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Treatment of Femoropopliteal Lesions With the BioMimics 3D Vascular Stent System: Two-Year Results From the MIMICS-2 Trial

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Abstract

Purpose: To report the safety and effectiveness outcomes through 2 years of the BioMimics 3D Vascular Stent System in the treatment of symptomatic patients with atherosclerotic femoropopliteal disease. **Materials and Methods:** The tubular, nitinol BioMimics 3D stent, which was designed to impart a helical shape to the arterial segment, was implanted in 271 patients (mean age 68.4±9.5 years; 180 men) with de novo femoropopliteal lesions enrolled at 43 investigational sites [31 US (n=162), 6 German (n=78), and 6 Japanese (n=31)] in the prospective, single-arm MIMICS-2 investigational device exemption trial (*ClinicalTrials.gov* identifier NCT02400905) between June 2015 and October 2016. Mean lesion length was 81.2±38.4 mm, 30.0% of patients had total occlusions, and 45.9% had moderate to severe calcification. Primary safety and effectiveness endpoints were compared at 1 year with prespecified objective performance goals (OPGs) set by the VIVA Physicians organization. Outcomes through 2 years are reported. **Results:** The primary effectiveness endpoint of 12-month primary stent patency was met by 182 of 249 patients (73.1%, 95% CI 67.3% to 78.2%), exceeding the OPG of 66%. The primary safety endpoint of 30-day freedom from major adverse events (MAEs) was met in 268 of 269 patients (99.6%, 95% CI 97.7% to 100%), exceeding the OPG of 88%. Kaplan-Meier estimates of freedom from loss of primary patency were 83.1% at 12 months and 70.2% at 24 months, freedom from MAEs estimates were 86.9% at 12 months and 79.2% at 24 months, and freedom from clinically-driven target lesion revascularization estimates were 88.0% at 12 months and 83.0% at 24 months. At 24 months, 88.2% of patients showed improvement of ≥1 Rutherford category; the ankle-brachial index was >0.9 for 64.4% vs 11.3% at baseline. There were no cases of stent fracture. **Conclusion:** Through 24 months, the BioMimics 3D Vascular Stent System provided safe and effective treatment for femoropopliteal lesions in patients with symptomatic peripheral artery disease.

Keywords

ankle-brachial index, femoropopliteal lesions, major adverse events, nitinol stents, objective performance goal, peripheral artery disease, stent patency, superficial femoral artery, target lesion revascularization

Introduction

Stents deployed in the femoropopliteal arterial segment are subjected to compression, flexion, extension, torsion, and pulsatile distension, suggesting the potential benefit of longitudinal device flexibility.[1,2] The inability of long and/or multiple overlapping straight stent segments to shorten or take up the slack during the thigh contraction and knee flexion involved in motion is conducive to considerable strains, kinking, and fatigue fractures.[3,4] The nonplanar curvature of the aortoiliac arteries promotes a laminar swirling flow pattern in the blood. When sustained in the superficial femoral

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artery (SFA), the swirling flow elevates wall shear stress on endothelial cells, increasing diffusion of oxygen to the arterial wall, and protecting against the development of atherosclerosis and restenosis.[5,6] It is now understood that this natural antirestenotic effect can be jeopardized by the implantation of a straight stent into the already relatively straight SFA, since the increased incidence of atherosclerosis and neointimal hyperplasia (NIH) in regions of low shear stress has been confirmed in adult humans.[5,6]

The BioMimics 3D Vascular Stent System (BioMimics 3D stent) (Veryan Medical Ltd, Horsham, UK) was designed to impart a helical shape to the arterial segment and thereby sustain and promote laminar swirling flow to generate an antirestenotic and atheroprotective elevation in wall shear stress. In the prospective, multicenter, randomized MIMICS trial,[7] 2-year freedom from loss of primary patency was significantly greater following primary stenting with the BioMimics 3D stent vs a control straight stent (88% vs 71%, p=0.05), and there was a significant advantage for the swirling flow stent in freedom from clinically-driven target lesion revascularization (CDTLR) (p=0.03) between 12 and 24 months following implantation. The BioMimics 3D stent received Conformité Européenne marking in November 2012, US Food and Drug Administration (FDA) premarket approval in October 2018, and Shonin approval by the Japanese Pharmaceuticals and Medical Device Agency (PMDA) in December 2019.

The purpose of the MIMICS-2 trial was (1) to evaluate the safety and effectiveness of the BioMimics 3D swirling flow stent in a larger patient population than the original randomized controlled trial[7] (RCT) and (2) to prospectively compare the performance of the swirling flow stent against the established objective performance goals (OPGs) for stent treatment of femoropopliteal lesions. This report presents results through 2 years from the MIMICS-2 trial to further characterize the performance of the BioMimics 3D swirling flow stent as a primary treatment modality of symptomatic peripheral artery disease (PAD) in the femoropopliteal segment.

