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PERIPHERAL

2-Year Results With a Sirolimus-Eluting Self-Expanding Stent for Femoropopliteal Lesions

The First-in-Human ILLUMINA Study

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ABSTRACT

OBJECTIVES The aim of the study was to assess 24-month efficacy and safety of a novel drug-eluting stent (DES) for femoropopliteal interventions with an innovative stent design and abluminal reservoir technology releasing the amphilimus formulation (sirolimus plus fatty acid) for efficient drug transfer and optimized release kinetics.

BACKGROUND DES releasing paclitaxel exhibited good patency rates after femoropopliteal interventions. No benefit has been reported when sirolimus or everolimus were used for antiproliferative stent coating.

METHODS Within a multicenter, first-in-man, single-arm study, 100 patients with symptomatic femoropopliteal disease (Rutherford category 2-4, mean lesion length 5.8 ± 3.9 cm, 35.0% total occlusions) were treated with the NiTiDES stent (Alvimedica). Two-year follow-up included assessment of primary patency (defined as absence of clinically driven target lesion revascularization or binary restenosis with a peak systolic velocity ratio >2.4 by duplex ultrasound), safety, functional, and clinical outcomes.

RESULTS At 24 months, Kaplan-Meier estimates of primary patency and freedom from clinically driven target lesion revascularization were 83.4% (95% CI: 73.9%-89.6%) and 93.1% (95% CI: 85.3%-96.9%), respectively. Over the study period, 3 deaths were reported with no major limb amputation. Functional and clinical benefits were sustained, as 82.1% of patients fell into Rutherford category 0 or 1 at 24 months, which was associated with preserved improvements in all walking disability questionnaire scores.

CONCLUSIONS The 2-year results of the ILLUMINA (Innovative siroLimus seLf expanding drUg-eluting stent for the treatMent of perIpheral disease: evaluation of safety aNd efficAcy) study demonstrate a sustained treatment benefit with a novel sirolimus-eluting stent that also compares favorably to other femoropopliteal intervention trials. Head-to-head comparisons of NiTiDES with a paclitaxel-based DES are warranted. (The ILLUMINA Study [ILLUMINA]; NCT03510676) (J Am Coll Cardiol Intv 2022;15:618-626) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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For revascularization of symptomatic femoropopliteal lesions, endovascular interventions have become the preferred treatment option in most clinical situations, caused by its minimally invasive nature.[1] Acute interventional failure secondary to vessel dissection or elastic recoil has been successfully addressed by the introduction of bare-metal stents (BMS), but durability is still compromised by high rates of restenosis, particularly in long, complex lesions. Drug-eluting technologies have been developed to inhibit neointimal hyperplasia responsible for restenosis and reocclusion. Using paclitaxel as an antiproliferative agent, both drug-eluting stents (DES) and drug-coated balloons (DCBs) improved primary patency rates compared with plain old balloon angioplasty in randomized controlled clinical trials in short- and medium-length lesions.[2-4] To date, 2 DES using paclitaxel as antiproliferative drug, one with a polymer coating and one without, are available on the market for treatment of femoropopliteal lesions. In a head-to-head comparison, noninferiority criteria were met for the primary efficacy and safety endpoints, and subsequent analyses showed superiority for the polymer-coated DES with respect to primary patency after 12 and 24 months.[4,5] In contrast to coronary interventions, in which DES eluting the immunosuppressant drugs sirolimus and everolimus were highly effective in reducing neointimal proliferation leading to coronary restenosis, initial studies investigating sirolimus- and everolimus-eluting stents for femoropopliteal interventions failed to show a sustained benefit.[6,7] Importantly, in both studies, acceptable short-term results were counteracted by a subsequent rapid increase in restenosis rates. Possible explanations for the observed failure were the combination of the drug with a copolymer for coating, low drug dosage, inappropriate elution kinetics, or unfavorable characteristics of the stent platform.[8] Recently, the ongoing discussion on the safety of paclitaxel-based devices for femoropopliteal interventions with regard to a controversial mortality signal beyond 2 years[9] has renewed interest in sirolimus for peripheral interventions.

