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ORIGINAL RESEARCH

One- versus three-month DAPT after everolimus-eluting stent implantation in diabetic patients at high bleeding risk: results from the XIENCE Short DAPT programme

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ABSTRACT

BACKGROUND: In patients with diabetes mellitus (DM) and high bleeding risk (HBR) undergoing percutaneous coronary intervention (PCI), the optimal duration of dual antiplatelet therapy (DAPT) remains uncertain.

AIMS: We sought to compare early DAPT discontinuation in DM and non-DM patients enrolled in the prospective XIENCE Short DAPT programme.

METHODS: The effects of 1- versus 3-month DAPT on ischaemic and bleeding outcomes were compared using propensity score stratification. The primary endpoint was a composite of all-cause death or myocardial infarction (MI) at 1 year. The incidence of Bleeding Academic Research Consortium (BARC) Type 2 to 5 bleeding was the key secondary endpoint.

RESULTS: Out of 3,352 included patients, 1,299 (38.8%) had DM; diabetic patients had a higher 1-year incidence of death or MI (DM vs non-DM: 10.1% vs 6.6%) and similar BARC 2-5 bleeding (DM vs non-DM: 9.5% vs 9.2%). With 1- versus 3-month DAPT, the incidence of death or MI did not statistically differ in DM patients (adjusted hazard ratio [adjHR] 0.70, 95% confidence interval [CI]: 0.47-1.05) and non-DM patients (adjHR 1.26, 95% CI: 0.87-1.81), although heterogeneity by DM status was evident (p for interaction=0.015). BARC 2-5 bleeding was numerically lower with 1-month DAPT in both groups (DM: adjHR 0.67, 95% CI: 0.45-1.01; non-DM: adjHR 0.78, 95% CI: 0.56-1.07; p for interaction=0.973).

CONCLUSIONS: Among HBR patients with DM undergoing PCI, 1-month DAPT, as compared to 3-month DAPT, was not associated with an excess of fatal or non-fatal MI and even reduced the occurrence of bleeding. These findings should be interpreted in the context of a predominantly stable patient population with low procedural complexity and may not be generalisable to higher-risk cases.

KEYWORDS: bleeding; DAPT; diabetes; high bleeding risk; percutaneous coronary intervention

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Bleeding and ischaemic events after percutaneous coronary intervention (PCI) are associated with substantial morbidity and mortality[1,2]. A course of 6-12 months of dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor is the default strategy to prevent thrombotic complications after coronary stenting[3]. However, DAPT is encumbered by a considerable risk of bleeding, particularly in patients with clinical conditions predisposing to high bleeding risk (HBR)[4]. Increasing awareness of the negative prognostic impact of bleeding and technology refinements with new-generation drug-eluting stents (DES) have allowed a progressive shortening of DAPT duration, without compromising safety[5-7].

Diabetes mellitus (DM) is an established cardiovascular risk factor that affects more than one-third of patients undergoing PCI[8]. Patients with DM are at higher risk for ischaemic events and are often considered for longer and more potent antithrombotic therapy after PCI[9-12]. However, the optimal strategy in patients with both DM and HBR status remains unclear[13].

In the XIENCE Short DAPT programme, a 1-month DAPT regimen followed by aspirin resulted in fewer bleeding complications than a 3-month regimen, without increasing ischaemic risk in HBR patients undergoing PCI[6]. Therefore, we aimed to evaluate the efficacy and safety of 1- versus 3-month DAPT in DM and non-DM patients with HBR undergoing PCI.

