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PERIPHERAL

The 24-Month Results of the Lutonix Global SFA Registry

Worldwide Experience With Lutonix Drug-Coated Balloon

Marcus Thieme, MD,[a,b] Peter Von Bilderling, MD,[c] Christian Paetzel, MD,[d] Dimitrios Karnabatidis, MD,[e] Julio Perez Delgado, MD,[f] Michael Lichtenberg, MD,[g] for the Lutonix Global SFA Registry Investigators

ABSTRACT

OBJECTIVES The Global SFA Registry sought to assess safety, clinical benefit, and outcomes of the Lutonix 035 drug-coated balloon (DCB) in a heterogeneous, real-world patient population at 12 and 24 months.

BACKGROUND Numerous clinical studies have evaluated the use of angioplasty for revascularization of femoropopliteal arteries in peripheral arterial disease with restenosis rates of 40% to 60% at 6 to 12 months. Data from recent studies document decreased restenosis rates and improvement in patency in patients receiving angioplasty of femoropopliteal arteries with DCBs.

METHODS The multicenter, prospective study enrolled 691 patients in 38 centers from 10 countries treated with the Lutonix 035 DCB in femoropopliteal lesions. The primary safety endpoint was freedom from a composite of target vessel restenosis, major index limb amputation, and device- or procedure-related death at 30 days. The primary effectiveness endpoint was freedom from target lesion restenosis at 12 months. Secondary endpoints were acute device and procedural success and clinically assessed primary patency.

RESULTS Freedom at 30 days from the composite safety endpoint was 99.4%. Freedom from target lesion restenosis was 93.4%/89.3% for the overall population, 93.2%/88.2% for long lesions up to 500 mm, and 90.7%/84.6% for in-stent restenosis at 12/24 months. Clinically assessed primary patency by Kaplan-Meier estimates was 85.4%/75.6% at 12/24 months. More than 76% of patients showed improvement of at least 1 Rutherford category.

CONCLUSIONS The Global SFA Registry 24-month outcomes confirm the Lutonix 035 DCB is a safe and effective long-term treatment option in real-world patients with peripheral arterial disease with superficial femoral artery lesions, also in long lesions and in-stent restenosis. (Lutonix Global SFA Registry; NCT01864278) (J Am Coll Cardiol Intv 2017;10:1682–90) © 2017 by the American College of Cardiology Foundation.

From the [a]Regiomed Vascular Center Sonneberg, Sonneberg, Germany; [b]Jena University Hospital, Jena, Germany; [c]Diakoniewerk Munchen, München, Germany; [d]Kliniken Nordoberpfalz AG, Weiden, Germany; [e]University Hospital of Patras, Patras, Greece; [f]Arberlandklinik Viechtach, Viechtach, Germany; and the [g]Klinikum Arnsberg, Karolinen-Hospital Huesten, Arnsberg, Germany.
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There have been numerous clinical studies evaluating the use of percutaneous transluminal angioplasty for treatment of peripheral arterial disease (PAD), with restenosis rates as high as 40% to 60% at 6 to 12 months. Drug-coated balloons (DCBs) have resulted in significantly higher primary patency at 6 to 12 months as compared with percutaneous transluminal angioplasty use (82.2% vs. 52.4%). Improved freedom from target lesion revascularization (TLR) rates for DCBs have been remarkable with increased primary patency over time. Until recently there have been limited clinical trials with DCBs for treatment of PAD in typical real-world setting. Patients in randomized controlled DCB trials usually had shorter lesions with a low degree of calcification and a lower proportion of chronic total occlusions (CTOs) (1–5).

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The Global SFA Registry documents safety, effectiveness, and outcomes of the Lutonix 035 DCB (Bard Lutonix, New Hope, Minnesota) in a heterogeneous real-world patient population.

METHODS

PATIENT POPULATION. This multicenter worldwide, prospective real-world study included 691 patients with stenosis or occlusion of a native femoropopliteal artery treated with the Lutonix 035 (with or without stenting). Enrollment criteria were intentionally broad and included: 1) patients age 18 years or older; 2) Rutherford Classification category of ≤4; 3) stenotic or obstructive vascular lesions of the femoropopliteal arteries; 4) lesions treatable with available Lutonix 035 DCB, size per current European Instructions for Use version 6 (IFU); 5) at least 1 patent native outflow artery to the ankle free from significant lesion (≥50% stenosis) as confirmed by angiography; and 6) informed consent and willingness to comply with the follow-up schedule. Exclusion criteria included patients who were: 1) enrolled in another clinical trial; 2) unable to take recommended medications as stated in IFU or had a noncontrollable allergy to contrast; 3) pregnant or planning on becoming pregnant; 4) intending to father a child; and 5) Rutherford category >4.