Materials and Methods

Study Design

The single-arm, prospective, multicenter MIMICS-2 trial was conducted under a US FDA investigational device exemption (IDE) and with the approval of the Japanese PMDA under the US-Japan Medical Device Harmonization by Doing initiative. The MIMICS-2 trial enrolled patients at 43 sites in the US, Germany, and Japan (Supplementary Table 1; available in the online version of the article). The trial used OPGs and endpoint assessments for femoropopliteal stents recommended by VIVA Physicians, Inc.[8] Key inclusion and exclusion criteria for the trial are summarized in Table 1.

Table 1. Patient Enrollment Criteria.

Key inclusion criteria
Age >18 and ≤85 years
Rutherford clinical categories 2 to 4
Peripheral artery disease documentation alternatives
Resting ABI ≤0.90
ABI ≤0.75 after exercise of the target limb
Toe-brachial index <0.70 when ABI not possible
Angiographic or duplex ultrasound evidence of ≥60% diameter stenosis when ABI normal
Angiographic criteria
Target lesion location ≥1 cm distal to the origin of the deep femoral artery and ≥3 cm above the bottom of the femur
Target lesion reference vessel diameter between 4.0 and 6.0 mm
Target lesion length ≥40 to ≤140 mm
Diameter stenosis ≥60%
Patent popliteal artery distal to the treated segment
At least 1 patent infrapopliteal artery with runoff to the ankle
Key exclusion criteria
Known or suspected infection
Contraindications to antiplatelet, anticoagulant, or thrombolytic therapies
Acute or chronic renal disease
Any comorbidity that would limit life expectancy to <36 months
Prior treatment of the target vessel with any type of surgical or endovascular procedure

Abbreviation: ABI, ankle-brachial index.

The trial was sponsored by Veryan Medical. The protocol was approved by all appropriate institutional review boards, and all patients provided written informed consent. Clinlogix LLC (Lower Gwynedd, PA, USA) provided independent monitoring at all study sites, while Veryan undertook all data management using an electronic data capture system from Datatrak International (Mayfield Heights, OH, USA). An independent Clinical Events Committee (CEC) adjudicated all safety events. Yale Cardiovascular Research Group (New Haven, CT, USA) was the angiographic and radiography core laboratory and VasCore (Boston, MA, USA) adjudicated the duplex ultrasound images. The MIMICS-2 trial was registered on the National Institutes of Health website (*ClinicalTrials.gov* identifier NCT02400905).

Study Device and Interventions

The self-expanding BioMimics 3D stent is laser-cut from a nitinol tube, setting a 3D helical geometry into the alloy's shape memory (Figure 1). The strut pattern of the stent, with short and long connectors between the crowns, promotes flexibility while still retaining sufficient curvature within the nitinol shape memory to impart helical shape to

Figure 1. The BioMimics 3D swirling flow stent (Veryan Medical, Horsham, UK).

the stented segment, even when it is moderately to severely calcified, thereby inducing swirling flow in the SFA. The stent ends are formed to be collinear with the adjacent vessel segments, and the final 3 crowns at each end have gradually decreasing radial force to avoid restenosis caused by flow disturbance at the stent ends. Three radiopaque tantalum markers at each end of the stent facilitate accurate deployment. The BioMimics 3D stent is mounted on a 6-F over-the-wire delivery system for use with a 0.035-inch guidewire; the stent is indicated for treatment of lesions up to 140 mm in length in reference vessels ranging from 3.5 to 6.0 mm in diameter.

All patients underwent qualifying angiography. Patients not already on aspirin or clopidogrel therapy received a minimum loading dose of 75 mg of aspirin and a minimum loading dose of 300 mg of clopidogrel or a similar antiplatelet agent within 24 hours of the index procedure. After the index procedure, patients were instructed to continue 75 mg of aspirin per day indefinitely and 75 mg of clopidogrel per day for a minimum of 30 days. Pre- and postdilation with standard balloon angioplasty were mandatory, and the duration and pressure were left to physician discretion. No other pretreatment therapies were permitted. Implantation of a second study stent was allowed as necessary, with overlap ≤10 mm, but no more than 2 study stents and no other commercially available stents were permitted under the protocol. Adjunctive use of drug-coated balloons was not permitted.