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The NiTiDES stent system (Alvimedica) represents a novel drug-eluting strategy, as it uses the amphilimus formulation, consisting of sirolimus formulated with an amphiphilic carrier (fatty acid), that is released through an abluminal reservoir technology from a BMS. The polymer-free platform is made of nitinol and covered with a second-generation pure carbon ultra-thin layer to increase hemocompatibility and biocompatibility.[10] The previously published 1-year outcomes of the first-in-human ILLUMINA (Innovative siroLimus seLf expanding drUg-eluting stent for the treatMent of perIpheral disease: evaluation of safety aNd efficAcy) study with a self-expanding NiTiDES stent for femoropopliteal interventions showed an excellent primary patency rate of 87% and a low clinically driven target lesion revascularization (CD-TLR) rate of 2%.[11] Presented here are the 2-year results.

ABBREVIATIONS AND ACRONYMS

ABI = ankle-brachial index
BMS = bare-metal stent(s)
CEC = clinical events committee
DCB = drug-coated balloon
DES = drug-eluting stent(s)
CD-TLR = clinically driven target lesion revascularization
WIQ = Walking Impairment Questionnaire

METHODS

STUDY DESIGN AND PARTICIPANTS. The ILLUMINA study was designed as a prospective, multicenter, single-arm study to assess efficacy and safety of the NiTiDES stent.

Patients with symptomatic ischemic obstruction of superficial femoral arteries or proximal popliteal arteries were enrolled in 10 centers in Germany, France, and Italy.

Enrolled patients had 1 or more (in tandem, with a distance between lesions ≤3 cm not exceeding the maximum lesion length) de novo or restenotic lesions of the above-the-knee femoropopliteal artery of one limb, meeting the general inclusion and exclusion criteria. Major inclusion criteria comprised Rutherford category 2 to 4 and resting ankle-brachial index (ABI) <0.9. Major exclusion criteria included lesions in the contralateral superficial femoral artery requiring intervention during the index procedure or within 30 days after the procedure and previous target vessel stenting. Angiographic criteria comprised lesion length ≤14 cm, >50% diameter stenosis, and at least 1 patent runoff vessel (<50% stenosis throughout its course).

The study was conducted in accordance with the Declaration of Helsinki, International Conference of Harmonization-Good Clinical Practices, and ISO

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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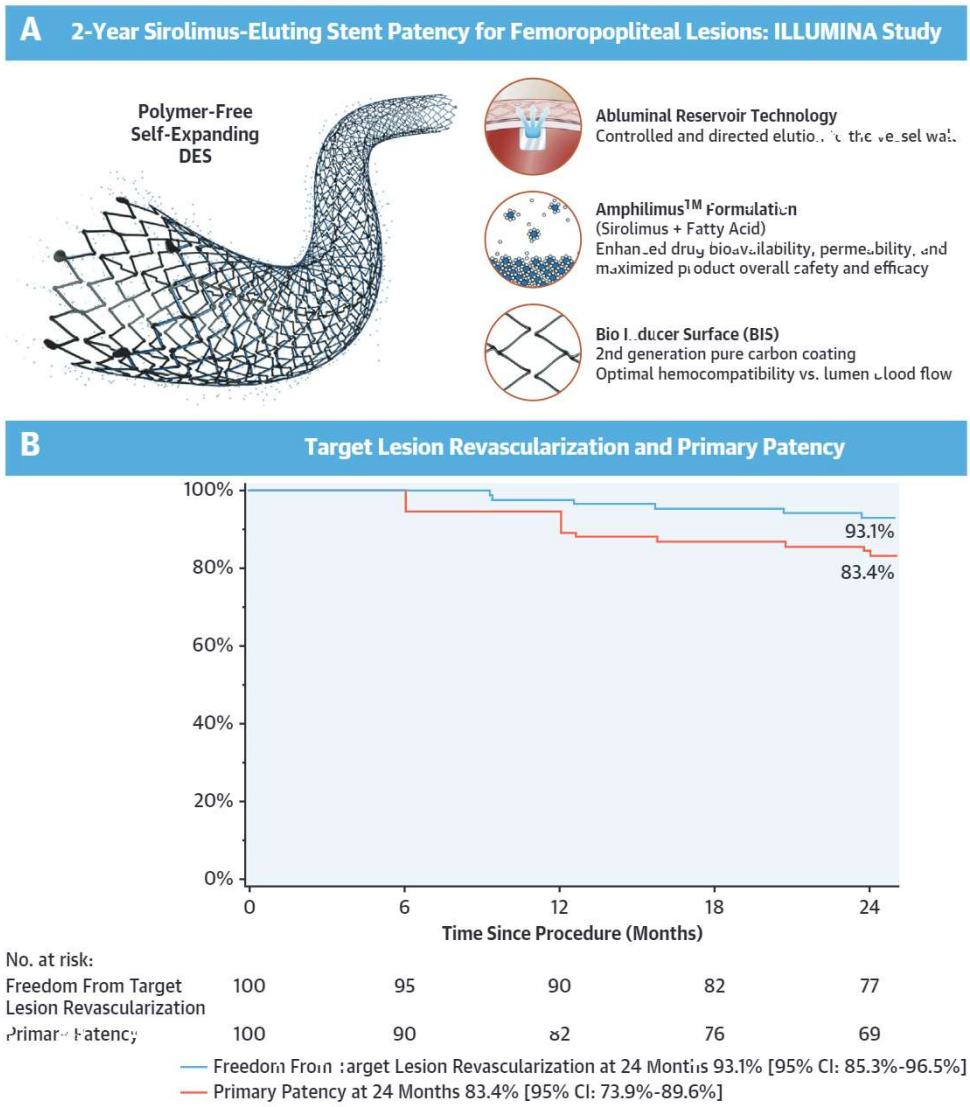
CENTRAL ILLUSTRATION **NiTiDES Stent for Femoropopliteal Disease: Design Characteristics and 2-Year Results**