Medical history was obtained on admission, and patients underwent physical examination focusing on PAD with Rutherford classification and measurement of ankle brachial index. The study was performed in compliance with local ethics committee requirements. Written informed consent was obtained before enrollment.

The lesion length, calcification, and vessel diameter were estimated visually by the investigator; no core laboratory review was performed.

STUDY DEVICES AND PROCEDURES. The Lutonix 035 DCB is a 0.035-inch over-the-wire drug-coated percutaneous transluminal angioplasty dilatation catheter with a semi-compliant balloon, coated with paclitaxel at a concentration of 2 μg/mm^2 with the excipients polysorbate and sorbitol to facilitate drug release and tissue deposition.

All endovascular treatment decisions, including DCB use, were at the discretion of the clinician. Instructions for use per device labeling were to be followed as a standard of care. Because this study was conducted in Europe, the IFU was followed and recommended the pre-dilatation with an uncoated balloon before DCB use. DCB treatment was to exceed the proximal and distal margins of the lesion segment by 5 mm to ensure the margins of the pre-dilated vessel were covered by the DCB. If multiple DCBs were needed to cover the full lesion length, balloons were to be positioned to ensure an overlap of the treated area. All procedural data regarding treated vessel segment, number and diameter of DCBs used, and the need for additional devices/stents were collected prospectively.

This registry was performed with marketed devices within the defined indications for use. There were no additional treatments or examinations that were required within this registry. The only differences to routine care were collection and analysis of patient data, informed consent, and the option of performing follow-up visits via telephone.

ENDPOINTS. The primary endpoints were defined in terms of safety and efficacy. The primary safety endpoint was freedom at 30 days from target vessel reintervention (TVR), major index limb amputation, and device- or procedure-related death. The primary efficacy endpoint was freedom from TLR at 12 months.

Secondary endpoints included: 1) acute device and procedural success; 2) primary patency at 6, 12, and 24 months; and 3) freedom from all-cause death, device- or procedure-related mortality, unexpected device or drug-related adverse events, index limb amputation, reintervention for treatment of thrombosis of the target vessel, reintervention for treatment of embolization to its distal vasculature, TLR, TVR, composite of all-cause perioperative (≤30 days)

ABBREVIATIONS AND ACRONYMS

CTO = chronic total occlusion

DCB = drug-coated balloon

IFU = European Instructions for Use

ISR = in-stent restenosis

PAD = peripheral arterial disease

RVD = reference vessel diameter

SFA = superficial femoral artery

TASC II = Trans-Atlantic Inter-Society Consensus II

TLR = target lesion revascularization

TVR = target vessel reintervention

TABLE 1 Baseline Demographics, Clinical Characteristics, and Medical History

	SFA Global Registry (n = 691)	Long Lesion (≥140 mm) (n = 140)	ISR (n = 89)
Age, yrs	68.2 ± 9.86 (691)	70.4 ± 9.19 (140)	68.2 ± 9.65 (89)
Median (min, max)	69.0 (37.0, 94.0)	70.5 (37.0, 94.0)	69.0 (38.0, 88.0)
Sex			
Female	32.1 (222/691)	30.7 (43/140)	40.4 (36/89)
Male	67.9 (469/691)	69.3 (97/140)	59.6 (53/89)
BMI, kg/m^2	27.2 ± 4.23 (665)	27.5 ± 3.89 (139)	26.4 ± 3.53 (83)
Median (min, max)	26.9 (15.9, 41.2)	26.9 (19.2, 40.8)	26.3 (19.8, 37.6)
BMI ≥30 kg/m^2	24.7 (164/665)	25.2 (35/139)	15.7 (13/83)
Rutherford category			
0	1.2 (8/689)	1.4 (2/140)	
1	2.3 (16/689)	0.7 (1/140)	1.1 (1/88)
2	20.6 (142/689)	16.4 (23/140)	28.4 (25/88)
3	66.9 (461/689)	75.7 (106/140)	61.4 (54/88)
4	7.4 (51/689)	5.0 (7/140)	8.0 (7/88)
5	1.5 (10/689)	0.7 (1/140)	1.1 (1/88)
6	0.1 (1/689)		
ABI of target limb	0.69 ± 0.24 (470)	0.68 ± 0.25 (110)	0.63 ± 0.24 (51)
Median (min, max)	0.70 (0.00, 1.40)	0.65 (0.01, 1.38)	0.62 (0.17, 1.34)
Smoker			
Current smoker	36.9 (254/689)	30.9 (43/139)	36.0 (32/89)
Nonsmoker	28.4 (196/689)	26.6 (37/139)	29.2 (26/89)
Previous smoker	34.7 (239/689)	42.4 (59/139)	34.8 (31/89)
Hypertension	84.9 (587/691)	91.4 (128/140)	86.5 (77/89)
Dyslipidemia	70.0 (484/691)	78.6 (110/140)	78.7 (70/89)
Diabetes	39.5 (273/691)	49.3 (69/140)	28.1 (25/89)
Type 1	12.1 (33/273)	10.1 (7/69)	8.0 (2/25)
Type 2	87.9 (240/273)	89.9 (62/69)	92.0 (23/25)
History of vascular disease	66.0 (456/691)	63.6 (89/140)	87.6 (78/89) 85.4 (76/89)
Prior PAD intervention in index leg	53.8 (196/364)	38.4 (28/73)	100.0 (77/77)
History of cardiac diseases	35.6 (246/691)	40.7 (57/140)	29.2 (26/89)
History of chronic renal disease	13.5 (93/691)	20.7 (29/140)	11.2 (10/89)

