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Long-term outcomes of hydrodynamic ultra-thin strut sirolimus-eluting stent with fluoropolymer containing triflusal: VELAZQUEZ-EPIC26 study

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ABSTRACT

Background: A new-generation coronary sirolimus eluting-stent(SES), whose novel characteristics are summarized in ultra-thin oval-shaped hydrodynamic struts (68 μm) and abluminal drug release with permanent fluoropolymer containing the platelet aggregation inhibitor triflusal, showed low target lesion failure(TLF) and absence of stent thrombosis(ST) at 1 year in a first-in-human study. Long-term clinical efficacy is unknown. We aim to investigate long-term clinical efficacy of this new SES in a real-world population undergoing PCI for native coronary artery.

Methods: VELAZQUEZ-EPIC26 is a prospective, observational and multicentre study of a large cohort undergoing PCI with the new SES (ihtDESTiny™). Primary endpoint was TLF at 2 years (composite of cardiovascular death, target vessel myocardial infarction, or clinically driven target lesion revascularization). Secondary clinical safety and efficacy endpoints included definitive or probable ST, target vessel failure (TVF), major adverse cardiac events (MACE), and BARC 3–5 bleeding.

Abbreviations: PCI, percutaneous coronary intervention; DES, drug eluting stents; DAPT, dual antiplatelet therapy; OAC, oral anticoagulation; TLF, target lesion failure; ST, stent thrombosis; SES, sirolimus-eluting stents; MI, myocardial infarction; ACS, acute coronary syndrome.

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Results: Between 2021 and 2023, 406 patients (mean age 65 ± 11 years, 75 % males, 26 % diabetes) were included. 519 SES were implanted over 482 target lesions. Mean stent diameter and length were 3.03 ± 0.49 mm and 22 ± 7,6 mm respectively. Procedural success rate was 97.3 %. TLF at 2 years was 2,2 % (n = 9). There were 3 cardiovascular deaths (0,7 %), none related to SES complications. 1 very late definite stent thrombosis was reported (0,2 %, n = 1). TVF, MACE and BARC 3–5 bleeding rates at years were 3 % (n = 12), 3,2 % (n = 13) and 3,5 % (n = 14) respectively.

Conclusions: In a large real-world population undergoing PCI for native coronary artery, a new hydrodynamic ultra-thin strut SES with abluminal permanent fluoropolymer containing triflusal shows low TLF and very low ST rates at 2 years.

1. Introduction

Percutaneous coronary intervention (PCI) with drug eluting stents (DES) is the most common coronary revascularization technique worldwide. It is recommended, if indicated, for any clinical scenario irrespective of clinical presentation, lesion type, anticipated duration of dual antiplatelet therapy (DAPT) or concomitant oral anticoagulation (OAC) therapy [1]. Since DES introduction into routine clinical practice, iterative refinements have been made to platform designs, strut thickness, different antiproliferative drugs and drug-carrier polymer conformation (from biocompatibility to reabsorption, or even absence) in order to improve long-term clinical outcomes. Consequently, newer-generation DES have demonstrated greater efficacy and safety, achieving a consistently lower rate of target lesion failure (TLF) through reductions in stent-related events such as restenosis, repeat revascularization, myocardial infarction or stent thrombosis (ST). However, mid-term outcomes have remained stable despite technical improvements, with TLF and ST rates of approximately 5–10 % and 1 %, respectively, at 1 year [2].

General comparisons among antiproliferative drugs, polymers or platform designs are difficult to interpret because these characteristics are all combined in the various new-generation DES currently available. However, current data suggest that there are no significant differences between sirolimus-eluting DES (SES) and other analogue drugs, or between biodegradable and permanent polymer-based DES [3]. Nevertheless, SES are associated with a lower tendency toward TLF and myocardial infarction (MI), and DES with ultra-thin struts (<70 μm) are associated with a significant reduction in TLF at the expense of a reduced risk of MI [4,5].

The ihtDESTiny™ stent consists of an ultrathin and oval-shaped hydrodynamic strut in a cobalt-chromium platform, and abluminal sirolimus release from a permanent fluoropolymer containing the platelet aggregation inhibitor triflusal. The mid-term endothelization pattern of this new SES was studied using optical coherence tomography in a first-in-human study. The platform was highly effective in limiting neointimal proliferation (late lumen loss of 0.11 mm and binary restenosis rate of 1.6 %), with low proportion of uncovered or malapposed struts (2.5 % and 1.1 % respectively), and absence of subclinical thrombi. At 12 months, target lesion revascularization rate was 3 % and no stent thrombosis was reported [6].

We conducted a study to investigate the long-term clinical efficacy and outcomes of this new SES platform in a broad real-world patient population undergoing PCI for native coronary artery in daily practice.

2. Methods

VELAZQUEZ-EPIC26 was a prospective, observational and multicentre study of a large cohort of patients with significant coronary stenosis treated with ihtDESTiny™ stent undergoing long-term (2 years) clinical follow-up.