Impact on daily practice

Diabetes mellitus is associated with a high ischaemic risk in patients with coronary artery disease undergoing percutaneous coronary intervention, often necessitating more intense and/or prolonged dual antiplatelet therapy (DAPT). In high bleeding risk (HBR) patients, shorter DAPT regimens have been proposed to mitigate bleeding events, though evidence supporting their safety in diabetic patients has been limited. Our analysis from the XIENCE Short DAPT programme demonstrates that a 1-month DAPT regimen is safe and effective, reducing bleeding complications without increasing ischaemic events in diabetic patients. These findings provide reassuring evidence for clinicians to consider shorter DAPT durations for HBR diabetic patients, particularly in stable presentations and low procedural complexity, as reflected in the majority of patients enrolled in the study. This approach helps balance the trade-off between bleeding and ischaemic risks in routine clinical practice.

Methods

STUDY DESIGN

The rationale, design and principal results of the XIENCE Short DAPT programme have been previously reported[14,15]. In brief, the programme consisted of three international, open-label, prospective, single-arm studies: the XIENCE 28 USA Study (ClinicalTrials.gov: NCT03815175) and XIENCE 28 Global Study (NCT03355742) testing 1-month DAPT, and the XIENCE 90 study (NCT03218787) testing 3-month DAPT. The two short DAPT regimens were tested in high bleeding risk patients undergoing PCI with the cobalt-chromium everolimus-eluting XIENCE stent (Abbott). Patients presenting with chronic coronary syndrome (CCS) or non-ST-segment elevation acute coronary syndrome (NSTE-ACS) were eligible for inclusion if they had up to 3 target lesions, with a maximum of 2 target lesions per epicardial vessel, excluding lesions located in the left main artery, grafts, or restenosis sites. The clinical programme was funded by Abbott, which designed the protocol together with the principal investigators and executive and steering committee members. The study protocol was approved by institutional review boards or ethics committees at each site. Enrolled patients signed written informed consent, and an independent data safety monitoring board ensured safety.

STUDY POPULATION AND TREATMENT

We designed this analysis to investigate the effect of 1- versus 3-month DAPT in diabetic and non-diabetic patients[15]. Key inclusion and exclusion criteria are reported in **Supplementary Table 1** and are the same as in the original studies. As per the XIENCE Short DAPT protocol, patients met HBR criteria if at least one of the following criteria was present: age ≥75 years, chronic therapy (>6 months) with anticoagulants, prior (within 12 months) history of major bleeding, prior stroke (ischaemic or haemorrhagic), anaemia (haemoglobin <11 g/dL), renal insufficiency (creatinine ≥2.0 mg/dL or dialysis), or systemic disease associated with higher bleeding risk (e.g., thrombocytopaenia or coagulation disorders). After the index PCI, patients received DAPT consisting of aspirin and a $P2Y_{12}$ inhibitor. Patients were assessed for DAPT discontinuation at 1- and at 3-month follow-up in the XIENCE 28 studies and the XIENCE 90 study, respectively. $P2Y_{12}$ inhibitor was discontinued in patients who were adherent to DAPT and did not experience myocardial infarction (MI), repeat revascularisation, stroke, or stent thrombosis. Follow-up occurred up to 12 months. For this analysis, the 1-month eligibility of patients from the XIENCE 90 study was retrospectively evaluated in order to match the design of the XIENCE 28 studies.

CLINICAL ENDPOINTS

The primary endpoint was the composite of all-cause death or MI between 1 and 12 months after the index PCI. Bleeding Academic Research Consortium (BARC) Type 2 to

Abbreviations

BARC	Bleeding Academic Research Consortium	**HBR**	high bleeding risk	**PCI**	percutaneous coronary intervention
CCS	chronic coronary syndrome	**MI**	myocardial infarction	**TLF**	target lesion failure
DAPT	dual antiplatelet therapy	**NACE**	net adverse clinical events	**TLR**	target lesion revascularisation
DES	drug-eluting stent	**NSTE-ACS**	non-ST-segment elevation acute coronary syndrome	**TVR**	target vessel revascularisation
DM	diabetes mellitus				

5 bleeding was the key secondary endpoint. Other endpoints included net adverse clinical events (NACE), defined as the composite of death, MI, BARC Type 3 to 5 bleeding, and stroke; target lesion failure (TLF), defined as the composite of cardiovascular death, target vessel MI, or clinically indicated target lesion revascularisation (TLR); target vessel revascularisation (TVR); definite or probable stent thrombosis; and the individual components of the composite outcomes. Outcomes were adjudicated by an independent clinical events committee. MI and stent thrombosis were defined according to the Academic Research Consortium 2 definitions[16]. The full endpoint definitions are provided in **Supplementary Table 2**.

