last decade, which is most likely due to our evolving understanding of the best techniques and best patients for CAS.[3-5]

During CREST, CAS was an evolving procedure, and much was learned and shared within the medical community. We expect that future studies will continue to show even more improvements in patient outcomes, although at a slower pace than during the first decade. However, there is no doubt that with the expanded indication of CAS (particularly if reimbursement can follow), private industry will reinvest in the field to develop better stent and embolic protection systems that can further improve patient outcomes. ■

Chuck Simonton, MD, is Chief Medical Officer of Abbott Vascular. He has disclosed that he is a salaried employee of Abbott Vascular. Dr. Simonton may be reached at (408) 845-1857; charles.simonton@av.abbott.com.

Patrick Verta, MD, is a Medical Director of Clinical Research at Abbott Vascular. He has disclosed that he is a full-time employee of Abbott Vascular and a shareholder of Abbott Laboratories.

1. Abbott Vascular Presentation to FDA Circulatory System Devices Advisory Panel. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM248647.pdf. Accessed August 18, 2011.
2. Department of Health & Human Services. Brief summary of the Circulatory System Devices Panel meeting. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM241779.pdf. Accessed August 18, 2011.
3. Gray WA, Hopkins LN, Yadav S, et al. Protected carotid stenting in high-surgical-risk patients: the ARCHeR results. J Vasc Surg. 2006;44:258-268.
4. Gray WA, Yadav JS, Verta P, et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. Catheter Cardiovasc Interv. 2007;69:341-348.
5. Gray WA, Chaturvedi S, Verta P; Investigators and the Executive Committees. Thirty-day outcomes for carotid artery stenting in 6320 patients from 2 prospective, multicenter, high-surgical-risk registries. Circ Cardiovasc Interv. 2009;2:159-166.

Please see page 44 for product indications and safety information.