Patient Population

From June 2015 to October 2016, the 43 investigational sites enrolled 271 patients (mean age 68.4±9.5 years; 180 men): 162 at the 31 US sites, 78 at the 6 German sites, and 31 at the 6 Japanese sites. Key baseline patient and lesion characteristics are summarized in Tables 2 and 3, respectively. Almost half of the patients (45.4%) were diabetic,

Table 2. Baseline Demographics and Clinical Characteristics of the 271 Patients in the Study.[a]

Age, y	68.4±9.5
Men	180/271 (66.4)
Race	
Asian	31/271 (11.4)
Black or African American	16/271 (5.9)
White	215/271 (79.3)
Other	1/271 (0.4)
Refuse to disclose	8/271 (3.0)
Body mass index, kg/m^2	28.1±5.5 (n=271)
Diabetes mellitus	123/271 (45.4)
Hypertension	244/271 (90.0)
Hypercholesterolemia	222/271 (81.9)
History of smoking	219/271 (80.8)
Previous myocardial infarction	50/271 (18.5)
Previous PCI	91/271 (33.6)
Previous CABG	56/271 (20.7)
Previous lower limb intervention	98/271 (36.2)
Rutherford category	
2	73/271 (26.9)
3	183/271 (67.5)
4	14/271 (5.2)
5	1/271 (0.4)
ABI per target limb	0.7±0.2 (n=257)

Abbreviations: ABI, ankle-brachial index; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.
[a]Continuous data are presented as the means ± standard deviation; categorical data are given as the counts/sample (percentage).

Table 3. Baseline Lesion Characteristics by Quantitative Vascular Angiography.[a,b]

Proximal lesion boundary[c]	
Proximal SFA	65/271 (24.0)
Mid SFA	130/271 (48.0)
Distal SFA	73/271 (26.9)
Proximal popliteal	3/271 (1.1)
Reference vessel diameter, mm[c]	5.4±0.6 (n=271)
Lesion length, mm	81.2±38.4 (n=269)
MLD, mm	1.1±1.0 (n=270)
Diameter stenosis by visual estimate, %	77.8±18.3 (n=269)
Total occlusion	81/270 (30.0)
Calcification	
None/mild	146/270 (54.1)
Moderate	84/270 (31.1)
Severe	40/270 (14.8)
Tibial vessel runoff <50% stenosed	237/240 (98.8)
Thrombus	10/270 (3.7)

Abbreviations: MLD, minimum lumen diameter; SFA, superficial femoral artery.
[a]Continuous data are presented as the means ± standard deviation; categorical data are given as the counts/sample (percentage).
[b]Except where indicated, values are those reported by the trial core laboratory.
[c]Values for this category are those reported by trial sites.

and most (90.0%) had hypertension. All lesions were de novo. The mean lesion length was 81.2±38.4 mm; 30.0% (81/270) of patients had total occlusions, and 45.9% (124/270) had >5-cm unilateral (grade 2) or bilateral (grade 4) calcification according to the Peripheral Arterial Calcium Scoring System.[9]

Study Follow-up and Endpoints

Scheduled follow-up at 30 days (±7 days), 12 months (365±30 days), and 24 months (730±60 days) included physical examination [Rutherford category, ankle-brachial index (ABI) or toe-brachial index, and review of symptoms], the Walking Improvement Questionnaire (WIQ), duplex ultrasound, and assessment of adverse events. At 12, 24, and 36 months, radiographs on the target limb in extension were scheduled to detect stent fracture.

The primary safety endpoint was a composite of major adverse events (MAEs) comprising death, any major amputation performed on the index limb, and CDTLR through 30 days. The primary effectiveness outcome was core laboratory–determined 12-month primary stent patency. Secondary outcomes included technical success, clinical and functional outcomes at 1, 12, and 24 months, and individual safety endpoints including the severity of adverse events and their relationship to the procedure or the device and severe adverse events (SAEs) at 1, 12, and 24 months. All outcome measures are defined in Table 4.

Table 4. MIMICS-2 Trial Endpoints.

Primary endpoints
Primary safety endpoint: Composite of death, any major amputation on the index limb, and CDTLR through 30 days (MAEs).
Primary effectiveness endpoint: Core laboratory–determined 12-month primary stent patency defined as no significant reduction in lumen diameter, assessed by duplex ultrasound (PSVR >2.0) OR angiography (≥50% diameter stenosis) OR occurrence of CDTLR, defined as either:
(1) revascularization of the target lesion with objective evidence of recurrent symptoms associated with an angiographic determination of ≥50% stenosis and new distal ischemic signs (worsening ABI or Rutherford category) associated with the index limb, or
(2) ≥70% diameter stenosis in the absence of objective evidence of recurrent symptoms.
Secondary endpoints
Technical success: achievement of ≤50% residual diameter stenosis at the index procedure.
Clinical outcome at 30 days and 12 and 24 months as determined by changes in Rutherford category and the 6-Minute Walk Test.
Functional outcome at 30 days and 12 and 24 months as determined by changes in the ABI and the Walking Impairment Questionnaire.
All individual safety endpoints including CDTLR and CDTVR, death, and index limb ischemia or amputation at 30 days and 12, 24, and 36 months.
Rating of adverse events for severity and relationship to the device or procedure.
Determination of SAEs
Stent integrity, ie, freedom from stent fracture (determined by core laboratory examination of radiographs taken with the leg in extension at 12, 24, and 36 months).