STATISTICAL ANALYSIS

Continuous variables are presented as means with standard deviations, while categorical variables are presented as frequencies and percentages. Comparisons between groups for continuous variables were performed using the Student's t-test, and comparisons between groups for categorical variables were performed using the chi-square test. Survival analysis was conducted using the Kaplan-Meier method, with comparisons between groups made using the log-rank test to assess the time to the first event. Cox proportional hazard models were applied to compare the unadjusted risks for the primary and secondary outcomes. Adjusted risks were derived using propensity score (PS) stratification into quintiles, consistent with the design of the main study[14]. For PS building, in case of missing data, multiple imputation with the Markov Chain Monte Carlo method and Rubin's combination rule was used. The stratification weight was determined by the proportion of the sample size of each stratum and the overall sample size for both groups. All analyses were conducted using R software, version 3.6.2 (R Foundation for Statistical Computing) or SAS software, version 9.4 (SAS Institute).

Results

POPULATION CHARACTERISTICS

Between July 2017 and February 2020, a total of 3,652 HBR patients were enrolled in the XIENCE Short DAPT programme. For the present analysis, the final cohort included in the study consisted of 3,352 patients, of whom 1,299 (38.8%) had DM **(Figure 1)**. The baseline and procedural characteristics of patients, stratified according to diabetic status, are reported in **Supplementary Table 3** and **Supplementary Table 4**. Diabetic patients were younger than non-diabetic patients but with more comorbidities; there were no differences between the groups in terms of clinical presentation, with most of the patients presenting with CCS (64.5% vs 65.9%; p=0.426) and up to one-third with NSTE-ACS (35.5% vs 34.1%; p=0.426). Among HBR criteria, anaemia and renal insufficiency were more frequently observed in the diabetic group. PCI complexity was generally low, with less than 6% receiving long stenting or more than 3-lesion, 3-stent, or 3-vessel PCI, with no difference between the groups.

When stratified according to DAPT duration, a total of 1,382 patients (41.2%) receiving 1-month DAPT and 1,970 patients (58.8%) receiving 3-month DAPT were included; of these, 512 and 787 were in the diabetic group, and 870 and 1,183 were in the non-diabetic group, respectively. The baseline clinical and procedural characteristics of patients with and without DM stratified according to the DAPT regimen are reported in **Table 1** and **Table 2**, respectively. Of note, patients receiving 1-month DAPT were more likely to present with non-ST-segment elevation myocardial infarction in both the DM (17.4% vs 7.5%; p<0.001) and non-DM (17.98% vs 6.69%; p<0.001) strata. Regarding the antithrombotic regimen, clopidogrel was the most common $P2Y_{12}$ inhibitor prescribed at discharge (>80%) across all groups **(Table 2)**. DAPT was continued

