

FDA Advisory Panel Recommends Expanded CAS Indication for Abbott Vascular's RX Acculink

BY THE ENDOVASCULAR TODAY STAFF

Abbott Vascular (Santa Clara, CA) announced that the US Food and Drug Administration (FDA) Circulatory System Devices Panel of the Medical Devices Advisory Committee voted that, for symptomatic and asymptomatic carotid artery disease patients with standard surgical risk, there is reasonable assurance that the benefits of carotid artery stenting (CAS) with the company's RX Acculink carotid stent system outweigh its risks. The FDA will take into account the panel's advice in making its decision on whether to expand the device's current indication to include patients at standard surgical risk. The company stated that it expects a decision later this year.

The RX Acculink currently is approved for the treatment of symptomatic and asymptomatic patients at high risk of adverse events from carotid endarterectomy (CEA) and is indicated to be used in conjunction with Abbott Vascular's RX Accunet embolic protection system (EPS).

According to Abbott Vascular, the committee's recommendation followed a review of data from CREST (Carotid Revascularization Endarterectomy Versus Stenting Trial), the largest prospective study comparing CAS to CEA conducted to date.

CREST demonstrated that CAS and CEA had similar safety and long-term outcomes for patients with symptomatic and asymptomatic carotid artery disease who were at standard surgical risk. In an analysis of 2,307 standard-risk patients with symptomatic and asymptomatic disease, CAS demonstrated noninferiority to CEA

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– Tyrone Collins, MD

for the primary composite endpoint of death, any stroke, and myocardial infarction within 30 days of the procedure plus ipsilateral stroke from 31 to 365 days. The results showed 7.1% of CAS patients and 6.6% of CEA patients experienced an event, the difference being nonsignificant. Thomas G. Brott, MD, et al published the CREST results in July in the *New England Journal of Medicine* (2010;363:11–23).

The October 2010 issue of *Endovascular Today*, "CAS: Data and Decisions," provides in-depth analyses of CREST and other major carotid revascularization trials and how their results will affect practices around the world. William A. Gray, MD, and Sumaira Macdonald, MBChB, served as co-chief medical editors of this issue.

Dr. Gray addressed the FDA advisory panel's deliberations and recommendations in comments to *Endovascular Today*.

Regarding the information that the panel had to consider, Dr. Gray noted, "The data presented from the CREST study, which served as the basis for the proposal for an expanded indication, interpreted both by the

sponsor and by the FDA, was consistent with the National Institutes of Health publication from 2010. The study met all of its prespecified endpoints. Additional analyses only further strengthened the results.”

He added, “Specifically, it was shown that patients over the age of 80 had increased rates of adverse outcomes with both CAS and CEA, but that there were no differences between them in this small cohort of patients. Further, a significant and consistent reduction in stroke and death for CAS was noted for the last 50% of the patients enrolled in the study (but no change in CEA outcomes), consistent with a learning curve improvement over the 8 years that also appeared to have been occurring outside during the period of the CREST trial according to both pivotal trials and prospective registries in this country.”

Looking toward the next phase of the regulatory process, Dr. Gray said, “This panel recommendation is important and will hopefully lead to an FDA approval for the extension of CAS to the standard surgical risk population. Assuming this approval, the Centers for Medicare & Medicaid Services extension of coverage to the standard risk population will be an important next step to making this technology and option available to patients requiring carotid revascularization.”

The Society for Cardiovascular Angiography and Interventions (SCAI) stated that it welcomed the FDA panel’s recommendation to expand the availability of CAS to patients at standard risk for adverse events while undergoing surgery. SCAI urged the FDA to approve this recommendation, so patients who are candidates for carotid revascularization will have access to a minimally invasive option for treatment of carotid artery disease.

Tyrone Collins, MD, chair of SCAI’s Carotid Stenting and Neurovascular Interventions Committee commented, “The FDA panel’s recommendation, supported principally by the data from CREST, reinforces the importance of scientifically rigorous clinical trials that study alternative treatment options for patients. Landmark trials such as CREST provide the evidence base that enables us to offer the right treatment to the right patients at the right time. We are hopeful more patients who may be at risk of stroke will have the full range of treatment options available to them.”

PANEL PROCEEDINGS

Jeffrey S. Borer, MD, of the University of Pennsylvania, served as Chair of the FDA panel’s public advisory committee meeting, which was held at the Holiday Inn, Gaithersburg, Maryland. The meeting was convened to discuss, make recommendations, and vote on the infor-

mation related to the premarket approval (PMA) supplement for the RX Acculink and RX Accunet. The FDA announced the meeting on December 20, 2010, and posted background materials, including an Executive Summary, on the its Web site.