Abbreviations: ABI, ankle-brachial index; CDTLR, clinically-driven target lesion revascularization; CDTVR, clinically-driven target vessel revascularization; MAEs, major adverse events; PSVR, peak systolic velocity ratio; SAEs, serious adverse events.

Statistical Analysis

Descriptive data were presented as the mean ± standard deviation for continuous data and the count (percentage) for categorical variables. Confidence intervals (CIs) were set at 95%. Primary and secondary outcomes were assessed using an intention-to-treat (ITT) analysis set that included all enrolled patients since no procedure was aborted due to non-deployment of the stent.

Sample size estimation for the MIMICS-2 trial was based on the OPGs of the VIVA Physicians, Inc.[8] and the results of the MIMICS RCT of the BioMimics 3D stent.[7] The primary safety objective was to demonstrate that the 30-day freedom from MAEs with the BioMimics 3D stent exceeded the VIVA OPG of 88%.[8] Success on the primary safety endpoint required that lower bound of the 1-sided 97.5% Agresti-Coull confidence limit be >88% for the proportion of patients treated with the study device who were free from MAEs through 30 days. The primary effectiveness objective was to determine that the 12-month rate of primary stent patency with the BioMimics 3D stent was statistically superior to the 66% VIVA OPG for bare nitinol stenting.[8] In order to statistically power both primary outcome measures at the same time with an 85% power to detect superiority for the primary effectiveness outcome, a target sample size of 230 patients was determined for the time period of 12 months. At this sample size, the power to detect superiority for the primary safety endpoint was >99%.

Freedom from CDTLR, clinically-driven target vessel revascularization, and MAEs were estimated using Kaplan-Meier analysis. The threshold of statistical significance was $p<0.05$ (2-sided). All analyses were performed using SAS (version 9.4 or higher; SAS Institute Inc, Cary, NC, USA).

Results

Procedural Results and Patient Disposition

Technical success was achieved in all patients whose baseline angiograms were reviewed by the core laboratory

