

Why Are There So Few Vascular Stents Approved?

An interview with Jennifer Goode of the FDA.

Endovascular Today: At ISET 2007, you indicated that there are more than 30 non-drug-eluting stents currently approved for vascular use in the US (18 coronary, five carotid, four iliac, two renal, two superficial femoral artery [SFA]), along with hundreds approved for nonvascular use. Why are there so few stents approved for peripheral use and so many nonvascular stents approved?

Ms. Goode: Although the numbers of coronary stents I reported at ISET were approximate numbers, and there are actually five approved iliac stents and stent grafts, it is clear that the number of approved vascular stents, and peripheral vascular stents in particular, are significantly fewer than the number of nonvascular stents cleared for market in the US. This may be due, in part, to the difference in submission requirements for nonvascular versus vascular stents.

Endovascular Today: What process must a stent go through to gain approval for vascular use? Does this differ from nonvascular approval?

Ms. Goode: Vascular stents are class III devices and require premarket approval. Approval is usually obtained through the submission of a premarket approval application. In these applications, a sponsor must submit documentation to demonstrate a reasonable assurance of safety and effectiveness, including engineering and clinical data. In contrast, nonvascular stents, such as biliary stents, are classified as class II devices and require clearance for marketing under the premarket notification [510(k)] program. There are fewer documentation

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requirements for 510(k) submissions as compared to pre-market approval submissions. In the case of biliary stents, the products are indicated for treatment of cancer patients who typically have a short life expectancy (ie, fewer than 9 to 12 months). Appropriately, the data requirements for biliary products are not as extensive as for vascular products that are intended for use in patients with long life expectancies. For example, clinical data are rarely required for biliary stent clearance. Additional information regarding the differences in marketing approval and clearance can be found in the April 2004 issue of *Endovascular Today*.¹

Endovascular Today: Are there currently any initiatives at the FDA to streamline or expedite the process of approving vascular stents, or is the FDA satisfied with the current model?

Ms. Goode: In the interest of encouraging the evaluation and labeling of stents for vascular use, the FDA has been working with the vascular community to identify appropriate clinical study designs. The FDA is open to discussion of alternatives to randomized controlled trials (RCTs) in support of marketing applications for first-generation vascular stents. The Agency recognizes that non-RCTs may facilitate patient enrollment and help get vas-

cular stent products to market more quickly. We are also willing to consider how to use a combination and balance of pre- and postmarket data collection to support marketing applications for second-generation devices.

Endovascular Today: Do stents designed for SFA use face particular scrutiny?

Ms. Goode: We do look carefully at SFA stents because we have seen information in the literature to suggest that the long-term fracture potential of some stent designs may be associated with adverse clinical outcomes. There is also some information in the Medical Device Reports to suggest that delivery of longer stents may be challenging. Because preclinical testing does not yet seem to be predictive of clinical performance, current clinical studies are designed to assess these potential failure modes. With the development of better preclinical testing and improvements in our understanding of the appropriate characteristics for SFA stents and delivery systems, the testing requirements may change.

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Endovascular Today: What type of testing and clinical trial work must be conducted for an SFA stent to be considered for approval?

Ms. Goode: The testing needed for vascular stents is detailed in the FDA's Guidance for Industry and FDA Staff entitled “Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems,” which was published on January 13, 2005. This guidance does not provide mandatory requirements, but rather, provides general information to help in the development of an appropriate testing strategy for a device. This strategy will be dependent on the device characteristics and the proposed intended clinical use. For SFA stents, it is appropriate to consider the effects of nonpulsatile loading modes, such as bending, torsion, compression, tension, and crush, on the fatigue life of the stents. In addition, the impact of “worst-case” anatomical constraints, such as vessel tortuosity and calcification, should be considered when designing simulated delivery, deployment, and stent system withdrawal

testing. If stent overlap is reasonably expected with clinical use, assessments of both single and overlapped stents should be considered with respect to the engineering and clinical testing.

Studies submitted in support of [SFA] vascular stents that have gained FDA approval have included the collection of 9- to 12-month primary endpoint data, as well as additional long-term follow-up (either in the pre- or post-market setting) to evaluate long-term safety and performance issues such as stent fracture and any associated clinical sequelae. As such, the FDA encourages manufacturers to discuss proposed study designs—both pre- and post-market—with us early in the process to ensure that appropriate data are collected to support a marketing application.

Endovascular Today: Does the FDA endorse the objective performance criteria (OPC) for SFA stenting recently published by VIVA Physicians, Inc. (VPI)?

Ms. Goode: As outlined in an editorial² my colleagues and I published in conjunction with the VPI article, we agree that the trial design and performance metrics they proposed is one potential option that can be used as the basis for a clinical study proposal. Specific comments in our editorial included the following:

“Because these VPI metrics were generated from patients with anatomically specific lesions in the superficial femoral and supragenicular popliteal arteries, as characterized by run-off circulation and Rutherford classifications, careful comparison of patient demographics from a single-arm registry study to the VPI data set would be important to determine the applicability of the performance goals to the registry patients. If the proposed trial design were used to support a marketing application for femoropopliteal stents, all eight of the 30-day and 12-month performance goals noted in the VPI's publication would be important for the assessment of this type of treatment.”

Endovascular Today: Can data from an ongoing SFA stent trial be gathered and presented for consideration in another vascular bed (ie, side registries involving iliac use)?

Ms. Goode: We encourage manufacturers to propose study platforms that may provide the basis for approval for more than one vascular bed. For example, we may be willing to consider the addition of side registries to ongoing SFA clinical trials, where data could be collected to support an expanded indication for use of the same stent system in treating iliac lesions, as well as lesions that extend across both iliac and SFA anatomy.

Endovascular Today: Several stent companies have invested in marketing SFA stent registries in Europe over the last several years. Do data for an SFA approval need to come from a single SFA study, or can datapoints be picked out of multiple studies to meet the OPC guidelines?

Ms. Goode: We believe that data from prospectively designed studies is optimal for use in support of marketing applications. However, other data available to a stent manufacturer may be useful in support of a marketing application and would be considered on the specifics of each individual case presented to the Agency.

Endovascular Today: The FDA has brought quite a lot of attention to the issue of stent fracture, yet the OPCs do not mention an acceptable fracture rate. What type of data are the FDA looking for on this issue?

Ms. Goode: As with most implantable cardiovascular device studies, assessment of device integrity is necessary for vascular stent studies. Clinical trials, which have supported many approved vascular stent and stent graft applications, have assessed whether fractures were occurring, the time frame in which fractures were detected, and whether there appeared to be any relationship between fractures and clinical sequelae. Where fractures have been noted, descriptive information is included in the labeling of approved vascular products.

Endovascular Today: Do you think we will see an increase in the number of SFA stents approved in the next several years?

Ms. Goode: From the amount of public discussion we have heard and participated in on this topic, we are encouraged by the vascular stent manufacturers' motivation to obtain vascular stent indications for their products, such as for SFA stenting. We think that this effort on their behalf will benefit both doctors and patients in terms of available treatment options, and we hope to facilitate this in whatever ways we can. ■

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1. Abel DB. Premarket approval and premarket notification: uncovering the mystery of FDA device regulation classifications. *Endovas Today*. 2004;3:53-54.

2. Goode J, Sapirstein W, Zuckerman B. FDA perspective on clinical trial design for femoropopliteal stent correction of peripheral vascular insufficiency cardiovascular devices. *Cathet Cardiovasc Interv*. 2007;69:920-921.