JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 20, 2017
ISSN 1936-8798
http://dx.doi.org/10.1016/j.jcin.2017.06.018

Drug-Coated Balloon Treatment for Femoropopliteal Artery Disease

The IN.PACT Global Study De Novo In-Stent Restenosis Imaging Cohort

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ABSTRACT

OBJECTIVES This study sought to evaluate the safety and effectiveness of a paclitaxel-coated drug-coated balloon (DCB) for the treatment of patients with de novo in-stent restenosis (ISR).

BACKGROUND Treatment of patients with ISR remains a challenge. Current strategies are plagued by high rates of recurrent restenosis and need for reintervention. The best intervention for ISR remains to be elucidated.

METHODS The IN.PACT Global study is an independently adjudicated multicenter, prospective, single-arm study that enrolled 1,535 subjects with symptomatic atherosclerotic disease of the superficial femoral and/or popliteal arteries, including de novo ISR lesions. Patients enrolled in the pre-specified ISR imaging cohort were evaluated for vessel patency and reintervention within the 12-month follow-up period.

RESULTS A total of 131 subjects with 149 ISR lesions were included for analysis. The mean age of the cohort was 67.8 years. Mean lesion length was 17.17 ± 10.47 cm, including 34.0% total occlusions and 59.1% calcified lesions. The 12-month Kaplan-Meier estimate of primary patency was 88.7%. The rate of clinically driven target lesion revascularization (CD TLR) at 12 months was 7.3%. The primary safety outcome, a composite of freedom from device- and procedure-related mortality through 30 days and freedom from major target limb amputation and CD TLR within 12 months, was 92.7%. There were no major target limb amputations, no deaths, and a low (0.8%) thrombosis rate.

CONCLUSIONS Results from the ISR imaging cohort demonstrate high patency and a low rate of CD TLR at 12 months. These data confirm the safety and effectiveness of the IN.PACT Admiral DCB (Medtronic, Dublin, Ireland) in complex femoropopliteal lesions, including this challenging subset. (J Am Coll Cardiol Intv 2017;10:2113–23)

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ABBREVIATIONS AND ACRONYMS

ABI = ankle-brachial index

CD = clinically driven

DCB = drug-coated balloon

DES = drug-eluting stent(s)

DUS = duplex ultrasonography

ISR = in-stent restenosis

PAD = peripheral artery disease

SFA = superficial femoral artery

TLR = target lesion revascularization

TVR = target vessel revascularization

WIQ = Walking Impairment Questionnaire

Endovascular interventions, including percutaneous transluminal angioplasty with a traditional uncoated balloon, implantation of bare-metal or drug-eluting stents (DES), angioplasty with a drug-coated balloon (DCB), and debulking with mechanical or laser atherectomy, have become the primary mode of revascularization in patients with symptomatic peripheral artery disease (PAD). Balloon angioplasty of the femoropopliteal segment is associated with a high incidence of restenosis, with the best results seen for very focal stenosis and noncomplex lesions (1). Stents yield better outcomes when compared with conventional angioplasty alone (2–5), but are associated with the risk of post-procedural in-stent restenosis (ISR) and other stent-related complications that can negatively affect the patient's long-term clinical outlook (6,7). Treatment of ISR with conventional methods remains a clinical challenge (8), with no clear frontline strategy.

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Technical improvements with DESs, DCBs, cutting balloons, and directional and laser atherectomy have been aimed at reducing the occurrence of ISR (9–15). DCBs and DESs deposit a long lasting antiproliferative therapeutic on the inner wall of the artery that supports the sustained inhibition of restenosis, but DCBs have the additional advantage of treating the lesion without leaving a permanent device at the target site (16). The safety and effectiveness of DCBs for the treatment of symptomatic PAD patients has been demonstrated in randomized controlled clinical trials (17–20). Although few, studies have reported positive outcomes with DCBs for the treatment of complex PAD lesions, including those that are formed by de novo ISR (10,15,21,22).

The IN.PACT Global Study was designed to evaluate the safety and effectiveness of a paclitaxel-coated DCB (IN.PACT Admiral, Medtronic, Dublin, Ireland) in the treatment of subjects with atherosclerotic femoropopliteal disease, including de novo ISR in the superficial femoral artery (SFA) or the entire length of the popliteal artery. Herein we report 12-month results from the ISR cohort.

METHODS

IN.PACT GLOBAL STUDY: DESIGN, SUBJECTS, AND TREATMENT. A prospective analysis of DCBs for the treatment of de novo ISR was incorporated into the design of the IN.PACT Global study, a prospective, multicenter, international, single-arm clinical trial assessing the safety and effectiveness of a paclitaxel-coated DCB for the treatment of patients with intermittent claudication or rest pain due to obstructive disease of the femoropopliteal artery, including the full native SFA and/or full popliteal artery (P1 to P3 segments).

Greater than 1,400 patients who satisfied the inclusion or exclusion criteria for the IN.PACT Global study were consecutively enrolled at participating centers into the clinical cohort (**Figure 1**). Patients enrolled at sited qualified by the VasCore Duplex Core Lab (Boston, Massachusetts) were screened to meet 1 or more of the imaging criteria based on an algorithm. The hierarchy for the imaging cohort subgroup assignment was as follows: 1) de novo ISR; 2) long lesions ≥15 cm; and 3) chronic total occlusions ≥5 cm. Enrollment in the respective imaging cohorts was only open to subjects that had a de novo ISR, long lesion, or chronic total occlusion at pre-procedure baseline. The only subjects who were included in the respective imaging cohort analyses, however, were those who had the primary target lesions that met the criteria of the respective cohort during the index procedure (i.e., no other types of lesions could have been treated during the index procedure).

Subjects with symptoms of intermittent claudication or ischemic rest pain (Rutherford clinical category 2 to 4) and angiographic evidence of occlusion or stenosis (length ≥2 cm) in the SFA or popliteal artery (including P1 to P3 segments) were eligible for enrollment in the IN.PACT Global study. Subjects with multiple lesions were allowed. Subjects with tissue loss were excluded.

Independent core laboratories analyzed all images, including duplex ultrasonography (DUS) (VasCore, Massachusetts General Hospital, Boston, Massachusetts) and angiography (SynvaCor Angiographic Core Lab, Springfield, Illinois). In cases where both angiography and duplex ultrasonography were available at the same assessment, then angiography was preferentially used. An independent Clinical Events

for research or clinical trials from 480 Biomedical, Abbott Vascular, B. Braun, Bard Peripheral Vascular, Bayer Pharma, Biotronik, Caveo Med, Contego Medical, Cook Medical, CSI, Gore & Associates, Innora, Intact Vascular, Medtronic, Mercator, Philips, Pluristem, Shockwave, Spectranetics, Terumo, TriReme, and Veryan.

Manuscript received December 8, 2016; revised manuscript received April 20, 2017, accepted June 13, 2017.