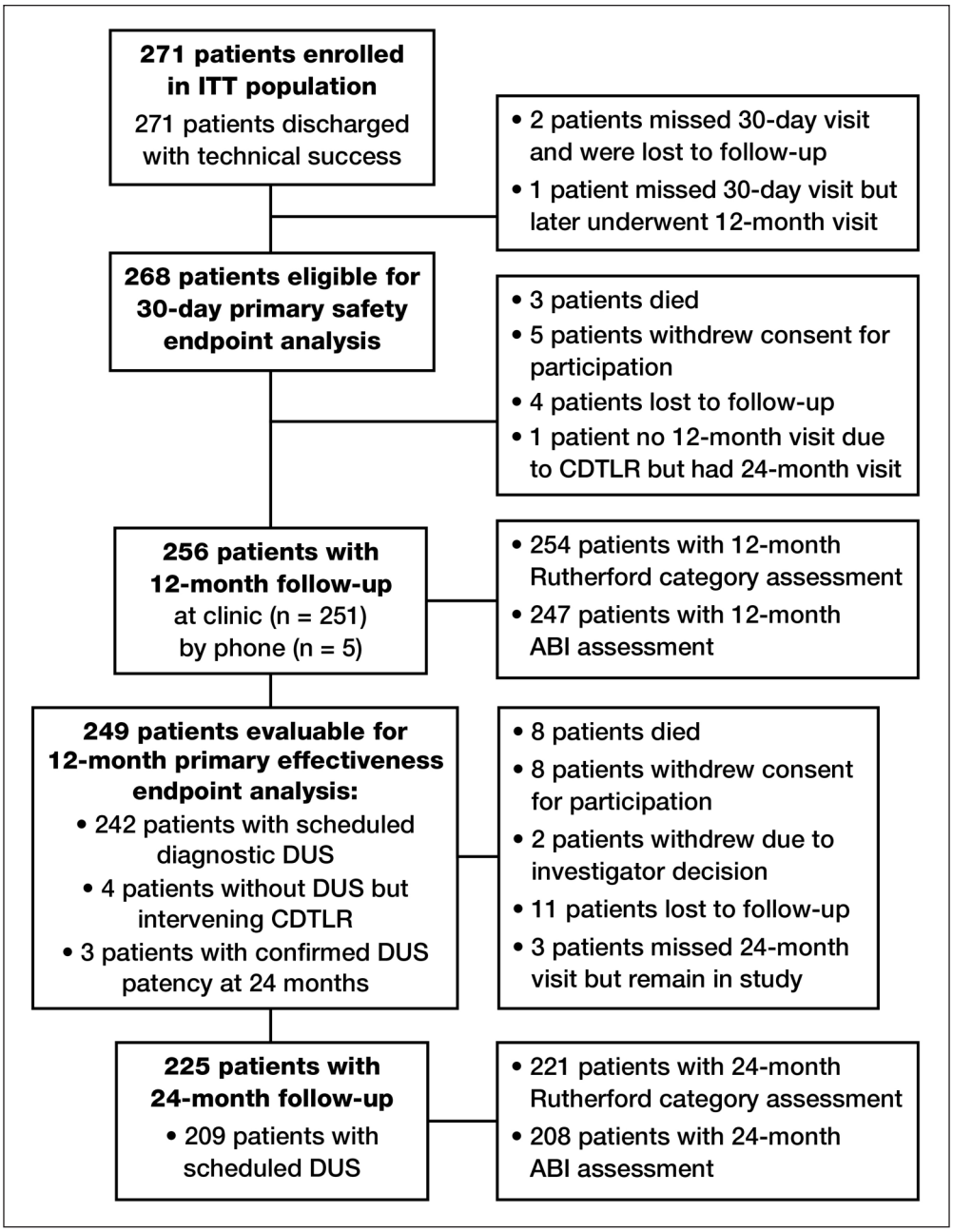

Figure 2. Patient disposition in the MIMICS-2 trial. ABI, ankle-brachial index; CDTLR, clinically-driven target lesion revascularization; DUS, duplex ultrasound; ITT, intention-to-treat.

(n=269). A total of 305 study devices were implanted in the 271 patients, with 1 stent implanted in 237 of 271 patients (87.5%) and 2 stents (overlapping) implanted in 34 (12.5%). No patient required more than 2 stents. The mean stented length was 112.3±36.3 mm overall (mean 105.1±31.8 mm in the 235 patients receiving single stents, mean 162.2±23.8 mm in the 34 patients with overlapping stents). In 22 of the 34 cases with stent overlapping, the second stent was required for a lesion ≤140 mm in length because 150-mm stents became available at approximately the midpoint in study enrollment.

Patient disposition through 24 months in the MIMICS-2 trial is summarized in Figure 2. Of the 271 patients enrolled, 3 missed the 30-day follow-up, leaving 268 patients eligible for the 30-day primary safety endpoint analysis. Through 12 months, 3 patients had died, 5 had withdrawn their consent to participate, and 6 were lost to follow-up. Of the total of 256 patients who underwent 12-month follow-up (Figure

Table 5. Primary Safety and Efficacy Endpoints.

Primary Endpoints	Rate	95% CI	VIVA OPG[a]
Safety: Freedom from MAEs at 30 days	99.6% (268/269)	97.7% to 100%	88%
Effectiveness: Primary stent patency at 12 months	73.1% (182/249)	67.3% to 78.2%	66%

Abbreviations: CI, confidence interval; MAEs, major adverse events; OPG, objective performance goal; VIVA, VIVA Physicians, Inc.
[a]Based on the lower bound of the 1-sided 97.5% Agresti-Coull confidence limit.

2), 249 were evaluable for the 12-month effectiveness analysis based on the availability of qualifying duplex ultrasound data, intervening CEC-adjudicated CDTLR, or (in 3 cases) already confirmed duplex ultrasound patency at 24 months, fulfilling the statistical requirement for a minimum of 230 evaluable patients.

Between 12 and 24 months, 8 patients died, 8 more withdrew consent, 2 were withdrawn by the investigator, 11 more were lost to follow-up, and 3 did not attend the 24-month visit, leaving 225 patients; duplex ultrasound imaging from the 24-month follow-up visit was available for 209 patients.

Through 24 months, 204 of 225 patients (90.7%) were compliant with the chronic aspirin therapy. Per protocol, clopidogrel or other antiplatelet medication was required only for 30 days, at which time 236 of 268 patients (88.1%) were compliant. At 24 months, 104 of 225 patients (46.2%) remained on clopidogrel or other antiplatelet medication.

Primary Endpoint Results

The results for the primary safety and effectiveness outcomes are summarized in Table 5. The primary safety outcome of freedom from MAEs at 30 days was reached by 268 of 269 patients (99.6%, 95% CI 97.7% to 100%). One patient underwent CDTLR (deployment of a drug-coated balloon and a drug-eluting stent) after abrupt closure of the treated segment 3 days after the index procedure. This patient completed the 30-day and 12-month follow-up visits but not the 24-month visit. After missing the 36-month visit, the patient was considered to be lost to follow-up. The lower bound of the 1-sided 97.5% Agresti-Coull confidence limit for the proportion of patients treated with the BioMimics 3D stent who were free from MAEs through 30 days was 97.7%, exceeding the endpoint-defined VIVA OPG of 88%. The MIMICS-2 primary safety outcome was therefore met.