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(A) Study device: drug-coating and -eluting properties of the NiTiDES stent. **(B)** 2-year survival curves for primary patency and freedom from clinically driven target lesion revascularization. DES = drug-eluting stent.

14155:2011. The protocol, informed consent form, and other study-specific documents were approved by each site's local ethics committee, and patients provided signed informed consent form before enrollment. A clinical trial registration was performed prospectively (NCT03510676).

The study was administrated and monitored by an independent clinical research organization (European Cardiovascular Research Center, Massy, France), overseeing clinical events committee and data safety monitoring board activities, data management, and statistical analysis. All endpoint-related adverse

TABLE 1 Baseline Patient Characteristics (N = 100)

Male	78 (78.0)
Age, y	67 ± 10
Body mass index, kg/m^2	26.74 ± 3.84
Smoker (active status)	39 (39.0)
Claudication (Rutherford class 2-3)	96 (96.0)
Critical limb ischemia (Rutherford class 4-5)	4 (4.0)
Ankle-brachial index	0.81 ± 0.13
Diabetes mellitus	35 (35.0)
Type 1	6 (17.1)
Type 2	29 (82.9)
No treatment	2 (5.7)
Controlled by diet	2 (5.7)
Oral treatment	21 (60.0)
Insulin	10 (28.6)
Hypercholesterolemia	54 (54.0)
Hypertension	69 (69.0)
Family history of cardiovascular disease	18 (18.0)
Renal disease	10 (10.0)
Cerebrovascular disease	13 (13.0)
Congestive heart failure	1 (1.0)
Myocardial infarction	9 (9.0)
Coronary artery disease	27 (27.0)

Values are n (%) or mean ± SD.

TABLE 2 Lesion and Procedural Characteristics (N = 100)

Lesion location	
Proximal SFA	8 (8.0)
Mid SFA	49 (49.0)
Distal SFA	38 (38.0)
Proximal popliteal artery	5 (5.0)
Lesion length, mm[a]	72.54 ± 37.99
Lesion length, mm[b]	57.49 ± 38.74
Percent diameter stenosis, %[a]	91.55 ± 8.94
Percent diameter stenosis, %[b]	84.32 ± 15.69
Total occlusions	35 (35.0)
Minimum lumen diameter, mm[a]	1.46 ± 2.36
Minimum lumen diameter, mm[b]	0.8 ± 0.8
Reference vessel diameter, mm[a]	5.72 ± 0.81
Reference vessel diameter, mm[b]	5.11 ± 0.72
Lesion calcification[a]	
None	25 (25.0)
Little	20 (20.0)
Moderate	35 (35.0)
Heavy	20 (20.0)
Lesion calcification according to PACSS (n = 93)[b]	
Grade 0 = none	10 (10.8)
Grade 1 = unilateral <5 cm	28 (30.1)
Grade 2 = unilateral ≥5 cm	0 (0)
Grade 3 = bilateral <5 cm	40 (43.0)
Grade 4 = bilateral ≥5 cm	15 (16.1)
Pre-dilatation	91 (91.0)
Stents/patient	1.09 ± 0.32
Total stent length, mm[a]	86.7 ± 40.8
Total stent length, mm[b]	92.01 ± 41.27
Post-dilatation	88 (88.0)
Maximum balloon diameter for post-dilatation, mm	5.62 ± 0.69
Post-procedural diameter stenosis, %[b]	17.96 ± 10.55
Device success[c]	100 (100.0)
Procedural success[d]	100 (100.0)