Values are mean ± SD (N) or % (n/N), unless otherwise indicated. Pressures >1.4 were excluded from this analysis per the measurement and interpretation of the ankle-brachial index guidelines from the American Heart Association.

ABI = ankle brachial index; BMI = body mass index; ISR = in-stent restenosis; PAD = peripheral arterial disease; SFA = superficial femoral artery.

death and index limb amputation, index limb reintervention, and index limb-related death at 6, 12, and 24 months.

Primary patency was assessed clinically based on patient symptoms and examination including Rutherford classification and ankle brachial index. Primary patency was defined as the onset of patency failure, being the earliest of TLR onset or the first visit date the investigator identified a failure. The censoring date was defined as the date of the last visit with investigator confirmation of no patency failure.

STATISTICAL ANALYSIS. Primary endpoints were analyzed using survival techniques based on time-to-event survival analysis, performed on the cohort of all patients enrolled and treated with the Lutonix DCB catheter. For each primary endpoint, the estimated mean ± SD or proportion and sample size was calculated and reported. Data were summarized using descriptive statistics, and the Kaplan-Meier survival analysis was used to evaluate survival percentages over the 6-, 12-, and 24-month periods. Statistical analysis was performed using SAS version 9.3 or higher (SAS Institute, Cary, North Carolina).

RESULTS

BASELINE CHARACTERISTICS. A total of 691 patients were enrolled across 38 centers and 10 countries. Patients were from real-world clinical

TABLE 2 Summary of Baseline Angiographic Data

	SFA Global Registry (n = 691)	Long Lesion (≥140 mm) (n = 140)	ISR (n = 89)
Number of treated lesions			
1	84.4 (583/691)	75.0 (105/140)	83.1 (74/89)
2	13.9 (96/691)	19.3 (27/140)	15.7 (14/89)
3	1.6 (11/691)	5.0 (7/140)	1.1 (1/89)
4	0.1 (1/691)	0.7 (1/140)	
Total target lesion, mm, site	101.2 ± 84.2 (685)	212.3 ± 65.3 (140)	154.4 ± 97.1 (89)
Median (min, max)	80.0 (2.3, 500.0)	200.0 (140.0, 500.0)	150.0 (10.0, 400.0)
Treated length, mm, site	136.6 ± 89.7 (689)	242.5 ± 83.3 (140)	182.1 ± 90.5 (89)
Median (min, max)	100.0 (6.0, 530.0)	220.0 (100.0, 520.0)	160.0 (40.0, 440.0)
Diameter stenosis, %, site	90.0 ± 11.0 (686)	93.6 ± 8.50 (140)	88.5 ± 13.3 (89)
Median (min, max)	90.0 (6.0, 100.0)	99.0 (50.0, 100.0)	90.0 (6.0, 100.0)
CTO	31.2 (214/686)	42.1 (59/140)	28.1 (25/89)
Average RVD, mm, site	5.2 ± 0.67 (681)	5.2 ± 0.62 (139)	5.4 ± 0.64 (89)
Median (min, max)	5.0 (2.0, 7.0)	5.0 (4.0, 6.0)	5.0 (4.0, 6.0)
Calcification	50.2 (238/474)	57.5 (46/80)	37.7 (26/69)
TASC II lesion class			
A	46.8 (231/494)	12.5 (11/88)	39.7 (25/63)
B	33.4 (165/494)	29.5 (26/88)	36.5 (23/63)
C	13.2 (65/494)	38.6 (34/88)	14.3 (9/63)
D	6.7 (33/494)	19.3 (17/88)	9.5 (6/63)
Most distal lesion			
Popliteal distal	3.0 (21/690)	4.3 (6/140)	5.6 (5/89)
Popliteal mid	10.1 (70/690)	13.6 (19/140)	5.6 (5/89)
Popliteal proximal	16.8 (116/690)	15.7 (22/140)	18.0 (16/89)
SFA distal	37.2 (257/690)	44.3 (62/140)	41.6 (37/89)
SFA mid	24.8 (171/690)	18.6 (26/140)	24.7 (22/89)
SFA proximal	8.0 (55/690)	3.6 (5/140)	4.5 (4/89)