The primary effectiveness outcome of primary stent patency at 12 months was met by 182 of 249 patients (73.1%, 95% CI 67.3% to 78.2%). The lower bound of the 1-sided 97.5% Agresti-Coull confidence limit for the proportion of patients treated with the BioMimics 3D stent who had stented segment patency through 12 months was 67.3%, exceeding the endpoint-defined VIVA OPG of 66%. The MIMICS-2 primary effectiveness outcome was therefore met. In 32 of 249 patients (12.9%), primary stent patency was determined to have been lost through intervening CDTLR.

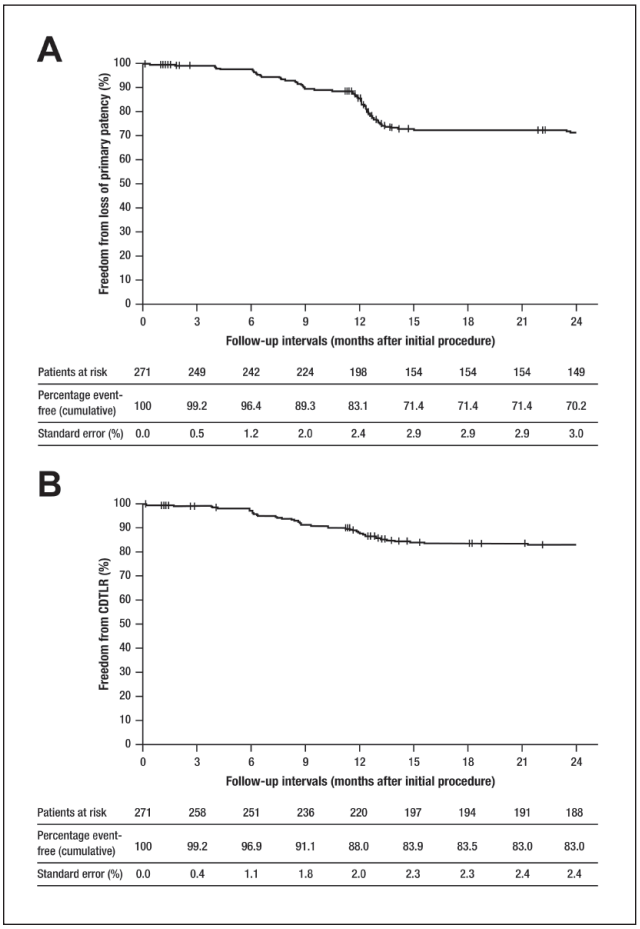

Figure 3. Kaplan-Meier survival analyses of freedom from loss of (A) primary patency and (B) clinically-driven target lesion revascularization (CDTLR) through 24 months (day 720) following implantation of the BioMimics 3D swirling flow stent.

The Kaplan-Meier estimates of freedom from loss of primary patency (Figure 3A) were 83.1% (95% CI 78.5% to 87.8%) at 12 months (day 360) and 70.2% (95% CI 64.4% to 76.1%) at 24 months (day 720).

Secondary Endpoint Results

Safety-related clinical outcomes through 24 months of follow-up are summarized in Table 6. The overall incidences

Table 6. Summary of CEC-Adjudicated MAEs Through 24 Months.[a]

Event	30 Days	12 Months	24 Months
MAEs[b]	1/269 (0.4)	35/261 (13.4)	54/243 (22.2)
Death	0/269 (0)	3/260 (1.2)	11/239 (4.6)
Cardiovascular	0/269 (0)	2/259 (0.8)	6/235 (2.6)
Noncardiovascular	0/269 (0)	1/259 (0.4)	5/233 (2.1)
Major target limb amputation	0/269 (0)	0/258 (0)	0/229 (0)
CDTLR	1/269 (0.4)	32/259 (12.4)	43/233 (18.5)
Objective evidence[c]	1/269 (0.4)	29/259 (11.2)	40/233 (17.2)
≥70% Stenosis	0/269 (0)	5/258 (1.9)	6/229 (2.6)

Abbreviations: CDTLR, clinically-driven target lesion revascularization; CEC, Clinical Events Committee; MAEs, major adverse events.
[a]Data are given as the counts/sample (percentage).
[b]MAEs were death, major amputation of the target limb, and CDTLR.
[c]Objective evidence of CDTLR was defined as recurrent symptoms associated with an angiographic determination of ≥50% stenosis and new distal ischemic signs (such as worsening of Rutherford category) associated with the index limb.

of MAEs were 0.4% (1/269) at 30 days, 13.4% (35/261) at 12 months, and 22.2% (54/243) at 24 months. Through 24 months, there were 11 deaths and no major target limb amputations. Up to 12 months, 1 death was due to metastatic disease, and 2 deaths were due to heart failure. Between 12 and 24 months, 3 deaths were due to cardiac arrest, 1 death was due to coronary artery disease, 2 deaths were due to chronic obstructive pulmonary disease, 1 death was due to pneumonia, and 1 was due to acute pancreatitis.