2.1. Patient population

Patients with coronary artery disease and clinical indication for elective or urgent PCI in 19 academic hospitals in 2 countries (Spain and Portugal) were eligible for enrolment under the following selection criteria.

Inclusion criteria: a) Patients older than 18 years of age eligible for PCI (according to European clinical practice guidelines on myocardial revascularization) [1]. b) Implantation of at least 1, or multiple, ihtDESTiny™ stents over de novo significant coronary lesions with a reference vessel diameter between 2 mm and 4 mm in diameter (no limitations according to lesion length, or number of lesions/vessels treated). c) Patients who were adequately informed about the study and provided written informed consent to participate.

Exclusion criteria: a) PCI with a different DES during the same procedure, or within 30 days before or after the procedure. b) PCI for in-stent restenosis or bypass graft stenosis. c) PCI for patients presenting Killip 3–4 acute coronary syndrome (ACS) or cardiogenic shock. d) Patients who are intolerant to dual antiplatelet therapy (DAPT), or who cannot complete DAPT for 3 months, or 6 months in case of ACS. e) Patients undergoing planned surgery (whether cardiac or not) 3 months after PCI. f) Patients with contraindications or hypersensitivity to sirolimus. g) Female patients in gestational age. h) Patients whose life expectancy is <2 years.

All procedures were performed in accordance with relevant laws and institutional guidelines. The study was approved by the clinical research committees of each participating institution. All patients provided informed consent to participate in the study.

2.2. Device description

The ihtDESTiny™ stent (IBERHOSPITEX S.A., Barcelona, Spain) is an open-cell ultrathin cobalt-chromium sirolimus eluting stent (0.9 μg/mm^2) with an oval-shape hydrodynamic strut with a thickness of 68 μm (EndoBoost®, Fig. 1). The stent geometry is based in offset mid-strut connectors arranged in an helicoidal pattern to balance radial strength and longitudinal stability. The strut oval structure is accomplished by using a 4-axis laser cutting stent system and a special electropolishing system. The coating consists of an abluminal dual layer (base plus barrier layer) with a biostable permanent fluoropolymer (BA-co-THEMA) containing the platelet aggregation inhibitor triflusal. Available diameters range from 2.0 to 4.0 mm and available lengths range from 8 to 40 mm.

2.3. Procedure

PCI was performed based on routine clinical practice: plaque preparation techniques, use of intravascular imaging, and optimization of the result with post-dilatation were all at the operator's discretion. Length and diameter of the stents should be selected through visual estimation or quantitative assessment. The selected stent length should guarantee complete lesion coverage. If more than 1 stent was needed, 1 mm to 2 mm of overlapping was recommended. For PCI involving bifurcation lesions, a single stent strategy (provisional stenting technique) was advised. Staged procedures within 30 days following the index PCI were permitted.

Anticoagulation with unfractionated heparin, bivalirudin, or low-molecular-weight heparin, with or without a glycoprotein IIb/IIIa inhibitor, was prescribed according to local standards. Before the procedure, all patients received DAPT with aspirin and P2Y12 inhibitor (clopidogrel, ticagrelor, or prasugrel) at recommended doses, at the operator's discretion. For patients in an acute setting who were not receiving chronic aspirin or P2Y12 inhibitor therapy, an oral loading dose should be administered according to the product label. DAPT was mandatory for a minimum of 3 months (or 6 months after ACS). In cases of concomitant OAC therapy, DAPT was recommended for at least 1 week. Using the High Bleeding

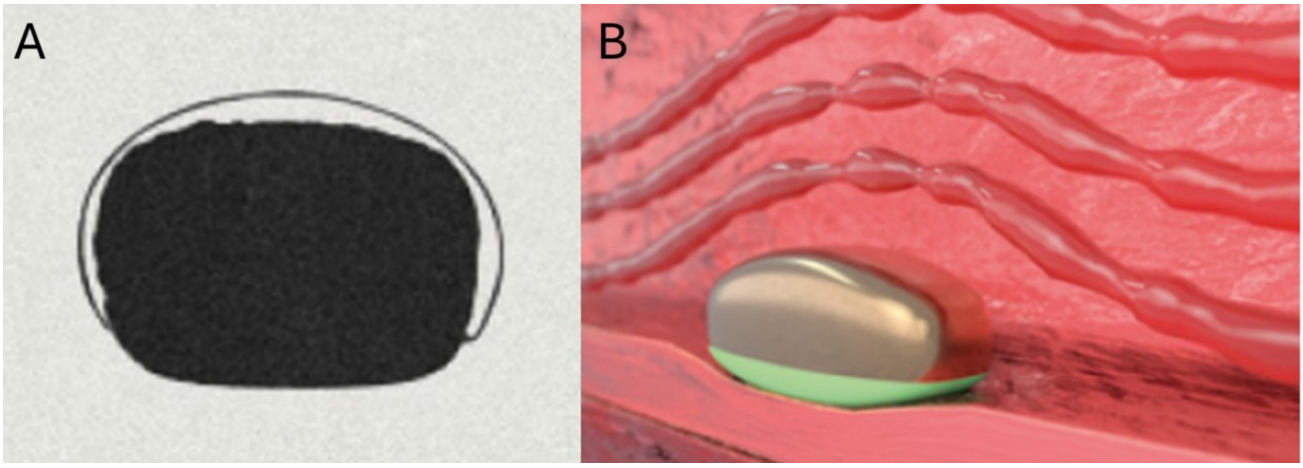

Fig. 1. EndoBoost® Technology: A) Scanning electron-microscopy showing the cross-section of the streamlined oval-shaped hydrodynamic struts. B) Hypothetical effect of the strut on coronary flow, minimizing flow recirculation zones and preserving endothelial shear stress.

