IN.PACT Global Study: Overview and 12-Month Outcomes of the Long Lesion and In-Stent Restenosis Imaging Cohorts

Positive overall safety and effectiveness for patients treated with the IN.PACT™ Admiral™ drug-coated balloon.

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Peripheral artery disease is a complex disease that is progressive in nature, often requiring multiple treatments to maintain blood flow and save patients' limbs. Balloon angioplasty has been the historical endovascular standard for treating peripheral artery disease, and in some centers in the world, it is still the go-to treatment. However, angioplasty is associated with a high incidence of restenosis and reocclusion.[1] Angioplasty followed by stenting with bare-metal nitinol stents, and more recently drug-eluting stents, has vastly improved the low patency rates observed with angioplasty. Recent studies have reported 12-month patency rates ranging from 63% to 83% in short- to intermediate-length lesions.[2-6] Despite improved outcomes with stents, concerns still remain about performance in more complex lesions, including long lesions, chronic total occlusions (CTOs), and in-stent restenosis (ISR). These complex lesion subsets continue to pose unique treatment challenges, with no current treatment standard identified. Lesion length is shown to be a predictor of lower patency at 12 months, with rates ranging from 35% to 65% (mean lesion length, > 20 cm).[7,8] Up to 40% of bare-metal stents placed in the superficial femoral artery (SFA) will develop ISR or occlusion within 1 year.[9] There remains a desire for minimally invasive treatment strategies that provide effective and durable outcomes in complex lesions while preserving future treatment options. Drug-coated balloons (DCBs) have emerged as an attractive option with promising results.

OVERVIEW

The IN.PACT Global Study is an independently adjudicated and monitored prospective, multicenter, single-arm study designed to expand evidence of the IN.PACT™ Admiral™ DCB (Medtronic, Inc.) in the treatment of patients with real-world femoropopliteal lesions, including long lesions, ISR, and CTOs; more than 1,500 patients were enrolled in the study.[10] More than 1,400 patients were enrolled as part of the clinical cohort. A subset of these subjects underwent duplex ultrasound (DUS) imaging at 12 months to assess patency and were included in the imaging cohort. The imaging cohort consisted of three subgroups: (1) de novo ISR, (2) long lesion ≥ 15 cm, and (3) CTOs ≥ 5 cm. The primary efficacy endpoint for the imaging cohort was primary patency at 12 months, defined as freedom from clinically driven target lesion revascularization (CD-TLR) and freedom from restenosis as determined by DUS peak systolic velocity ratio

TABLE 1. CONSISTENT CLINICAL OUTCOMES WITH THE IN.PACT ADMIRAL DCB ACROSS STUDIES AND COMPLEX LESION SUBSETS

	IN.PACT SFA (DCB Arm) (N = 220)	IN.PACT Global Long Lesion Imaging Cohort (N = 157)	IN.PACT Global De Novo ISR Imaging Cohort (N = 131)
Lesion length	8.9 cm	26.4 cm	17.2 cm
Primary patency (12-month Kaplan-Meier)	87.5%	91.1%	88.7%
CD-TLR	2.4%	6.0%	7.3%
CD-TVR	4.3%	6.0%	8.9%
Thrombosis	1.4%	3.7%	0.8%

(PSVR) ≤ 2.4. The safety endpoint was a composite of freedom from device- and procedure-related mortality through 30 days and freedom from major target limb amputation and clinically driven target vessel revascularization (CD-TVR) within 12 months. Twelve-month outcomes from the long lesion imaging cohort were presented at EuroPCR in May 2015, and outcomes from the ISR imaging cohort were presented at the Vascular Interventional Advances (VIVA) conference in November 2015. Findings from these two complex lesion subsets are summarized as follows.

LONG LESION IMAGING COHORT

As presented by Prof. Dierk Scheinert, 157 patients (mean age, 69.5 years; 66.2% males) with 164 lesions ≥ 15 cm in length were enrolled in the long lesion imaging cohort of the IN.PACT Global Study.[10] The mean lesion length treated was 26.4 cm, markedly longer than that reported in traditional pivotal studies evaluating outcomes in the SFA, and included 60.4% total occlusions and 71.8% calcified lesions. At 12 months, the Kaplan-Meier estimate of primary patency was 91.1%. When stratified by lesion length subgroups (lesion lengths, 15–25 cm vs > 25 cm), primary patency was 97.7% in patients with lesion lengths of 15 to 25 cm and 79.2% in patients with lesion lengths > 25 cm. The CD-TLR rate at 12 months was 6.0%. The primary safety endpoint outcome was 94.0%. There were no major target limb amputations reported within 12 months, and the rate of thrombosis was low at 3.7%.

DE NOVO ISR IMAGING COHORT

To evaluate the effectiveness of the IN.PACT Admiral DCB in treating ISR lesions, 131 patients with pure de novo ISR lesions were enrolled into the ISR imaging cohort of the IN.PACT Global Study and underwent DUS imaging at 12 months.[11] The mean age was 67.8 years, and 69.5% of the patients were male. The mean lesion length treated was 17.2 cm, including 34.0% CTOs and 59.1% calcified lesions. The 12-month Kaplan-Meier estimate of primary patency was 88.7%. The CD-TLR rate at 12 months was 7.3%. The primary safety outcome was 91.1%. There were no major target limb amputations, no deaths, and a low (0.8%) thrombosis rate within the 12-month follow-up period.

DISCUSSION

The IN.PACT Admiral DCB has shown consistent clinical effectiveness across the IN.PACT Admiral clinical studies (Table 1). Very high patency was observed in the randomized trial and in the complex subsets in the IN.PACT Global Study. This is noteworthy, given that the mean lesion length in the randomized controlled trial was 8.9 cm compared to 26.4 cm in the long lesion imaging cohort. Restenosis after SFA interventions, particularly with stents, is common and remains an ongoing major challenge. Patency rates for reintervention are usually lower than those for the primary intervention with the exception of the results from the IN.PACT Global ISR imaging cohort. To the best of my knowledge, this is the highest 12-month primary patency rate reported for ISR interventions.

Intended for markets where mentioned products and indications are approved.

SUMMARY

DCBs have emerged as an important therapeutic modality for the treatment of femoropopliteal lesions. Results from the IN.PACT Global Study demonstrate positive overall safety and effectiveness for patients treated with the IN.PACT Admiral DCB. Importantly, the high patency and low CD-TLR rates were consistently observed across IN.PACT Admiral studies and SFA lesions, including the long lesion and ISR subsets. ■

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