Values are % (n/N) or mean ± SD (N), unless otherwise indicated.
CTO = chronic total occlusion; RVD = reference vessel diameter; TASC = Trans-Atlantic Inter-Society Consensus II; other abbreviations as in Table 1.

practice undergoing interventions in the superficial femoral and/or popliteal arteries with the Lutonix 035 DCB between December 2012 and July 2014.

Demographics, clinical characteristics, and medical history are presented in Table 1. Patients were on average 68.2 ± 9.86 years of age and cardiovascular risk factors were highly prevalent. Most patients (75.9%) presented with Rutherford category 3 or higher at the time of enrollment and 7.4% in category 4. Although patients with Rutherford category 5 and 6 were excluded from being enrolled, 11 patients (1.6%) with category 5 or 6 were included. Slightly more than one-half (53.8%) of the patients had a previous target limb intervention.

Baseline angiographic data in Table 1 show the average total target lesion length was 101.2 ± 84.2 mm. A total of 70.1% of the lesions were located in the SFA and 29.9% in the popliteal artery. Lesion characteristics were assessed by TASC II (Trans-Atlantic Inter-Society Consensus II) guidelines. Baseline ankle brachial index of the target limb was 0.69 ± 0.24. Calcification was present in 50.2% of the lesions, with CTO occurring in 31.2% (Table 2).

The summary of procedural outcomes is presented in Table 3. The DCB device average inflation time was 108.1 ± 39.49 s, with an average pressure of 9.5 ± 2.16 atm. Average balloon to vessel ratio (balloon diameter/reference vessel diameter [RVD]) was 1.00 ± 0.09 for the DCB. Percent diameter stenosis pre-procedure was on average 90%. Final percent diameter stenosis was reduced to 14.6%. Vessel preparation before DCB also included atherectomy in 1.3%, cutting balloon in 0.1%, laser in 0.1%, stent in 0.6%, and other (not defined) in 3.2%.

Additionally, 2 subgroups were analyzed: patients with long lesions (≥140 mm; n = 140) and patients with in-stent restenosis (ISR) (n = 89). The demographics, clinical characteristics, medical history, and baseline angiographic data for the 2 subgroups were similar to the overall global registry patients (Table 1). The long-lesion and ISR patients had longer lesions, with the ISR groups having less calcification.

TABLE 3 Summary of Procedural Data

	SFA Global Registry (n = 691)	Long Lesion (≥140 mm) (n = 140)	ISR (n = 89)
Pre-dilatation			
Pre-dilatation performed	64.9 (448/690)	76.4 (107/140)	59.6 (53/89)
Study device treatment			
Inflation time per balloon, s	108.1 ± 39.49 (676)	111.1 ± 35.84 (137)	104.6 ± 40.47 (89)
Median (min, max)	120.0 (30.0, 240.0)	120.0 (30.0, 180.0)	120.0 (30.0, 180.0)
Balloon pressure, atm	9.5 ± 2.16 (674)	10.3 ± 1.81 (137)	9.6 ± 2.19 (89)
Median (min, max)	10.0 (2.0, 20.0)	10.0 (6.0, 14.0)	10.0 (2.0, 14.0)
Balloon to vessel ratio (inflated diameter/RVD)	1.00 ± 0.09 (681)	0.99 ± 0.08 (139)	1.01 ± 0.09 (89)
Median (min, max)	1.00 (0.50, 1.63)	1.00 (0.77, 1.50)	1.00 (0.83, 1.50)
Final procedure outcome			
Diameter stenosis post-procedure, %	14.6 ± 18.69 (680)	19.0 ± 21.00 (140)	13.2 ± 17.65 (89)
Median (min, max)	10.0 (0.0, 100.0)	10.0 (0.0, 90.0)	10.0 (0.0, 100.0)
Final dissection	18.4% (127/690)	34.3% (48/140)	13.5% (12/89)
Final dissection treatment grade			
A	67.7 (86/127)	64.6 (31/48)	75.0 (9/12)
B	18.9 (24/127)	10.4 (5/48)	8.3 (1/12)
C	3.9 (5/127)	8.3 (4/48)	
D	5.5 (7/127)	8.3 (4/48)	16.7 (2/12)
E	2.4 (3/127)	4.2 (2/48)	
F	1.6 (2/127)	4.2 (2/48)	
Bailout spot stenting	25.2 (174/690)	35.7 (50/140)	33.7 (30/89)

Values are % (n/N) or mean ± SD (N), unless otherwise indicated.
Abbreviations as in Table 1.