Overall, through 24 months, there were 46 (14.4%) device-related site-reported SAEs, and there were 27 (8.9%) procedure-related site-reported SAEs. There were 15 in-hospital SAEs in 13 patients, none of which were adjudicated as being related to the study device.

The Kaplan-Meier estimates of freedom from MAEs were 86.9% (95% CI 82.8% to 91.0%) at 12 months (day 360) and 79.2% (95% CI 74.2% to 84.2%) at 24 months (day 720). The Kaplan-Meier estimates of freedom from CEC-adjudicated CDTLR were 88.0% (95% CI 84.0% to 92.0%) at 12 months and 83.0% (95% CI 78.4% to 87.7%) at 24 months (Figure 3B).

Changes in Clinical and Functional Outcome Measures

The changes from baseline to 24 months in Rutherford category are summarized in Figure 4. At baseline, the majority of patients suffered from moderate intermittent claudication (category 2, 26.9%) or severe claudication (category 3, 67.5%); 5.2% had rest pain (category 4), and 0.4% had tissue loss (category 5). There was an improvement of ≥1 category for 86.9% of patients at 30 days, 85.0% of patients at 12 months, and 88.2% of patients at 24 months. At 24 months, almost two-thirds of patients (65.2%, 144/221) had an improvement of ≥2 categories, and more than one-third (37.6%, 83/221) had an improvement of ≥3 categories. At 24 months, there were 7 patients for whom Rutherford categories worsened compared with baseline; of these patients, 4 experienced worsening in both the treated and the non-treated legs.

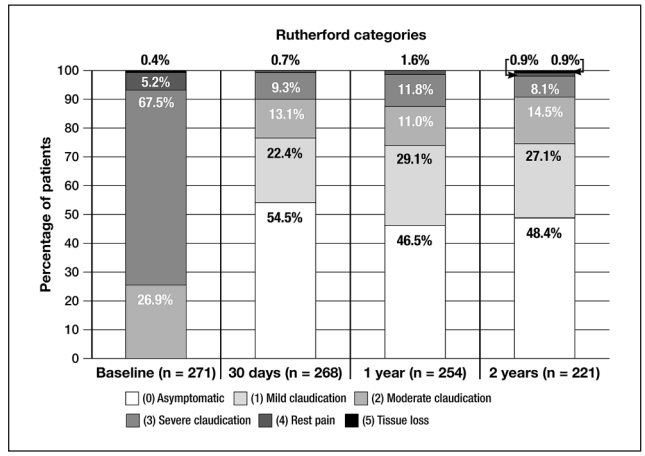

Figure 4. Changes in Rutherford category classification from baseline through 24 months.

Mean ABI improved from 0.70±0.2 at baseline (n=257) to 0.98±0.16 at 30 days (n=263). Improvement was then maintained at 12 months (0.92±0.19, n=247) and at 24 months (0.94±0.20, n=208). At baseline, 11.3% of patients had an ABI assessment of >0.9; at 24 months, 64.4% of patients had an ABI assessment of >0.9 (Table 7).

Using a matched baseline comparison, there was a mean improvement in the overall WIQ score of 0.30±0.30 at 30 days (n=259), 0.29±0.30 at 12 months (n=248), and 0.26±0.28 at 24 months (n=215). From 30 days through 24 months, there was sustained improvement in all the component WIQ categories, walking distance, walking speed, and stair climbing.

Stent Fracture

Through 24 months postimplant, with radiography assessment performed by the core laboratory in 204 of 271

Table 7. Changes in Target Limb Ankle-Brachial Index (ABI).[a]

ABI	Before Procedure	30 Days	12 Months	24 Months
≤0.4	8/257 (3.1)	0/263 (0)	3/247 (1.2)	1/208 (0.5)
>0.4 to ≤0.9	220/257 (85.6)	74/263 (28.1)	100/247 (40.5)	73/208 (35.1)
>0.9	29/257 (11.3)	189/263 (71.9)	144/247 (58.3)	134/208 (64.4)

[a]Data are given as the counts/sample (percentage).

patients (75.3%), there were no detected cases of stent fracture.

