

DURABILITY II Trial

A new standard in femoropopliteal artery nitinol stent trial design.

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The DURABILITY II trial, which initiated enrollment in October 2007, is a prospective, single-arm investigational device exemption (IDE) trial evaluating the clinical safety and effectiveness of the Protégé EverFlex nitinol stent (ev3 Inc., Plymouth, MN) for the treatment of patients with lifestyle-limiting claudication (Rutherford categories 2–4) due to femoropopliteal atherosclerotic disease. Data from this trial will support the premarket approval application of the Protégé EverFlex stent system. This landmark trial presents the largest prospective evaluation of nitinol stents for the treatment of claudication and includes duplex Doppler core lab assessment of 12-month restenosis, hemodynamic endpoints (ie, ankle-brachial indices), and stent fractures. However, beyond these essential study design features, the DURABILITY II trial is novel in its advancement of three new paradigms in femoropopliteal nitinol IDE trials and thus represents a new benchmark in trial design.

The DURABILITY II trial is the first IDE trial to use the VIVA Physicians, Inc., in collaboration with the US Food and Drug Administration, proposed femoropopliteal percutaneous balloon angioplasty (PTA) objective performance criteria¹ as a 12-month restenosis rate as a comparator to which superiority must be established. This PTA comparator therefore obviates the need of a randomized trial design of PTA versus stenting, thereby promoting a “least burdensome pathway” for device approval.² Importantly, this objective performance criteria has now been accepted by other

industry members as the standard for IDE trials to support premarket approval application in the femoropopliteal artery.

Another distinguishing aspect of the DURABILITY II trial design, and an important first, is the inclusion of a claudication treadmill test as a “therapeutic endpoint.” Increasingly, government regulators and payors, includ-



Figure 1. A 13-cm total left femoropopliteal occlusion with a symptomatic DURABILITY II patient (Rutherford class 3) (A). After successful deployment of a 20-cm Protégé nitinol stent (B).

ing the Centers for Medicare & Medicaid Services, have challenged clinician scientists and industry members to integrate clinical endpoints that are relevant to the Medicare population.³

As part of a patient subcohort, the DURABILITY II trial will evaluate patients with moderate to severe claudication with a preprocedure and 12-month objective assessment of absolute walking distance using a claudication treadmill protocol to document potential clinical improvement after successful stent implantation. The patient's claudication treadmill time will be correlated with the duplex Doppler assessment of restenosis and with quality-of-life assessment. This is important, because the Centers for Medicare & Medicaid Services is now requesting physicians and industry members to demonstrate that the procedures actually have a relevant clinical benefit to patients—not just the assessment of a surrogate endpoint (eg, peak systolic velocity at 12 months). This is the first trial to challenge clinicians to enroll patients, objectively evaluate their treadmill walking distance, and then perform an intervention and establish an improvement in the therapeutic endpoint at 12 months. Notably, this important substudy has challenged the rate of enrollment, because many physicians do not routinely assess a patient's walking distance as part of their routine preprocedure assessment. Nonetheless, this important subcohort has completed enrollment, and the trial investigators look forward to gaining new clinical insights into the effect of stenting on this therapeutic endpoint.

Finally, this trial tests the hypothesis that the placement of a single nitinol stent, potentially up to 200 mm in length (Figure 1), may translate into a reduced incidence of stent fractures and, in turn, may reduce 12-month duplex Doppler-defined restenosis rates and target lesion revascularization rates. Previous trials of nitinol stents in the femoropopliteal artery have suggested that use of multiple overlapping stents, particularly three or more, is associated with high rates of stent fractures and restenosis. By treating lesion lengths between 4 and 18 cm and having available stent lengths up to 20 cm, this trial will provide important insights into this “single stent” hypothesis. These three important “firsts” of the DURABILITY II trial distinguish this trial from others in its importance and relevance in patients, physicians, and payors.

An important preview into the potential results of the DURABILITY II trial have been evaluated in the DURABILITY I trial.⁴ This trial, performed at 14 sites in Western Europe, evaluated 151 patients and followed them with 6- and 12-month duplex ultrasonography.

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Additionally, angiography and x-ray surveillance for stent fractures were performed under core lab surveillance. The 12-month primary endpoint was patency as assessed by duplex ultrasound peak systolic velocity ratio < 2.5 with no reintervention. Review of the details of this trial noted a mean lesion length of 9.6 cm; 40% of these patients had occlusive disease with 55% of patients gauged as Rutherford class 3, and 12% of patients were Rutherford 4 and 5. More than 50% of patients had the deployment of a single 15-cm stent with a technical success rate of 100%. The primary 12-month endpoint of patency, as defined by duplex Doppler ultrasound, was noted at 72.2% with freedom from target lesion revascularization of 79.1%.

Additionally, this was the first European study to evaluate the use of a single long stent in patients with challenging atherosclerosis. Combined with the pending results of the DURABILITY II trial, the investigators will have access to important procedural, clinical, and follow-up data in more than 400 patients after receiving long Protégé EverFlex stents. This represents an important contribution to the medical literature in the assessment of the efficacy and durability of nitinol stents in the femoropopliteal artery. ■

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