Most of the long-lesion patient group lesions were TASC B and C, compared with the overall global registry (Table 2).

The IFU recommended a pre-dilatation before using the DCB; however, only 64.9% of the patients had a pre-dilatation. Although 83.6% (179 of 214) of the CTO patients had a pre-dilatation, only 56.4% (269 of 477) of the stenotic lesions were pre-dilated. There was no significant difference in freedom from TLR at 12 or 24 months between the 2 subgroups (Table 4).

PATIENT DISPOSITION. Follow-up data were available for 89.9% and 83.9% of patients at 12 and 24 months, respectively. The average follow-up time period was 726.4 ± 195.4 days. A total of 44 patients exited the study by 12 months and a total of 54 patients by 24 months. Follow-up evaluations included mortality, rate of reintervention, TLR, and occurrence of minor or major amputations.

ENDPOINT RESULTS. Primary safety endpoint. Freedom at 30 days from the composite of TVR, major index limb amputation, and device- and procedure-related death was 99.4% (Table 5). Freedom from primary safety events by Kaplan-Meier estimates was 92.1% at 12 months and 86.7% at 24 months (Table 6).

Primary efficacy endpoint. Effective therapy was demonstrated for all patients and long-lesion and ISR subgroups. Freedom from TLR for all patients at 12 months was 93.4% and at 24 months was 89.3% (Table 5). The Kaplan-Meier estimate for TLR-free survival was 94.1% at 12 months and at 24 months was 90.3% (Table 6, Figure 1).

The 12- and 24-month TLR-free rate by Kaplan-Meier estimate for selected subgroups of CTO, calcification, diabetes, dyslipidemia, and female are presented in Table 4. The 12- and 24-month TLR-free

TABLE 4 TLR-Free Survival With Kaplan-Meier Method Selected Subgroups 12 and 24 Months

	12 Months Survival	24 Months Survival
Chronic total occlusion	94.3 (90.2-96.7)	90.6 (85.6-93.9)
Calcification	94.4 (90.6-96.7)	89.7 (84.9-93.1)
Diabetes	96.6 (93.7-98.2)	91.7 (87.5-94.5)
Dyslipidemia	94.1 (91.5-95.9)	90.9 (87.8-93.2)
Females	88.9 (83.9-92.4)	85.8 (80.2-89.8)
Without pre-dilatation	94.7 (90.9-97.2)	90.4 (85.5-94.0)
With pre-dilatation	94.7 (90.9-97.2)	88.7 (85.1-91.7)
Without bailout-stent	93.6 (91.0-95.6)	88.9 (85.6-91.7)
With bailout-stent	92.8 (87.8-96.2)	90.3 (84.5-94.5)

Values are % (95% confidence interval).
CI = confidence interval; TLR = target lesion revascularization.

rates were 94.3%, 94.4%, 96.6%, 94.1% for 12 months; and 88.9%, 90.6%, 89.7%, 91.7%, 90.9%, and 85.8% for 24 months. The results demonstrate effective therapy in these subgroups.

Secondary endpoints. The clinically assessed primary patency success rate at 12 and 24 months was 83.1% and 73.5%. The clinical primary patency rate for all patients by Kaplan-Meier estimates resulted in 85.4% for 12 months and 75.6%% at 24 months (Figure 2).

A secondary safety composite endpoint analysis was performed to determine the percent of patients who were free of composite of all-cause perioperative (≤30 day) death and from index limb amputation, index limb reintervention, and index limb-related death at 12 and 24 months. The success rate was 86.8% at 12 months and 80.2% at 24 months for all patients. Freedom from secondary safety composite endpoint by Kaplan-Meier estimates for 12 months was 88.4% and at 24 months was 82.1% (Figure 3).