Risk (HBR) criteria or PRECISE-DAPT score to guide DAPT duration was encouraged [7,8].

2.4. Data collection and follow-up

All patient data, both baseline and follow-up, were collected in an electronic database designed specifically for the study in which guaranteed complete anonymization of the data. Data collected included patient's clinical and laboratory profiles, cardiovascular medications, angiographic lesions characteristics and PCI procedures and results. Quantitative coronary angiography (QCA) measurements were recommended for evaluating lesions and results. Based on daily clinical practice, cardiac enzyme measurements were protocolized in case of ACS, or when data suggested periprocedural MI according to the operator's judgement.

Events were assessed during hospital stays, and at 1 year and 2 years (± 45 days) after index PCI through outpatient clinical visits or telephone contact. Local investigators evaluated and reported clinical events, which were then adjudicated by the 2 principal investigators after they monitored the provided clinical data. All study endpoints were defined based on standardized consensus criteria established by the Academic Research Consortium-2 (ARC-2) [9]. A Contract Research Organization (EPIC) oversaw the monitoring process.

This study is registered with ClinicalTrials.gov under the number NCT04899141.

2.5. Endpoints and definitions

The primary endpoint was target lesion failure at 2 years, defined as the composite of cardiovascular death, target vessel myocardial infarction, or clinically driven target lesion revascularization (presence of restenosis with FFR values ≤ 0.80 or iFR values ≤ 0.89, QCA > 70 % or QCA > 50 % with ischemic signs or a positive vessel-dependent stress-induced myocardial ischemia test).

Secondary clinical safety and efficacy endpoints included definitive or probable ST according to ARC-2 criteria, target vessel failure (TVF, composite endpoint of cardiovascular death, target vessel MI o target vessel revascularization), major adverse cardiac events (MACE, composite endpoint of cardiovascular death, any MI or any stroke), patient-oriented composite endpoint (POCE, composite endpoint of all-cause death, any MI, any revascularization or any stroke), the individual components of the composite endpoints, and BARC 3 to 5 bleeding rate. Any death due to any proximate cardiac cause, unwitnessed death, or death of unknown cause was considered as cardiovascular death.

Device success was defined as final diameter stenosis <30 %, with TIMI grade 3 flow and without residual dissection ≥ C (NHLBI Classification). Procedural success was defined as device success and uneventful stent implantation (absence of periprocedural MI, perforation, emergency cardiac surgery or death) or repeated unplanned revascularization within the first 3 days after stent implantation.

Planned staged PCI within 30 days for lesions present at the time of index PCI was not considered as repeated or new revascularization. It was adequately registered in a form specifically designed for the electronic database. For patients treated with staged PCI, the follow-up calendar began on the date of the index PCI.

Periprocedural myocardial infarction was defined as absolute increased troponin levels ≥ 35 with respect to the upper reference limit within the first 48 h after the PCI followed by the appearance of: a) sudden closure of the main vessel (TIMI grade 0 flow, including cases with basal TIMI grade 0 flow and TIMI grade 2–3 flow achieved during PCI); b) loss of a lateral branch (>1.5 mm, TIMI grade 0–1 flow after PCI with TIMI grade 2–3 flow before PCI); c) embolization (sudden distal closure of the target vessel); d) new Q-waves in electrocardiogram; e) significant myocardial loss on imaging modalities [9].

2.6. Statistical analysis and sample size

The sample size was estimated based on the following premises: a) In a real-life registry of new-generation ultra-thin SES (and bioresorbable polymer), TLF rate was 8.1 % at 2-year follow-up [10]. b) In a large study treating native coronary artery lesions, the most validated stable fluoropolymer everolimus-eluting stent showed a TLF rate of 6.3 % at 2-year follow-up [11]. In clinical trials comparing DES, the most common inferiority margin typically ranges from 1.5 % to 3 % for the primary endpoint, which is usually TLF at a certain follow-up period (1 or 2 years). The hypothesis is that the ihtDEStiny™ is not inferior to the most validated ultra-thin, stable polymer-based or sirolimus DES. Assuming a TLF 7 % at 2 years for the most validated DES and a TFL < 10 % for the ihtDEStiny™, and a non-inferiority margin of 3 % along with a one-sided type I error rate of 0.025 and a statistical power of 80 %, the estimated required sample size for each arm in a comparative study would be 364 patients. Considering a 10 % loss to follow-up, a final sample size of 401 patients is deemed appropriate for assessing the efficacy and safety of the ihtDEStiny™ stent.