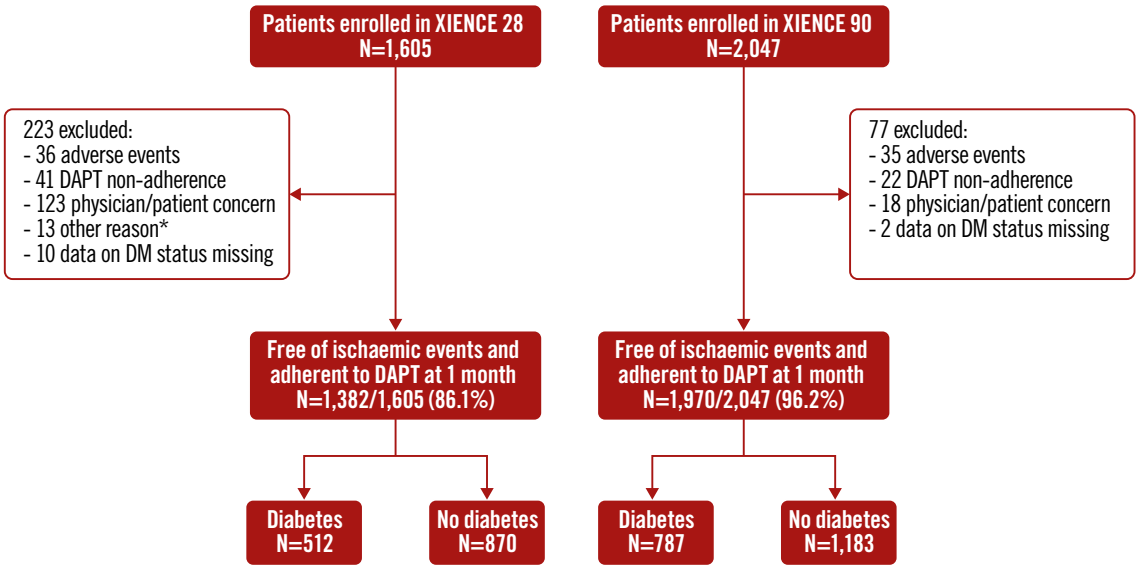


Figure 1. *Patient flow diagram. *1 duplicate subject enrolment, 12 missed the 1-month visit. DAPT: dual antiplatelet therapy; DM: diabetes mellitus*

Table 1. Baseline clinical characteristics in patients with and without diabetes, stratified according to DAPT regimen.