There were no reported device-, procedure-, or limb-related deaths throughout the 24 months of follow-up. The perioperative freedom from death rate was 99.7%. Freedom from all-cause death was 97.2% at 12 months and 94.1% at 24 months. Freedom from major or minor amputation was ≥99% at both time points. The rate of freedom from any index limb intervention was 87.1% at 12 months and 80.4% at 24 months and from intervention caused by TLR was 93.4% and 89.3% at 12 and 24 months, respectively. TVR-free rate at 12 and 24 months was 91.4% and 85.6%, respectively. Freedom from reintervention for treatment of thrombus was 98.3% at 12 months and 97.3% at 24 months. Freedom from reintervention for treatment of distal vascular events was 99.4% at 12 months and 99.3% at 24 months. No unanticipated adverse events were reported.

LONG-LESION AND IN-STENT RESTENOSIS SUBGROUPS.

Primary safety endpoint. Freedom from the composite of TVR, major index limb amputation, and device- and procedure-related death at 30 days was 99.3% and 100.0% for long-lesion and ISR patients, respectively (Table 5). Freedom from primary safety events by Kaplan-Meier estimates at 12 months was 90.5% for long lesions and 89.6% for ISR. For 24 months, freedom from primary safety events by Kaplan-Meier estimates was 85.7% for long lesions and 82.0% for ISR (Table 6).

Primary efficacy endpoint. Freedom from TLR at 12 months was 93.2% and 88.2% at 24 months for long lesions. For ISR patients, results were 90.7% and 84.6% at 12 and 24 months, respectively (Table 5). The Kaplan-Meier estimates for TLR-free survival at 12 and 24 months were 93.4% and 89.4% for long lesions and 90.7% and 85.5% for ISR (Table 6, Figure 1).

Secondary endpoints. The clinically assessed primary patency rate by Kaplan-Meier estimates was 76.9% at 12 months and 67.3% at 24 months for long lesions. For ISR patients the 12-month rate was 83.3% and 66.0% for 24 months (Figure 2). Freedom from reintervention for treatment of thrombus was 96.2% at 12 months and 95.0% at 24 months for long lesions and 98.8% and 94.8% at 12 and 24 months, respectively, in the ISR subgroup. Freedom from reintervention for treatment of distal vascular

TABLE 5 Primary Safety and Efficacy Endpoints

Primary Endpoints	Success	95% CI*
SFA Global Registry		
Safety: freedom from TVR, major amputation, device- and procedure-related death within 30 days	99.4 (681/681)	98.5–99.8
Efficacy: freedom from TLR at 12 months	93.4 (605/648)	91.2–95.2
Freedom from TLR at 24 months	89.3 (526/589)	86.5–91.7
Long-lesion subgroup (≥140 mm)		
Safety: freedom from TVR, major amputation, device- and procedure-related death within 30 days	99.3 (138/139)	961–100.0
Efficacy: freedom from TLR at 12 months	93.2 (123/132)	87.5–96.8
Freedom from TLR at 24 months	88.2 (105/119)	81.0–93.4
ISR		
Safety: freedom from TVR, major amputation, device- and procedure-related death within 30 days	100.0 (88/88)	95.9–100.0
Efficacy: freedom from TLR at 12 months	90.7 (78/86)	82.5–95.9
Freedom from TLR at 24 months	84.6 (66/78)	74.7–91.8

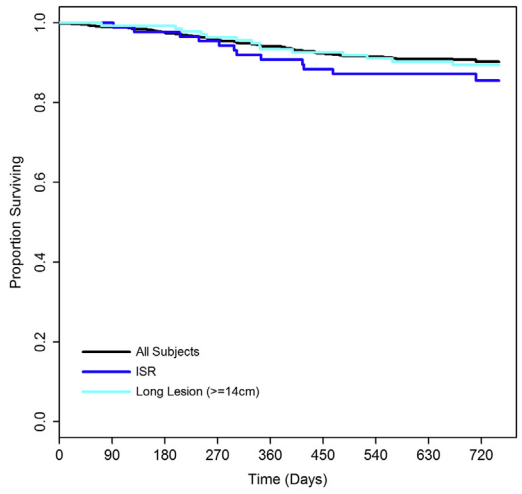
Values are % (n/N), unless otherwise indicated. *Exact binomial confidence interval.
TVR = target vessel reintervention; other abbreviations as in Tables 1 and 4.