A statistical analysis was conducted using SPSS 21.0. Descriptive statistics are presented, with continuous variables expressed as mean ± standard deviation, and categorical variables reported as absolute and relative frequencies. Event incidence will be expressed as a cumulative incidence rate at the end of follow-up period. Event-free survival, defined as the time from stent implantation to the occurrence of the primary end-point event, was assessed using the Kaplan-Meier method.

3. Results

A total of 411 patients were recruited between November 15, 2021, and May 12, 2023. 6 patients were excluded for meeting exclusion criteria or for having duplicated registrations due to staged procedures (Fig. 2). Finally, 405 patients were included in the study, with 519 stents implanted in 482 target lesions. Baseline patient characteristics are shown in Table 1 and are consistent with daily clinical practice. Patients were, on average, 65 years of age, and approximately one-quarter had diabetes mellitus. ACS was the most common PCI indication (ST elevation ACS in 25 % of patients). Only 10 % of patients presented HBR, but one-quarter of patients had a high PRECISE-DAPT score > 25.

Table 2 shows the coronary anatomic features, PCI characteristics and immediate results. Half of the lesions were complex (B2/C), but high-risk PCI was rare (CTO or 2-stent bifurcations). The prevalence of calcified or tortuous lesions was 25 %. Three-quarters of the lesions received predilatation, and half received post-dilatation. Mean stent size and length were compatible with large vessels (3 mm and 22 mm respectively), with a total length of 28 mm implanted. 7,9 % of patients (n:32) received overlapping stents. In summary, most patients presented with and were treated for one-vessel coronary artery disease (73,3 % and 88,4 % respectively), and PCI was performed in 1 lesion (83,7 %) with a single stent (93,5 %, n:482). 22 patients (5,4 %) underwent staged PCI.

Device and procedural success rates were 97,9 % and 97,3 % respectively. Final TIMI 2 flow was observed in 8 patients and 2 lesions presented residual stenosis > 30 % (both in the same patient). 2 patients experienced coronary perforation following stent post-dilatation (Ellis types I and III). The patient with type III perforation experienced periprocedural MI due to side branch occlusion after covered-stent implantation. No additional periprocedural MIs were reported. No patients required emergency surgery or died during the procedure. There were no reports of repeated revascularization within the first 3 days.

Clinical outcomes are presented in Table 3. 2 patients died during the index PCI hospital stay, due to myocardial free-wall rupture after MI and severe BARC 5b gastrointestinal bleeding. One patient lost follow-up after the first year due to moving to another country. 6 patients (1,5 %, n:405) and 9 patients (2,2 %, n:404) met the primary endpoint of target lesion failure at 1 and 2 years, respectively. Fig. 3 shows a Kaplan-Meier plot of the cumulative incidence of target lesion failure. Only 1 very late definite stent thrombosis was reported, following voluntary aspirin discontinuation. All 3 cardiovascular deaths occurred in the first year, but none were related to stent (one was due to myocardial rupture, and 2 due to acute heart failure without target vessel ischemia). One same patient underwent consecutive non-target vessel revascularizations, none of which resulted in myocardial infarction.

Adherence to DAPT and OAC were 50,4 % (n:204) and 9,3 % (n:38) at 1 year, and 11,1 % (n:45) and 11,3 % (n:46) at 2 years, respectively. During the first year of follow-up, 7 patients experienced unplanned DAPT interruptions (2 major surgeries, and 5 significant bleeding) without events. By the end of follow-up 5 patients had discontinued antiplatelet therapy. BARC 3–5 bleeding occurred more frequently during the first year, on

Table 1
Baseline clinical characteristics. Data are n (%) or mean ± SD.

Clinical characteristics	Patients N = 405
Age, years	65 ± 11
Hypertension	260 (64,2 %)
Dyslipidemia	231 (57 %)
Diabetes mellitus	106 (26,2 %)
Insulin-requiring	17 (4,2 %)
Current smoker	124 (30,6 %)
Renal disease (GF < 60 ml/min)	56 (13,8 %)
Previous myocardial infarction	48 (11,9 %)
Previous PCI	56 (13,8 %)
Previous CABG	3 (0,7 %)
Atrial fibrillation	22 (5,4 %)
Oral anticoagulation	25 (6,2 %)
DOAC	11 (2,7 %)
AVK	14 (3,5 %)
High Bleeding Risk	42 (10,4 %)
PRECISE-DAPT	18 ± 11
PRECISE-DAPT > 25	105 (25,9 %)
LVEF (%)	54 ± 10
Clinical presentation	
Stable angina	74 (18,3 %)
Unstable angina	47 (11,6 %)
Non-STEMI	155 (38,3 %)
STEMI	105 (25,9 %)
Heart failure/other	24 (5,9 %)

Abbreviations. GF: glomerular filtration. PCI: percutaneous coronary intervention. CABG: coronary artery bypass grafts. DOAC: direct oral anticoagulant. AVK: anti-vitamin K anticoagulant. LVEF: left ventricular ejection fraction. STEMI: ST elevation myocardial infarction.