Values are n (%) or mean ± SD. [a]Visual estimation. [b]Core lab assessment. [c]Defined as successful delivery and deployment of the investigational stent(s, at the intended target lesion and final residual stenosis of the target lesion ≤30% assessed by visual estimation. [d]Defined as device success without the occurrence of major adverse events during the hospital stay.

PACSS = Peripheral Artery Calcification Scoring System; SFA = superficial femoral artery.

events were adjudicated by the independent clinical events committee (CEC), consisting of 2 vascular surgeons and 1 angiologist, to assess their relationship to the study procedure or device.

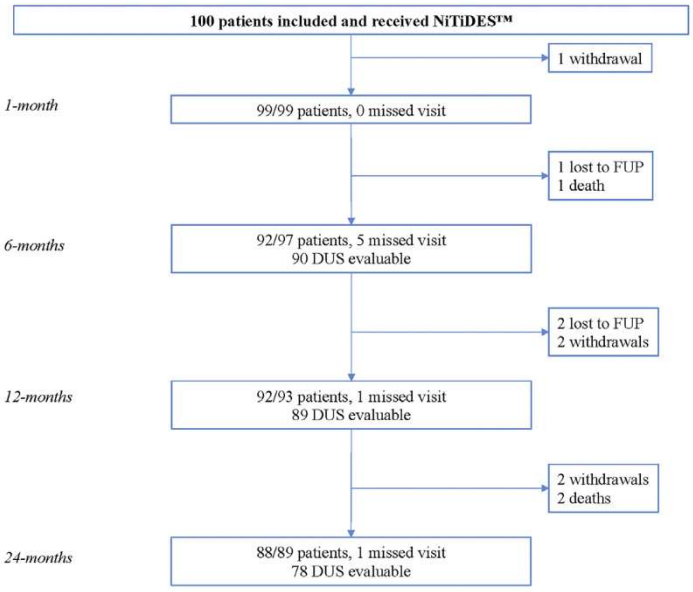
The data safety monitoring board comprised 3 independent members from the specialties of radiology, vascular surgery, and statistics. Angiographic and duplex ultrasound images were independently analyzed by a core laboratory (Core Lab Black Forest, Bad Krozingen, Germany).

STUDY DEVICE. The NiTiDES stent was developed by CID S.p.A. (member of Alvimedica Group). NiTiDES is a CE-certified, polymer-free self-expanding DES in nitinol alloy, loaded with the amphilimus formulation (sirolimus plus fatty acid) enhancing drug bioavailability (**Central Illustration**). The drug is contained within grooves (reservoirs) on the outer surface of the stent (Abluminal Reservoir Technology), and therefore it is eluted only toward the vessel wall, allowing a fast stent re-endothelialization. The entire structure, including the reservoirs, is homogeneously coated with an ultra-thin film of pure carbon (*i*-Carbofilm [Bio Inducer Surface]) in order to increase hemocompatibility and biocompatibility and ensure thromboresistance.

Available stent sizes for the ILLUMINA study included lengths of 20, 40, 60, 80, 100, 120, and 150 mm and diameters of 6, 7, and 8 mm.

INTERVENTIONS AND CONCOMITANT MEDICAL THERAPY. Rutherford classification, ABI, and Walking Impairment Questionnaire (WIQ)[12] were documented before the procedure. Vessel access was performed according to local practices. A bolus of 5,000 IU heparin was recommended for periprocedural anticoagulation. In case angiographic inclusion criteria were met and the guidewire successfully

FIGURE 1 Patient Flow Diagram



Patient flow through 24 months. DUS = duplex ultrasound; FU = follow up.

passed the lesion, the patient could be enrolled in the study. Pre-dilatation was mandatory using a standard balloon at least 0.5 mm smaller than the planned stent. Stents were placed to fully cover the lesion, and stent length had to exceed the target lesion length by10 mm (5 mm for each side). Post-dilatation was at the operator's discretion to achieve a residual stenosis <30%. The recommended antiplatelet regimen consisted of aspirin 325 mg/d and clopidogrel 300 mg (or ticlopidine 250 mg twice a day or prasugrel 60 mg) as a loading dose before the procedure. After the procedure, aspirin 100 mg/d should be administered indefinitely in conjunction with an adenosine diphosphate receptor antagonist (preferably clopidogrel 75 mg/d, or as an alternative. ticlopidine 250 mg twice a day or prasugrel 10 mg/d) for at least 2 months.