	Patients with DM (n=1,299)			Patients without DM (n=2,053)		
	XIENCE 28 1-month DAPT (n=512)	XIENCE 90 3-month DAPT (n=787)	*p*-value	XIENCE 28 1-month DAPT (n=870)	XIENCE 90 3-month DAPT (n=1,183)	*p*-value
Clinical characteristics						
Age, years	74.2±9.0	72.8±9.8	0.011	77.0±7.8	76.6±8.8	0.236
Female sex	171 (33.4)	264 (33.5)	0.956	279 (32.1)	436 (36.9)	0.024
Race						
White	280 (76.3)	651 (82.7)	0.01	522 (87.6)	1,086 (91.8)	0.004
Asian	68 (18.5)	29 (3.7)	<0.001	55 (9.2)	16 (1.4)	<0.001
Hispanic or Latino ethnicity	49 (10.1)	29 (3.7)	<0.001	88 (10.7)	27 (2.3)	<0.001
Black or African American	17 (4.6)	71 (9.0)	0.009	19 (3.2)	46 (3.9)	0.457
Hypertension	460 (89.8)	745 (94.7)	0.001	712 (81.8)	1,025 (86.6)	0.003
Dyslipidaemia	376 (73.4)	688 (87.4)	<0.001	558 (64.1)	932 (78.8)	<0.001
Chronic kidney disease	238 (48.0)	311 (39.8)	0.004	389 (47.2)	489 (41.7)	0.016
Prior PCI	163 (31.8)	257 (32.7)	0.758	225 (25.9)	350 (29.6)	0.063
Prior CABG	51 (10.0)	115 (14.6)	0.014	61 (7.0)	131 (11.1)	0.002
Chronic coronary syndrome	333 (65.0)	505 (64.2)	0.748	576 (66.2)	776 (65.6)	0.773
Acute coronary syndrome	179 (35.0)	282 (35.8)	0.748	294 (33.8)	407 (34.4)	0.773
NSTEMI	89 (17.4)	59 (7.5)	<0.001	155 (17.8)	82 (6.9)	<0.001
Unstable angina	90 (17.6)	223 (28.3)	<0.001	139 (16.0)	325 (27.5)	<0.001
PARIS bleeding score	6.3±2.2	6.0±2.4	0.038	6.0±2.3	6.0±2.3	0.814
PRECISE-DAPT score	27.8±12.3	26.3±12.4	0.038	27.6±10.6	26.1±11.1	0.004
High bleeding risk criteria						
Age ≥75 years	307 (60.0)	436 (55.4)	0.105	635 (73.0)	854 (72.2)	0.689
Chronic anticoagulant therapy	230 (44.9)	319 (40.5)	0.118	384 (44.2)	486 (41.1)	0.159
Anaemia	99 (19.3)	172 (21.9)	0.275	99 (11.4)	141 (11.9)	0.714
History of stroke	62 (12.1)	108 (13.7)	0.399	82 (9.4)	115 (9.7)	0.829
Renal insufficiency	73 (14.3)	118 (15.0)	0.714	42 (4.8)	39 (3.3)	0.077
Thrombocytopaenia	11 (2.2)	23 (3.0)	0.404	20 (2.4)	14 (1.2)	0.043
History of major bleeding	17 (3.3)	20 (2.5)	0.409	29 (3.3)	37 (3.1)	0.79
Number of HBR criteria	1.6±0.8	1.5±0.7	0.505	1.5±0.7	1.4±0.6	0.062
ESC thrombotic risk enhancers[40]						
Diabetes	512 (100)	787 (100)	N/A	-	-	-
Insulin-dependent diabetes	160 (31.2)	264 (33.5)	0.389	-	-	-
Prior MI	98 (19.3)	143 (18.5)	0.715	128 (14.8)	174 (14.9)	0.946
Multivessel CAD	253 (49.4)	399 (50.7)	0.651	317 (36.4)	519 (43.9)	<0.001
eGFR 15-59 ml/min/1.73 m²	203 (39.6)	269 (34.2)	0.045	358 (41.1)	447 (37.8)	0.123
Premature CAD (age <45 years)	2 (0.4)	4 (0.5)	0.76	2 (0.2)	3 (0.3)	0.914
Number of risk enhancers	2.1±0.9	2.0±0.9	0.277	0.9±0.8	1.0±0.8	0.312
Moderate or high thrombotic risk	512 (100)	787 (100)	N/A	583 (67.0)	809 (68.4)	0.51

Continuous variables are reported as mean±SD. Categorical variables are reported as n (%). CABG: coronary artery bypass graft; CAD: coronary artery disease; DAPT: dual antiplatelet therapy; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; ESC: European Society of Cardiology; HBR: high bleeding risk; MI: myocardial infarction; N/A: not applicable; NSTEMI: non-ST-segment elevation myocardial infarction; PARIS: Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients; PCI: percutaneous coronary intervention; PRECISE-DAPT: Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy; SD: standard deviation

Table 2. Procedural features and therapy at discharge in patients with and without diabetes, stratified according to DAPT regimen.