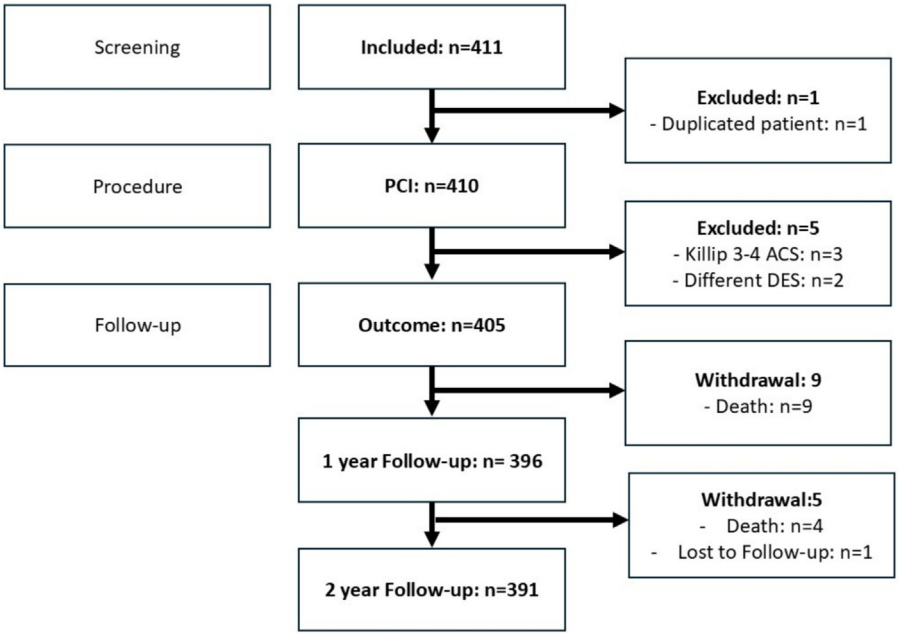

Fig. 2. Flow chart of the study.

Table 2
Angiographic characteristics, PCI characteristics and results. Data are n (%) or mean ± SD.

	Patients N = 405[a] Lesions *N* = 482
Angiographic characteristics	
Number of vessels diseased[a]	
1	297 (73,3 %)
2	86 (21,2 %)
3	22 (5,4 %)
Target lesion vessel	
Left Anterior Descending	212 (44 %)
Left Circumflex	119 (24,7 %)
Right Coronary Artery	148 (30,7 %)
Left Main Coronary Artery	3 (0,6 %)
AHA Lesion Classification	
A	76 (15,8 %)
B1	190 (39,4 %)
B2	141 (29,3 %)
C	75 (15,6 %)
Initial TIMI Flow grade	
0	92 (19,1 %)
1	22 (4,6 %)
2	62 (12,9 %)
3	306 (63,5 %)
Calcification (moderate-severe)	142 (29,7 %)
Vessel tortuosity (moderate-severe)	120 (24,9 %)
Bifurcation	62 (12,9 %)
2-Stent technique	3 (0,6 %)
Chronic total occlusion	6 (1,2 %)
Minimum lumen diameter (mm)	0,75 ± 0,76
Proximal reference vessel diameter (mm)	3,18 ± 0,55
Distal reference vessel diameter (mm)	2,92 ± 0,57
Stenosis (%)	86 ± 14
Lesion length (mm)	18 ± 8
PCI characteristics	
P2Y12 inhibitor[a]	
Clopidogrel	180 (44,4 %)
Ticagrelor	174 (43 %)
Prasugrel	51 (12,6 %)
IIb/IIIa platelet inhibitors	37 (9,1 %)
Radial approach[a]	375 (92,6 %)
Pre-dilatation	361 (74,9 %)
Non-compliant balloon	85 (17,6 %)
Cutting balloon	56 (11,6 %)
Rotational atherectomy	10 (2,1 %)
Intracoronary lythotripsy	3 (0,6 %)
Guide extension catheter	17 (3,5 %)
Post-dilatation	226 (46,9 %)
Non-compliant balloon	197 (40,9 %)
Intracoronary imaging	34 (7,1 %)
Stent size (mm)	3,03 ± 0,49
Stent length (mm)	22 ± 7,6
Pressure inflation (atm)	14 ± 2,9
Number of stents per patient[a]	1,28 ± 0,61
1	319 (78,8 %)
2	64 (15,8 %)
3	18 (4,4 %)
4	2 (0,5 %)
5	2 (0,5 %)
Number of stents per lesion	1,07 ± 0,33
1	451 (93,5 %)
2	28 (5,7 %)
3	4 (0,8 %)
Total stent length per patient (mm)	28 ± 17
PCI results	
Number of vessels treated[a]	1,12 ± 0,34
1	358 (88,4 %)
2	45 (11,1 %)
3	2 (0,5 %)
Number of lesions treated[a]	1,19 ± 0,45
1	339 (83,7 %)
2	55 (13,6 %)
3	11 (2,7 %)
Complete revascularization[a]	290 (71,6 %)
Final minimal luminal diameter (mm)	3,03 ± 0,52
Final stenosis (%)	4 ± 4
Device success	472 (97,9 %)
Final TIMI Flow Grade	
2	8 (1,7 %)
3	474 (98,3 %)
Residual stenosis > 30 %	2 (0,4 %)
Residual dissection ≥ C	0 (0 %)
Procedure success[a]	394 (97,3 %)
Periprocedural myocardial infarction	1 (0,2 %)
Coronary perforation	2 (0,5 %)
Urgent cardiac surgery	0 (0 %)
Periprocedural death	0 (0 %)
Unplanned revascularization (3 days)	0 (0 %)
DAPT duration recommended (at discharge)	
≤1 month	27 (6,7 %)
3 months	14 (3,7 %)
6 months	49 (12,1 %)
12 months	309 (76,3 %)
>12 months	4 (1 %)