FOLLOW-UP AND ENDPOINTS. A phone call was scheduled at 1 month. At 6, 12, and 24 months after the procedure, an in-house visit was performed, including physical examination, evaluation of adverse events and pharmacological treatments, symptoms evaluation through Rutherford classification, ABI measurement at rest, WIQ completion, and ultrasound assessment of the target lesion.

The primary safety endpoint was the composite rate of CEC-adjudicated major adverse events including all-cause death, target limb amputation, target limb ischemia requiring surgical intervention or surgical repair of the target vessel, or CD-TLR (and worsening of the Rutherford score by 2 classes, or to class 5 or 6 at 12 months. CD-TLR was defined as a reintervention performed for ≥50% diameter stenosis (confirmed by angiography) within ±5 mm proximal or distal to the target lesion after documentation of recurrent clinical symptoms of peripheral artery disease following the initial procedure. The primary efficacy endpoint was primary patency defined as absence of CD-TLR or binary restenosis as indicated by a peak systolic velocity ratio >2.4 by duplex ultrasound core laboratory analysis at 12 months. Protocol prespecified secondary endpoints included CD-TLR, target limb major amputation, all-cause mortality, and changes in Rutherford classification and WIQ scores through 24 months. All data were 100% source identified.

STATISTICAL ANALYSIS. Outcomes were analyzed using the intention-to-treat population. Continuous variables are presented as mean ± SD; categorical variables are expressed as number and percentage. Comparisons between baseline and follow-up were performed using a 1-sample Student's *t*-test. For primary patency and CD-TLR, Kaplan-Meier curves through 24-month follow-up are given. All analyses were performed with SAS software (version 9.4, SAS Institute).

RESULTS

The ILLUMINA study enrolled 100 patients between January 26, 2016, and February 7, 2017. Key baseline characteristics and results through 12 months were previously reported.[11] Detailed patient characteristics are given in **Table 1**. The vast majority of patients presented with claudication, only 4.0% with ischemic rest pain. Lesion and procedural characteristics are shown in **Table 2**. Mean lesion length was 5.75 cm as assessed by the core laboratory, and more than one-half of the lesions were classified as grade 3 or 4 according to the Peripheral Artery Calcification Scoring System. Pre-dilatation was performed in 91.0% and post-dilatation in 88.0% of procedures. Patients were treated with 1.09 ± 0.32 NiTiDES stents (total mean stent length 92.01 ± 41.27 mm) as per core lab assessment. Device and procedural success were both 100%, with no patient exhibiting residual stenosis >30%.

The final 2-year visit was completed by 88 patients (**Figure 1**), and over the study course, 3 patients died,

TABLE 3 Efficacy Endpoints at 12 and 24 Months

	12 mo (n = 8J)	24 mo (n · 78,
Primary patency: standard definition Absence of clinically driven target lesion revascularization or binary restenosis; binary restenosis is defined as a peak systolic velocity ratio (PSVR) >2.4 by core lab evaluation	79 (88.8)	63 (80.9)
Primary patency: alternative definition Absence of clinically driven target lesion revascularization or binary restenosis; binary restenosis is defined as a PSVR >2.0 by core lab evaluation	78 (87.6)	60 (76.9)
Binary restenosis defined by PSVR >2.4[a]	8 (9.0)	9 (11.5)
Binary restenosis defined by PSVR >2.0[a]	9 (10.1)	12 (15.4)

Values are n (%). [a]2 patients had PSVR > 2.4 at 6 months and were submitted to target lesion revascularization at 12 months

PSVR = peak systolic velocity ratio.