TABLE 6 Freedom From Primary Safety and Efficacy Events by Kaplan-Meier Method at 12 and 24 Months

	12 Months	24 Months
SFA Global Registry		
Freedom from TVR, major amputation, device- or procedure-related death	92.1 (89.8–93.9)	86.7 (83.9–89.1)
TLR-free survival	94.1 (92.0–95.6)	90.3 (87.7–92.3)
Long lesion subgroup (≥140 mm)		
Freedom from TVR, major amputation, device- and procedure-related death	90.5 (84.1–94.4)	85.7 (78.5–90.7)
TLR-free survival	93.4 (87.7–96.5)	89.4 (82.8–93.6)
ISR		
Freedom from TVR, major amputation, device- and procedure-related death	89.6 (80.9–94.4)	82.0 (71.8–88.8)
TLR-free survival	90.7 (82.3–95.3)	85.5 (75.7–91.5)

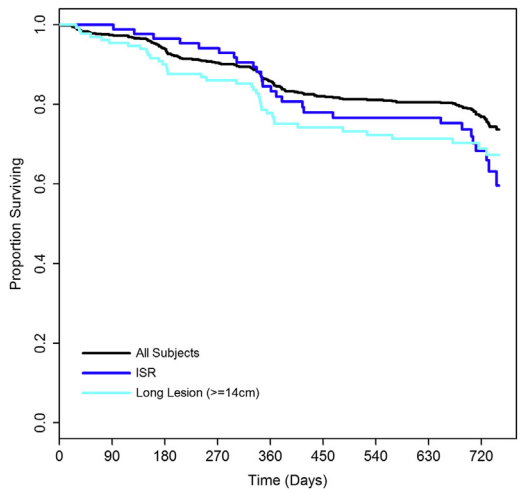
Values are Kaplan-Meier Estimates Survival, % (95% confidence interval).
Abbreviations as in Tables 1, 4, and 5.

FIGURE 1 Kaplan-Meier Curve for TLR-Free Survival Including Subgroups



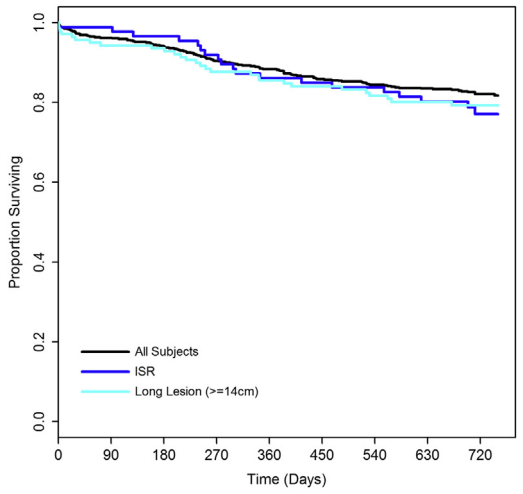
TLR-free survival shown for all patients, ISR, and long-lesion subgroups. The Kaplan-Meier estimate for TLR-free survival for all subjects was 94.1% at 12 months and 90.3% at 24 months. The Kaplan-Meier estimates for TLR-free survival at 12 and 24 months were 93.4% and 89.4% for long lesions, and 90.7% and 85.5% for ISR. ISR = in-stent restenosis; TLR = target lesion revascularization.

FIGURE 2 Kaplan-Meier Curve for Primary Patency Including Subgroups



Clinical primary patency reported for all patients, ISR, and long-lesion subgroups. The clinical primary patency rate for all patients by Kaplan-Meier estimates resulted in 85.4% for 12 months and 75.6%% at 24 months. The clinical primary patency rate by Kaplan-Meier estimates was 76.9% at 12 months and 67.3% at 24 months for long lesions. For ISR patients, the 12-month rate was 83.3% and 66.0% for 24 months. Abbreviations as in Figure 1.

FIGURE 3 Kaplan-Meier Curve for Freedom From Secondary Composite Endpoint Including Subgroups



Freedom from secondary safety composite endpoints reported for all patients, ISR, and long-lesion subgroups. Secondary safety composite endpoint was defined as freedom from composite of all-cause perioperative (<30 day) death and from index limb amputation, index limb reintervention, and index limb-related death at 12 and 24 months. Freedom from secondary safety composite endpoint by Kaplan-Meier estimates for 12 months was 88.4% and at 24 months was 82.1%. For the long-lesion subgroup freedom from secondary safety composite endpoint by Kaplan-Meier estimates at 12 and 24 months were 85.5% and 79.3%. For ISR the rates at 12 and 24 months were 86.1% and 77.1%. Abbreviations as in Figure 1.

events was 99.4% at 12 months and 99.3% at 24 months.

Freedom from the secondary safety composite endpoint by Kaplan-Meier estimates for the long lesion and ISR subgroups were similar to the global registry patients.

DISCUSSION

Numerous options are available for the treatment of femoropopliteal artery disease. This registry documents significant success of the Lutonix 035 DCB catheter in real-world use over 24 months, with a variety of lesion lengths and in patients with substantial comorbidities. Longer lesion lengths and ISR were intentionally included in the study. The study population consisted of patients with significant comorbidities including coronary artery disease (60.2%), dyslipidemia (70%), hypertension (84.9%), and diabetes (39.5%).