Abbreviations. PCI: percutaneous coronary intervention. DAPT: dual antiplatelet therapy.
[a] Patient-level analysis variable.

DAPT (9 patients) or on OAC plus single antiplatelet therapy (3 patients). 4 strokes were reported: 1 haemorrhagic and 3 ischemic. 1 patient taking OAC for atrial fibrillation experienced an early haemorrhagic stroke due to concomitant clopidogrel use, and a late ischemic stroke while on OAC monotherapy. The other 2 strokes occurred late in patients on single antiplatelet therapy and were not related to atrial fibrillation.

4. Discussion

The main findings of this study are: 1) in a real-world population, daily practice PCI for native coronary artery disease with the ihtDEStiny™ stent shows very high efficacy as evidenced by a low TLF rate at 2 years; 2) the use of this new stent is associated with a very low definite or probable ST rates at 2 years.

We decided to evaluate the clinical efficacy of this new stent after 2 years to assess its long-term efficacy and safety following DAPT cessation. The 2-year TLF rates for DES implantation vary depending on the type of stent used and the clinical context. Due to the heterogeneity of end-point definitions across studies, long-term TLF outcomes are unavailable for some DES. In summary, published 2-year TLF rates of commercially available stents range from 5,1 % to 11,9 % [12–20]. Although cross-

Table 3
Clinical outcomes during 2 years follow-up. Data are n (%).

Clinical outcomes	1 year (N = 405)	2 year (*N* = 404)
Target lesion failure	6 (1,5 %)	9 (2,2 %)
Cardiovascular death	3 (0,7 %)	3 (0,7 %)
Target vessel myocardial infarction	3 (0,7 %)	5 (1,2 %)
Clinically driven target lesion revascularization	2 (0,5 %)	4 (1 %)
Death from any cause	8 (2 %)	13 (3,2 %)
Target vessel failure	9 (2,2 %)	12 (3 %)
Cardiovascular death	3 (0,7 %)	3 (0,7 %)
Target vessel myocardial infarction	3 (0,7 %)	5 (1,2 %)
Target vessel revascularization	5 (1,2 %)	8 (2 %)
Stent thrombosis	0 (0 %)	1 (0,2 %)
Definite	0 (0 %)	1 (0,2 %)
Probable	0 (0 %)	0 (0 %)
Any myocardial infarction	4 (1 %)	7 (1,7 %)
Any revascularization	9 (2,2 %)	13 (3,2 %)
Stroke	1 (0,2 %)	3 (0,7 %)
Bleeding BARC 3–5	12 (3 %)	14 (3,5 %)
MACE	8 (2 %)	13 (3,2 %)
POCE	18 (4,4 %)	29 (7,2 %)

Abbreviations. BARC: Bleeding Academic Research Consortium. MACE: major adverse cardiovascular events. POCE: patient-oriented composite endpoint.