TABLE 4 Safety Endpoints at 12 and 24 Months

	12 mo (n = 93)	24 mo (n = 90)
Safety endpoint: composite event-free survival[a]	90 (96.8)	79 (87.8)
Kaplan-Meier estimate (95% CI), %	95.7 (89.1-98.4)	87.7 (78.9-93.0)
Death	1 (1.1)	3 (3.3)
Target limb amputation	0 (0.0)	0 (0.0)
Target limb ischemia requiring surgical intervention or surgical repair of target vessel	0 (0.0)	1 (1.1)
Clinically driven TLR	2 (2.2)	6 (7.7)

Values are n (%), unless otherwise indicated. [a]Freedom from clinical events committee-adjudicated major adverse events (death, target limb amputation, target limb ischemia requiring surgical intervention or surgical repair of target vessel or clinically driven TLR) and freedom from worsening of the Rutherford score by 2 classes, or to class 5 or 6.

TLR = target lesion revascularization.

including 1 death caused by myocardial infarction after 5 months, 1 death caused by severe septic shock at 13 months, and 1 death caused by lung cancer at 17 months post-procedure. No death was considered a device- or procedure-related death by the CEC. Three patients were lost to follow-up and 5 patients withdrew consent over the study period.

EFFECTIVENESS, SAFETY, AND CLINICAL BENEFIT. At 12 and 24 months, Kaplan-Meier estimates of primary patency were 89.3% (95% CI: 81.0%-94.1%) and 83.4% (95% CI: 73.9%-89.6%), respectively (**Central Illustration**). Using an alternative cutoff for binary restenosis by duplex ultrasound (peak systolic velocity ratio >2.0 instead of peak systolic velocity ratio >2.4) had little impact on the observed absolute primary patency and binary restenosis rates through the 24-month follow-up (**Table 3**). Likewise, freedom from CD-TLR was over 90.0% through 24 months (**Central Illustration**), and repeat revascularization of the target lesion was performed in 6 patients in the study period after a median follow-up of 429 (interquartile range: 284-627) days (**Table 4**). One surgical repair of the target vessel was performed by thrombendarterectomy proximally from the target lesions in the common femoral artery at 18 months and was adjudicated as not device related by the CEC. In addition, 11 patients underwent non-target limb contralateral revascularization during the course of the study: 5 patients were treated in the first year after the index intervention, 6 patients in the second year, and 1 of these patients required both TLR and contralateral revascularization.

No target limb amputation occurred, and worsening of the Rutherford score by 2 classes or to class 5 or 6 was seen in 1 patient beyond 12 months after index intervention who was asymptomatic at 1 year follow-up but suffered a femoral fracture 5 months before the final visit.

Distribution of Rutherford clinical classification at baseline, 12 months, and 24 months is given in **Figure 2**. More than 80.0% of patients presented with no or minimal clinical symptoms, and in parallel, 86.9% reported an improved Rutherford clinical category compared with baseline at 24 months (**Table 5**).

Likewise, functional benefits were preserved over time, with significant improvements in all walking disability questionnaire scores as well as ABI measurements compared with baseline (**Table 5**).

DISCUSSION

The results of ILLUMINA trial showed that the use of the NiTiDES DES for the treatment of patients with symptomatic femoropopliteal lesions is safe and effective. The reassuring primary patency and freedom from TLR rates through 24 months of 83.4% and 93.1%, respectively, were paralleled by sustained clinical and functional improvements. Patient characteristics were in line with other recent trials in the field of femoropopliteal interventions using drug-eluting devices,[2-4] with treated lesions predominantly classified as TASC (Trans-Atlantic Inter-Society Consensus) II Document A and B and a maximum lesion length up to 14 cm. Importantly, chronic total occlusions as a relevant predictor for restenosis after femoropopliteal revascularizations[13,14] were treated in about one-third

