FDA INSIGHTS

Regulation of Peripheral Vascular Devices

Current issues in the regulation of SFA stents.

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The views and opinions presented in this article are those of the authors and do not necessarily reflect those of the US FDA, the US Department of Health and Human Services, or the Public Health Service.

In recent years, the pace of technological development of medical devices has continued to increase. The rapid development, turnover, and obsolescence of medical devices in general, and peripheral vascular devices in particular, have put increasing pressure on both industry and the FDA to keep pace with changes in the clinical application of the devices. Part of the FDA's response to this situation has been to develop an application of the Total Product Life Cycle as described in the Strategic Plan for the Center for Devices and Radiological Health, and, in so doing, to construct innovative ways to strike the proper balance between premarket review and postmarket assessment and surveillance of devices.

The Peripheral Vascular Devices Branch (PVDB) has also responded to this challenge by developing a set of ongoing initiatives to ensure that the clinical trials and regulatory mechanisms involved in the premarket review of device applications are consistent with current clinical practice, while considering that the burden on manufacturers should be minimized in terms of resource expenditures and time-to-market issues. The majority of these initiatives are related to defining data requirements for some of the devices regulated by the branch and for specific indications for a broad range of devices. For example, the PVDB is working to identify appropriate clinical study designs for superficial femoral artery (SFA) stents and the clinical study standards of evidence needed for permanent and retrievable inferior vena cava filters, as well as defining comparison datasets or objective performance criteria for iliac artery stents and abdominal aortic aneurysm and thoracic aortic aneurysm endovascular grafts. Data requirements for devices intended to treat in-stent restenosis are also being discussed. Other initiatives include developing suggested standardized formats for information being provided to clinicians, such as the clinical updates for endovascular grafts. This article on SFA stenting is the first of several articles that will describe some of these initiatives.

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SFA STENT REGULATORY CHALLENGES

Stenting as a therapy for treatment of SFA disease has been reported in the literature for many years. In the perspective of the FDA, therapeutic intervention in the SFA is one of the more challenging and complex peripheral vascular environments. For a variety of reasons, the performance of stents in the SFA appears to be more problematic than in other peripheral vascular beds, such as the iliac and carotid arteries. This may be due to the significant mechanical stresses placed on the devices in the dynamic SFA environment relative to other vasculature, as well as the vessel length and the severity of stenotic and occlusive disease. These performance challenges are further complicated by clinical study design challenges related to the lack of a generally accepted standard of care for patients with SFA disease.

There are presently two devices approved for use in the treatment of SFA disease: the ev3 IntraCoil (ev3 Inc., Plymouth, MN) bare metal stent approved under P000033 in 2002 and the recently approved Gore Viabahn (W. L. Gore & Associates, Flagstaff, AZ) covered stent approved under P040037. Both of these device approvals involved clinical trials of the investigational

devices that included percutaneous transluminal balloon angioplasty (PTA) as the control arm.

At the time the clinical trials of the currently approved devices were designed, PTA was the only FDA-approved device for treatment of SFA disease, and was therefore considered an appropriate control against which the performance of the investigational devices in terms of safety and effectiveness could be assessed. However, PTA may not be as useful as a control given the current clinical environment. In particular, it appears that PTA may be more commonly used clinically to treat certain types of lesions such as short, focal lesions, whereas clinical expectations are that stents may be more effective with longer lesions or diffuse disease. This differential may result in bias in the selection of patients for each therapy and lead to difficulty in interpretation of the study results because the patient populations may not be equivalent in terms of risks and benefits to be derived from each type of intervention. In addition, crossover contributes to challenges in interpreting results.

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Differences in patient populations with SFA disease must also be considered in designing appropriate clinical studies. As with all clinical studies, SFA stent study subject inclusion and exclusion criteria should be constructed to ensure that the study subjects are representative of the patient population that is the target of the therapy. In general, for SFA stents, the target population is patients with claudication (Rutherford-Becker Category 2 through 4), and the study design should be directed toward demonstrating the safety and effectiveness of the investigational device in this patient population. Another possible target population is patients who are at risk of limb amputation due to critical limb ischemia, wherein the therapeutic effect of the investigational device may be to support efforts to salvage the at-risk limb. The FDA believes that these two populations likely have different risk/benefit profiles and therefore that the clinical trials that involve these patients should have safety and effectiveness metrics that are optimized to demonstrate the risks and benefits to each population.

The advent of drug-eluting stents (DES) has presented another confounding factor in SFA stent clinical trial design. In contrast to DESs indicated for coronary arteries, DESs in the SFA vasculature are subjected to significant mechanical stresses that may result in fractures and delaminations that could, in turn, result in failure of the DES to perform appropriately or lead to adverse events. The longer devices, when placed in single or overlapping configurations, may produce high serum and tissue drug concentrations relative to DES in coronary arteries. These factors should be considered when designing both preclinical as well as clinical trials for DES to be used in the SFA indication.

PVDB SFA INITIATIVE

In light of these issues, PVDB is reconsidering the appropriate controls for SFA stent study designs as well as taking a fresh look at the possibility of developing objective performance criteria or point estimates that could serve as quantitative metrics to evaluate safety and effectiveness of investigational bare metal SFA stents. Because of the significant safety and effectiveness issues associated with inclusion of a drug substance on a stent, such criteria would not be applicable to DESs. With respect to DESs, we are willing to consider a trial that compares a DES to a bare metal stent, in which the bare metal stent (if not approved for use in the SFA) performance is compared to objective performance criteria or point estimates. Such a trial design could potentially result in product approvals for both the DES and the bare metal stent, if the data are supportive.

We welcome the participation of industry, clinicians, and other stakeholders to participate in the process of defining optimal clinical trial designs for SFA stent studies. ■

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REGULATORY QUESTIONS?

The goal of Dorothy B. Abel's FDA Insights column is to clarify misconceptions regarding device approval and the regulation of endovascular care. If there is a particular question you would like addressed in this column, please submit it via email to evteditorial@bmctoday.com.