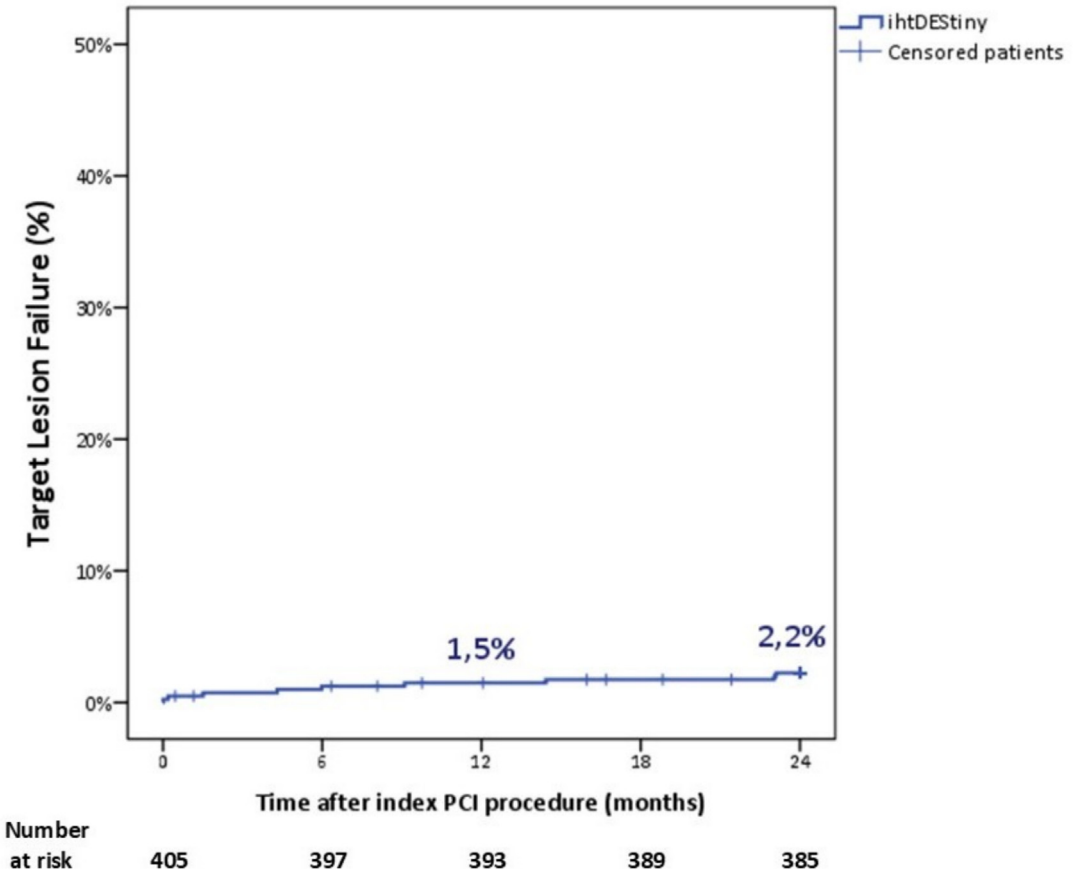

Fig. 3. Kaplan-Meier plot of cumulative incidence of target lesion failure from 0 to 24 months.

comparison with results from other studies has limitations, it helps to put our results in context. ihtDEStiny™ shows the lowest reported 2-year TLF rate for treating native coronary artery disease, likely due to multiple contributing factors. One main reason is that, despite an unrestrictive patient and lesion inclusion criteria, most patients underwent PCI for a single vessel and lesion and received a single stent. Patients undergoing extensive and more complex PCI experience higher rates of TLF (HR: 1.41), MI (HR: 1.48) and stent thrombosis (HR: 2.26), at short- and long-term follow-ups [21,22]. As expected in a real-world registry, patients were not low risk (one-fourth of the sample was diabetic, or presented with ST elevation ACS), but operators decided to use this new stent out from high-risk coronary anatomies (prevalence of type C AHA lesions were only 15 %). Moreover, operators sought optimal stent implantation, as evidenced by high pre- and post-dilatation rates, which are also associated with improved clinical outcomes [23]. However, our study's findings generally align with those of contemporary studies evaluating the efficacy and safety of new stents, in which per-protocol PCI for high-risk lesions is limited [24].

In an effort to improve efficacy and safety, DES characteristics have continually changed in recent years, primarily regarding the released drug, polymer properties and, overall, the strut thickness. The clinical significance of strut shape design has been poorly studied. According to evidence from a recent large network meta-analysis, sirolimus is the DES drug associated with lower rates of TLF compared to everolimus (OR: 0.84, p = 0.03), zotarolimus (OR: 0.81, p = 0.01) or biolimus (OR: 0.81, p = 0.03). Sirolimus was also associated with a lower long-term ST rate compared to zotarolimus (OR: 0.66, p = 0.04) or biolimus (OR: 0.60, p = 0.04) [4]. Some studies advanced better outcomes for biodegradable polymer over permanent polymer, but these studies compared first-generation DES with second-generation DES, or with newer generation DES [24,25]. A meta-analysis comparing biodegradable polymer DES with second-generation durable polymer DES shows no difference in TLF or ST [26]. ihtDEStiny™ presents a fixed ultra-thin strut thickness of 68 μm for all stent sizes. The effect of strut thickness on clinical outcomes is well-established. Ultra-thin strut DES are associated with a significant reduction in target lesion failure (around 15 %), driven by fewer MI and ST during the first year, and fewer clinically indicated target lesion revascularization at long-term (2 years), independently of the drug or polymer [5,27,28]. The design of stent struts influences endothelial shear stress (ESS) by reducing it and disturbing the flow within the stented segment. Low ESS is associated with endothelial dysfunction, inflammation, and platelet activation, which can lead to restenosis and stent thrombosis [29]. Streamlined stent strut profiles, such an oval shape, reduce the impact on ESS and minimize flow recirculation zones compared to traditional square or circular profiles [30]. Recently, Nguyen et al. found in a preclinical model that reducing the thickness and streamlining the shape of stent struts can promote endothelization, which is crucial for reducing the risk of stent thrombosis [31]. ihtDEStiny™ features an oval-shaped hydrodynamic strut (EndoBoost®). To the best of our knowledge, this is the first clinical evaluation of a DES with a streamlined oval-shaped strut.