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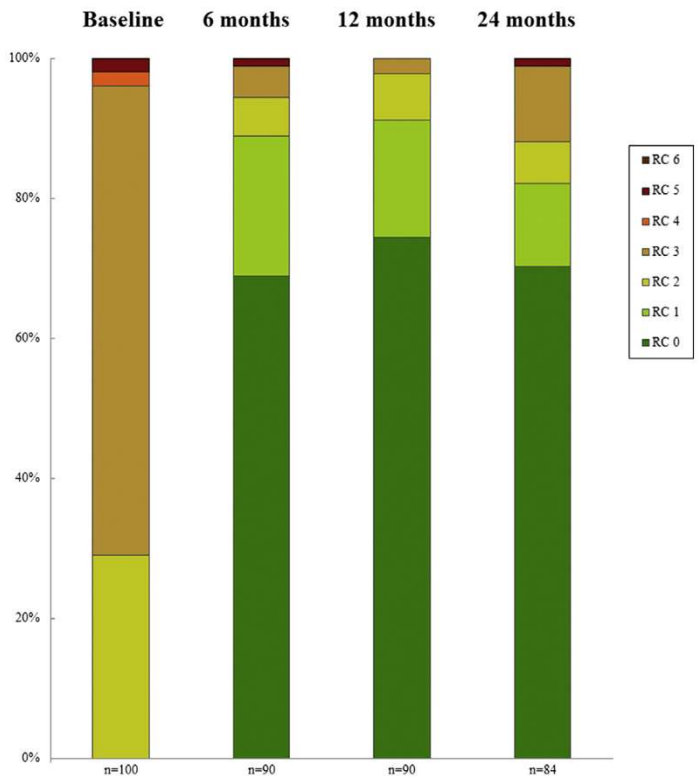
FIGURE 2 Distribution of RC at Baseline, 12 and 24-Months After Treatment of 100 Patients With Femoropopliteal Disease Using the NiTiDES Stent



The number at risk for each follow-up period is given **below each bar**. RC = Rutherford category.

of cases, and more than one-half of lesions exhibited extensive calcification according to Peripheral Artery Calcification Scoring System criteria. The observed primary patency rate of 83.4% in the ILLUMINA study compares well with other trials investigating DES for femoropopliteal interventions. In the recently published IMPERIAL (A Randomized Trial Comparing the ELUVIA™ Drug-eluting Stent Versus Zilver® PTX® Stent for Treatment of Superficial Femoral and/or Proximal Popliteal Arteries) trial comparing 2 paclitaxel-eluting stents, one with a polymer coating (Eluvia [Boston Scientific]) and one without (Zilver PTX [Cook Medical]), the primary patency rate was 83.0% for Eluvia and 77.1% for Zilver PTX after 24 months of follow-up.[5] In the BATTLE (Bare Metal Stent vs. Paclitaxel Eluting Stent in the Setting of Primary Stenting of Intermediate-Length Femoropopliteal Lesions) trial, a head-to-head randomized comparison of the Zilver PTX vs a BMS, patency rates of 78.8% and 74.6% were reported at 2 years for the DES and BMS, respectively.[15] The observed 6.9% CD-TLR rate in the ILLUMINA study after 2 years is also the lowest reported rate so far after femoropopliteal interventions. Thus, in the IMPERIAL trial 2-year CD-TLR rates were 12.7% and 20.1% for the aforementioned devices, and in the BATTLE trial, 2-year TLR rates were 12.4% and 14.4% for the DES and BMS, respectively.

As an alternative to DES, the use of DCBs improved patency and reduced CD-TLR compared with standard balloon angioplasty in short- and medium-length femoral lesions without the need of a permanent implant that would affect vascular vasomotion.[2] However, high provisional stenting rates up to 50% were reported for DCB use in long, complex lesions,[16] underscoring the continued need for the use of femoropopliteal stents. Keeping in mind the limitations of between trial comparisons with differences in characteristics of the included patients and lesions, the observed primary patency rate through 24 months ranged from about 64% to 90% in the intervention arms of recent DCB trials,[17-20] and thus the results from the ILLUMINA trial also fall at the high end of this range. So far, direct comparisons between DCBs and DES did not show superiority of a stent-based approach up to 3 years either.[14,21]

A prior trial investigating a sirolimus-eluting self-expanding stent for femoropopliteal lesions showed high restenosis rates after initially good results, indicating a catch-up phenomenon when compared with its bare-metal counterpart.[6,22] In contrast, the excellent 12-month results were sustained through 24-month in the ILLUMINA study. Importantly, the design of the NiTiDES stent is completely different and unique, as a novel elution technology has been developed combining abluminal drug-elution from dedicated reservoirs with a new antiproliferative drug formulation (sirolimus plus fatty acid) in order to optimize drug transfer into the vessel wall while minimizing systemic drug effect. The polymer-free concept is attractive, as chronic inflammation has been linked to the presence of durable polymers of coronary DES before.[23] The amphilimus drug formulation supports enhanced drug tissue permeation through utilizing fatty acid pathways,[24] which might be particularly beneficial in diabetics as an increased uptake of fatty acids has been described in diabetic cells. Importantly, prior studies suggested a relative ineffectiveness for restenosis inhibition by coronary DES eluting paclitaxel or mTOR inhibitors (-*limus* drugs) in diabetics, which could be overcome by the amphilimus formulation[24,25] and thereby contribute to the observed efficacy in the ILLUMINA study, with 35% of patients being diabetics.