Discussion

Based on the MIMICS-2 trial outcomes through 2 years, the BioMimics 3D stent provided safe and effective treatment of femoropopliteal lesions in patients with symptomatic PAD. Both the safety and effectiveness outcomes of primary stent patency through 12 months exceeded the prespecified OPGs. In this patient population at high risk for cardiovascular events, the incidences of MAEs and CDTLR were acceptable at 2 years, with no major target limb amputations and sustained clinical improvement.

Granted the difficulty inherent in such comparisons, the 83.1% rate of freedom from loss of primary patency at 12 months for the BioMimics 3D swirling flow stent is similar to values reported in other recent trials of bare metal stents in the femoropopliteal segment. The 12-month freedom from loss of primary patency was 77.2% for the Protégé Everflex,[10] 81.3% for the LifeStent FlexStar and FlexStar XL,[11] 81.7% for the S.M.A.R.T. stent,[12] 86.3% for the Supera interwoven nitinol stent,[13] and 82.9% for the Misago self-expanding nitinol bare metal stent.[14]

In the MIMICS RCT, there were no cases of CDTLR between 12 and 24 months: freedom from CDTLR was 91.0% at 12 months and 91.0% at 24 months.[7] In the current IDE study, a flattening of the CDTLR Kaplan-Meier curve was also observed beginning at 12 months: freedom from CDTLR was 88.0% at 12 months and 83.0% at 24 months. In both trials, these results occurred in treatment of relatively complex lesions: moderate or severe calcification was present in 52% of the patients receiving the helical centerline stent in the MIMICS RCT (mean lesion length of 65.8 mm) and 45.9% of the MIMICS-2 trial patients (mean lesion length of 81.2 mm). The 24-month freedom from CDTLR estimate of 83.0% for the helical centerline stent can be compared (again with caution) with the rates reported for drug-eluting devices to provide some context about the value of swirling flow induced by the BioMimics 3D stent. For the polymer-free, paclitaxel-eluting Zilver PTX, 24-month freedom from CDTLR was reported as 86.6%.[15] For the polymer- and paclitaxel-coated Eluvia stent, the 24-month freedom from CDTLR was reported as 92.8%.[16] In a study of the paclitaxel-coated IN.PACT Admiral balloon, the 24-month freedom from CDTLR was 91.0%.[17]

In this IDE study, core laboratory review of radiographic imaging concluded that there was no evidence of stent fracture for the helical centerline stent through 24 months. For other nitinol stents, reported 12-month rates of stent fracture were 0.4% for the Protégé Everflex,[10] 3.1% for the LifeStent FlexStar and FlexStar XL,[11] 2.0% for the S.M.A.R.T. stent,[12] 0% for the Supera stent,[13] and 0.5% for the Misago stent.[14] There were no cases of stent fracture for the helical centerline stent through 24 months in the MIMICS RCT.[18]

The design concept of the BioMimics 3D stent has been described elsewhere, as have the post hoc computational fluid dynamic analyses from the MIMICS RCT that measured wall shear stress associated with the swirling flow stent vs a straight nitinol stent.[18] Because the SFA is a long, relatively straight vessel, it is exposed to low wall shear stress under resting conditions, predisposing it to atherosclerotic disease and confounding the healing process after endovascular injury.[19] Conventional straight stents further straighten the vessel and disturb blood flow, creating areas of low wall shear stress, a phenomenon associated with the NIH cascade.[5,20,21] The strategy of elevating wall shear stress by promoting swirling flow and thereby limiting the intervention-activated NIH cascade could be used as an alternative to the deployment of drug-eluting stents or employed as a complementary strategy along with use of drug-coated balloons for the femoropopliteal segment.

Limitations

MIMICS-2 is an IDE trial with endpoints accepted by the FDA for comparison with those from other trials of bare nitinol stents. While customary and considered acceptable for such IDE evaluations of new devices in which the expected outcomes are framed in terms of similar patient eligibility criteria, baseline angiographic lesion characteristics, endpoint structure, and clinical and imaging follow-up methodology, the single-arm nonrandomized design is more susceptible to bias than an RCT.

Conclusion

In this multicenter international IDE study, the BioMimics 3D Vascular Stent System achieved the prespecified 12-month OPGs and was safe and effective as primary treatment of

occlusive femoropopliteal lesions in patients with symptomatic PAD through 24 months, confirming the outcomes of the MIMICS RCT. In both the MIMICS and the MIMICS-2 trials, there were no cases of stent fracture. The prospective observational MIMICS-3D registry is evaluating the swirling flow stent in a real-world clinical population, with enrollment of more than 500 patients and with a dedicated subgroup analysis of device performance as a complementary treatment in procedures involving drug-coated balloons.

Authors' Note

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Supplemental Material

Supplemental material for this article is available online.

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