Although advancements in stent technology and antiplatelet therapy have significantly reduced the incidence of stent thrombosis to below 1 % per year, a 0 % rate has never been documented in large-scale studies. In our cohort, only 1 patient suffered a very late definite stent thrombosis (ST) after aspirin withdrawal, despite unplanned dual antiplatelet therapy (DAPT) interruption in 7 patients and scheduled interruption according to medical criteria in most patients. These results support the safety of the studied stent. Regarding the anecdotal ST rate observed in our study, the streamlined ultra-thin strut and the polymer feature could have played a significant role. First, fluoropolymers are among the least thrombogenic polymers used in current DES, with less platelet aggregation and less inflammatory cell attachment [32]. Second, the antiplatelet agent triflusal in the coating would potentially increase the device's local thromboresistant profile. Mid-term subclinical thrombi

detection by optical coherence tomography after new generation DES implantation ranges from 1 % to 5.3 % [33,34]. The PROMETHEUS study showed a remarkable absence of subclinical thrombi in a first-in-human use of the ihtDESTiny™. Apart from this data, our study is the first to report the long-term clinical effects of a triflusal-containing stent [6].

We hypothesize that the combination of all these characteristics in the investigated device (streamlined ultra-thin strut and sirolimus eluting from a permanent fluoropolymer containing triflusal) facilitates the low TLF and ST rates observed in our study. Recently, 2-year follow up data was published from a large prospective study using a DES with similar design (thin-strut and sirolimus eluting from a permanent polymer), presenting similar TLF and ST rates (3.4 % and 0.7 % respectively) than those observed in our study [35]. According to our results, conducting randomized studies comparing ihtDESTiny™ against the most validated DES should be considered.

4.1. Limitations

Notwithstanding the large size cohort, the study is a single-arm prospective observational study, which is its major limitation. Furthermore, since the study was not designed as an "all-comers" study, the operators decided which patients and lesions would receive the new stent, and patient-selection bias was not controlled.

Although the stents were implanted as closely as possible to daily clinical practice, patient and lesions included in the study were selected under a set of inclusion and exclusion criteria. Therefore, the results are applicable only to those settings. Since the study did not control treatment protocols, variations in practice could have affected the outcomes.

A core-lab for lesion characterization and PCI results evaluation was not considered. Although academic centres were selected based on high PCI volumes and broad experienced operators, data collected may be affected by variability in data entry, measurement, or interpretation.

Although the study protocol strictly defined periprocedural MI and included it as a mandatory specific form in the electronic database to ensure its exclusion, cardiac enzyme analyses were not protocolized for every patient included in the study, which may have led to under-reporting. Systematic post-PCI analysis could have increased the diagnosis of periprocedural MI and, consequently, a higher TLF rate.

5. Conclusions

In a large real-world population undergoing PCI for native coronary artery, a new hydrodynamic ultra-thin strut SES with abluminal permanent fluoropolymer containing triflusal shows low TLF and very low ST rates at 2 years.

CRediT authorship contribution statement

Jose Antonio Linares Vicente: Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Writing – original draft. **Fermín Sainz Laso:** Investigation, Data curation. **Juan Manuel Casanova Sandoval:** Investigation, Data curation. **Jose Ramón Rumoroso Cueva:** Supervision, Investigation, Data curation. **Antonio Gómez Menchero:** Investigation, Data curation. **Joan Antoni Gómez Hospital:** Investigation, Data curation. **Ainhoa Pérez Guerrero:** Investigation, Data curation. **Sandra Santos Martinez:** Investigation, Data curation. **Javier Fernández Portalés:** Investigation, Data curation. **Sebastián Romani:** Investigation, Data curation. **Bruno García Del Blanco:** Investigation, Data curation. **Raymundo Ocaranza Sánchez:** Investigation, Data curation. **Cristóbal Urbano Carrillo:** Investigation, Data curation. **Koldobika García San Roman:** Investigation, Data curation. **Hugo Vinhas:** Investigation, Data curation. **Belén Cid Álvarez:** Investigation, Data curation. **Juan Sanchís Fores:** Investigation, Data curation. **Miren Tellería Arrieta:** Investigation, Data curation. **Alfonso Torres Bosco:** Investigation, Data curation. **Eduardo Pinar Bermúdez:** Investigation, Data curation. **Jose Juan Méndez Castro:** Investigation, Data curation. **Fernando Lozano Ruiz de Poveda:** Investigation, Data curation. **Armando Pérez de Prado:** Supervision, Funding acquisition, Conceptualization. **Jose María De la Torre Hernández:** Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Writing – original draft.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jose A Linares Vicente reports financial support was provided by IHT Cordynamic. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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