The DCB data provided safe and effective therapy for patients with regard to Rutherford category scale. Most patients were classified as Rutherford Classification 3 (66.9%) at baseline. From baseline to 24 months 47.3% of patients improved to Rutherford category 0 and 21.7% of patients shifted to Rutherford stage 1. At 24 months most (76.1%) of the subjects improved by at least 1 stage. Despite treatment of lesions up to 500 mm with the DCB, the rate of reintervention for thrombus was low.

This study, to date, is the first multicenter study to report 24-month outcomes for PAD patients treated with DCB in a prospective real world setting. Schmidt et al. (6) reported 24-month retrospective single center data on the use of DCB to treat PAD. Comparing this multicenter prospective study in real-world patients with a retrospective single-center study is not a feasible comparison because of the different study design, the mixed patient group, and different lesion lengths.

Pre-dilatation before treating with the Lutonix 035 DCB is in the IFU. However, because this is a real-world study, the physicians treated patients by standard of care. Pre-dilatation was performed in approximately 65% of the patients enrolled. Most of the patients (83.6%) with CTO were pre-dilated, but only 56.4% of the patients with stenotic lesions. No significant differences in the outcome were found, if no pre-dilatation occurred.

The DCB device procedural data showed an average inflation time of 108.1 ± 39.49 s, with an average pressure of 9.5 ± 2.16 atm. Average balloon to vessel ratio (inflated diameter/RVD) was 1.00 ± 0.09 resulting in an average diameter stenosis post-DCB of 14.6 ± 18.69%. Higher balloon pressures and balloon to vessel ratios were used to provide better balloon to tissue apposition and thus better delivery of drug. Balloon pressures used in this study were on average 9.5 atm, which was higher than nominal pressures of 6 to 8 atm. The use of bailout stents was at the discretion of the investigator. Lesion lengths up to 500 mm were treated in this study with a mean bailout stenting rate of 25.2%. Freedom from TLR was similar between subjects at 12 months with and without bailout stents, 92.8% and 93.6%, respectively. Indicating that stenting did not contribute to the observed freedom from TLR rates.

The data confirm that the Lutonix 035 DCB is an excellent option for treatment of PAD in a variety of lesions including long lesions and ISR and in patients with multiple comorbidities including extensive vascular disease.

STUDY LIMITATIONS. The trial was a prospective, multicenter, single-arm registry, and did not include a comparison control group. Rather, reference to past clinical experience was used as a point of comparison. Physicians enrolled patients for whom they believed the therapy would be appropriate, and the decision to enroll was not based on randomization or sequential patient identification. The study included patients seen in typical real-world clinical practice with a commercially available product used consistent with established IFU. The intent of this study was to evaluate the DCB outcomes in standard of care practice. Reporting the TLR outcomes are real-world results and were not adjusted by core laboratory review.

CONCLUSIONS

The Global SFA Registry 24-month outcomes confirm the Lutonix 035 DCB is a safe and effective treatment option in femoropopliteal lesions, with good long term results in real-world PAD patients, challenging comorbidities and difficult lesions (CTO and calcified). Benefit was also shown in patients with long lesions and ISR.

ADDRESS FOR CORRESPONDENCE: Dr. Marcus Thieme, Department of Angiology/Cardiology/Diabetology, Regiomed Vascular Center Sonneberg, Neustadter Strasse 61, 96515 Sonneberg, Germany. E-mail: marcus.thieme@medinos-kliniken.de.

PERSPECTIVES

WHAT IS KNOWN? The angioplasty of femoropopliteal arteries in PAD presents restenosis rates of 40% to 60% at 6 to 12 months. Data from recent studies document improvement in patency in patients receiving treatment with drug-coated balloons.

WHAT IS NEW? The Global SFA Registry assesses safety, clinical benefit, and outcomes of the Lutonix 035 DCB in femoropopliteal lesions in a heterogeneous, real-world patient population in 38 centers from 10 countries at 12 and 24 months. This study, to date, is the first multicenter study to report 24-month outcomes for PAD patients treated with DCB in a prospective real-world setting.

WHAT IS NEXT? The outcome confirms the Lutonix 035 DCB as a safe and effective long-term treatment option in PAD patients with femoropopliteal lesions, challenging comorbidities, and difficult lesions. Further studies are required to confirm these results and to clarify whether it is a group effect of DCBs, and the benefits of DCBs in below-the-knee-arteries.

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KEY WORDS amputation, angioplasty, drug-coated balloon, paclitaxel, peripheral artery disease, restenosis