According to the FDA, Abbott Vascular is seeking to expand the indications for their RX Acculink device for CAS to include patients at standard risk for adverse events from CEA. These patients must meet the same criteria outlined for the high-risk patients, with the exception that patients without neurological symptoms may be treated if they have $\geq 70\%$ stenosis of the common or internal carotid artery (a reduction from $\geq 80\%$ stenosis that is required for high-risk patients).

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Questions for Panel Voting

At the meeting, a majority of the panel voted affirmatively on each of the three questions that they were asked to consider. The questions and votes were:

- Is there reasonable assurance that the RX Acculink carotid stent system is safe for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication? The panel votes were: 6 Yes, 4 No, 1 Abstained.
- Is there reasonable assurance that the RX Acculink carotid stent system is effective for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication? The panel votes were: 8 Yes, 2 No, 1 Abstained.
- Do the benefits of the RX Acculink carotid stent system for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication outweigh the risks of the RX Acculink carotid stent system for use in patients requiring carotid revascularization who meet the criteria specified in the proposed indication? The panel votes were: 7 Yes, 3 No, 1 Abstained.

Current and Proposed Indications

The FDA outlined the approved indication and the proposed expanded indication for the Abbott Vascular RX Acculink carotid stent system, based on data from the CREST study.

High Surgical Risk (Current Indication)

The RX Acculink carotid stent system, used in conjunction with Abbott Vascular's Accunet or Emboshield family of EPS, is indicated for the treatment of patients at high risk for adverse events from CEA who require carotid revascularization and meet the criteria outlined below:

- Patients with neurological symptoms and $\geq 50\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram or patients without neurological symptoms and $\geq 80\%$ stenosis of the common or internal carotid artery by ultrasound or angiogram; and
- Patients must have a reference vessel diameter within the range of 4 to 9 mm at the target lesion.

Standard Surgical Risk**(Proposed Additional Indication)**

The RX Acculink carotid stent system, used in conjunction with the Accunet EPS, is indicated for the treatment of patients at standard risk for adverse events from CEA who require carotid revascularization and meet the criteria outlined below:

- Patients with neurological symptoms and $\geq 70\%$ stenosis of the common or internal carotid artery by ultrasound or $\geq 50\%$ stenosis of the common or internal carotid artery by angiogram or patients without neurological symptoms and $\geq 70\%$ stenosis of the common or internal carotid artery by ultrasound or $\geq 60\%$ stenosis of the common or internal carotid artery by angiogram; and
- Patients must have a reference vessel diameter within the range of 4 to 9 mm at the target lesion.

The data presented in the subject PMA supplement characterize the safety and effectiveness of the RX Acculink carotid stent system when used to treat standard surgical risk patients requiring carotid revascularization, said the FDA. The panel members were asked to fully assess the significance of these results and comment on the risk-to-benefit ratio of using the RX Acculink to treat these patients.

According to the agency, the proposed indications are supported by a primary analysis of the CREST trial data and by multiple important secondary and tertiary analyses. The panel was advised that these additional analyses, particularly for patient subgroups, should be used to determine whether all elements of the proposed indications are supported by the study data. The FDA believes that the separate analyses of symptomatic and asymptomatic subjects should be carefully considered when determining whether the CREST results demonstrate safety and effectiveness in both populations. Similarly, the FDA believes that the comparisons of results in octogenarian

subjects can influence whether this important population should be specifically included or excluded in the indications for use.

Additionally, the FDA advised that the specification of the percent stenosis criteria is a critical issue. The agency pointed out that American Heart Association guidelines state that revascularization is acceptable in asymptomatic subjects with stenosis $\geq 75\%$, with less certainty about lower degrees of stenosis. In addition, there are other opinions that revascularization should not be attempted in asymptomatic subjects with $< 70\%$ stenosis. Consideration of the appropriate percent stenosis criteria may be important in refining the indications for use and device labeling, the FDA said.

SCAI, in supporting the confirmation of the panel's recommendation, emphasized the importance of the following if the new indication is approved:

- Participation in registries to collect clinical data to study CAS in real-world settings to benchmark outcomes for continuous quality improvement.
- Participation in accreditation programs requiring independent peer review of CAS procedures.
- Creation of continuing medical education and physician training programs to develop more physicians skilled in CAS.

According to SCAI, the American Heart Association/American Stroke Association's recently updated guidelines for secondary stroke prevention include broader recommendations for CAS than those currently covered by Medicare. Currently, Medicare and most insurers in the United States cover CAS only for symptomatic patients at increased surgical risk and those enrolled in clinical trials. All other patients must pay out of pocket for the procedure, receive medications only, or undergo CEA, SCAI noted.

"SCAI urges the FDA to accept the panel's recommendation, as it would provide patients with a safe, effective, and minimally invasive treatment option for carotid artery disease," commented SCAI president-elect Christopher J. White, MD. "This recommendation by the FDA panel to expand the labeled indication for the use of CAS would be a step forward in preventing stroke, the third leading cause of death in the United States." ■

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