The use of paclitaxel-eluting devices for endovascular femoropopliteal interventions is currently scrutinized by regulatory agencies after the publication of a meta-analysis of randomized controlled trials identifying a safety signal with increased mortality in patients undergoing interventions with paclitaxel-containing balloons and stents compared with noncoated devices.[26] In the light of these data, the NiTiDES stent may be an attractive candidate for an alternative drug-eluting device for femoropopliteal interventions without paclitaxel exposure.

STUDY LIMITATIONS. As the study was a single-arm, clinical trial, results should be confirmed in appropriately powered, randomized trials against clinically proven DES. So far, only lesions with moderate complexity were included, and the role of the NiTiDES DES for complex lesions has to be tested. Long-term follow-up is required to show durability and safety of the intervention.

CONCLUSIONS

The ILLUMINA study demonstrated promising primary patency and reassuring safety for treatment of symptomatic femoropopliteal lesions with the NiTiDES stent system using the amphilimus drug formulation through 24 months. The observed safety and efficacy outcomes of the ILLUMINA study represent excellent results after femoropopliteal interventions. Future studies directly comparing NiTiDES with other DES used in clinical routine are desirable.

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TABLE 5 Clinical and Functional Benefit

Improvement in Rutherford Clinical Classification			
	6 mo (n = 90)	12 mo (n = 90)	24 mo (n = 84)
Improvement by ≥2 classes	73 (81.1)	81 (90.0)	66 (78.6)
Improvement by 1 class	10 (11.1)	4 (4.4)	7 (8.3)
Unchanged	6 (6.7)	5 (5.5)	8 (9.5)
Worsening by 1 class	1 (1.1)	0 (0.0)	2 (2.4)
Worsening by ≥2 classes	0 (0.0)	0 (0.0)	1 (1.2)
Worsening to class 5-6	0 (0.0)	0 (0.0)	1 (1.2)

WIQ Scores				
	Baseline (n = 100)	6 mo (n = 90)	12 mo (n = 90)	24 mo (n = 84)
Pain severity	39.1 ± 27.5	82.5 ± 25.8[a]	82.8 ± 26.7[a]	83.4 ± 27.1[a]
Walking distance	35.8 ± 29.7	76.6 ± 34.0[a]	83.8 ± 30.2[a]	80.2 ± 32.6[a]
Walking speed	30.7 ± 22.6	53.5 ± 31.7[a]	56.7 ± 30.8[a]	57.9 ± 32.2[a]
Stair climbing	56.3 ± 32.5	76.1 ± 33.4[a]	78.4 ± 31.1[a]	75.4 ± 32.8[a]
Overall WIQ score	40.9 ± 13.5	68.7 ± 13.2[a]	72.9 ± 14.3[a]	71.2 ± 11.7[a]

ABI Measurements				
	Baseline (n = 100)	6 mo (n = 89)	12 mo (n = 89)	24 mo (n = 77)
Resting ABI	0.81 ± 0.13	0.95 ± 0.11[a]	0.94 ± 0.14[a]	0.92 ± 0.14[a]

Values are n (%) or mean ± SD. [a]$P < 0.0001$ against baseline.
ABI = ankle-brachial index; WIQ = Walking Impairment Questionnaire.

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PERSPECTIVES

WHAT IS KNOWN? Endovascular femoropopliteal interventions are increasingly performed worldwide, and significant advances in the treatment have been associated with improved patency rates. While the effectiveness of paclitaxel-containing balloons and stents has been demonstrated in several randomized controlled trials, the safety of these devices has been challenged by a recent meta-analysis identifying an increased mortality risk beyond 2 years after the procedure.

WHAT IS NEW? The first-in-human ILLUMINA study demonstrated an excellent primary patency and low reintervention rate through 2 years with the novel sirolimus-eluting NiTiDES stent.

WHAT IS NEXT? Additional research should directly compare NiTiDES with other DES used in clinical routine including also more complex lesions

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KEY WORDS drug-eluting stent(s), patency, peripheral vascular disease, sirolimus, superficial femoral artery disease