	Patients with DM (n=1,299)			Patients without DM (n=2,053)		
	XIENCE 28 1-month DAPT (n=512)	XIENCE 90 3-month DAPT (n=787)	*p*-value	XIENCE 28 1-month DAPT (n=870)	XIENCE 90 3-month DAPT (n=1,183)	*p*-value
Procedural characteristics						
Radial access	349 (68.2)	398 (50.6)	<0.001	629 (72.3)	629 (53.2)	<0.001
Number of lesions treated	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.577	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.704
Type B2/C lesion	178 (34.8)	299 (38.0)	0.238	318 (36.6)	387 (32.7)	0.07
Bifurcation lesion	46 (9.0)	61 (7.8)	0.429	115 (13.2)	92 (7.8)	<0.001
Number of stents implanted	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.76	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.593
Total stent length, mm	26.9±14.4	26.1±13.5	0.305	27.4±14.5	25.2±14.0	<0.001
Preprocedure RVD, mm	3.0±0.5	3.0±0.5	0.377	3.0±0.5	3.0±0.5	0.625
Preprocedure %DS	83.2±9.7	83.8±9.8	0.278	82.1±10.7	84.0±9.4	<0.001
Complex PCI, any of the following	30 (5.9)	45 (5.7)	0.915	44 (5.1)	62 (5.2)	0.853
≥3 stents implanted	18 (3.5)	31 (3.9)	0.696	29 (3.3)	40 (3.4)	0.953
≥3 lesions treated	11 (2.1)	19 (2.4)	0.755	23 (2.6)	33 (2.8)	0.841
≥3 vessel treated	1 (0.2)	0 (0)	0.215	1 (0.1)	5 (0.4)	0.202
Total stent length >60 mm	17 (3.3)	28 (3.6)	0.819	35 (4.0)	46 (3.9)	0.877
Antiplatelet therapy at discharge						
Aspirin	417 (81.4)	728 (92.5)	<0.001	705 (81.0)	1,071 (90.5)	<0.001
Clopidogrel	436 (85.2)	634 (80.6)	0.034	759 (87.2)	977 (82.6)	0.004
Prasugrel	10 (2.0)	19 (2.4)	0.583	4 (0.5)	27 (2.3)	<0.001
Ticagrelor	66 (12.9)	135 (17.2)	0.038	107 (12.3)	181 (15.3)	0.053

Continuous variables are reported as mean±SD, or median [IQR]. Categorical variables are reported as n (%). DAPT: dual antiplatelet therapy; DM: diabetes mellitus; DS: diameter stenosis; IQR: interquartile range; PCI: percutaneous coronary intervention; RVD: reference vessel diameter; SD: standard deviation

after the protocol-mandated time in 3.1% and 14.5% of patients in the 1- and 3-month DAPT groups, respectively, without differences according to diabetes status. In the latter group, 70.0% of patients completed 3-month DAPT, 14.5% were still on DAPT at 6 months, and 12.9% were on DAPT at 12-month follow-up. Within 90 days of follow-up, DAPT discontinuation occurred more frequently in non-diabetic patients on 3-month DAPT **(Figure 2)**.

OUTCOMES ACCORDING TO DIABETES STATUS

At 1-year follow-up, patients with DM had a higher incidence of the primary endpoint (10.1% vs 6.6%, hazard ratio [HR] 1.51, 95% confidence interval [CI]: 1.18-1.94; p=0.001) **(Figure 3A)**. Diabetic patients also experienced significantly higher risks of MI, TLF, TVR, and NACE **(Supplementary Table 5)**. With respect to bleeding, there were no significant differences between diabetic and non-diabetic patients for either BARC Type 2-5 (9.5% vs 9.2%, HR 1.02, 95% CI: 0.80-1.29; p=0.902) **(Figure 3B)** or BARC Type 3-5 bleeding (4.6% vs 4.2%, HR 1.09, 95% CI: 0.78-1.54; p=0.610).

OUTCOMES ACCORDING TO DAPT DURATION

The incidence and adjusted HRs (adjHRs) for clinical outcomes, stratified by DAPT duration and diabetic status, are reported in **Table 3** and the **Central illustration**. Between 1 and 12 months after PCI, in patients with DM, all-cause death or MI occurred in 39 (8.4%) patients receiving 1-month DAPT and in 81 (11.3%) patients on 3-month DAPT; in the non-DM group, the primary endpoint occurred in 64 (7.8%) patients on 1-month DAPT and in 64 (5.7%) patients on 3-month DAPT. After PS stratification, there was a signal of treatment effect modification of 1- versus 3-month DAPT by diabetic status for the risk of the primary endpoint (DM: adjHR 0.70, 95% CI: 0.47-1.05; p=0.083; non-DM: adjHR 1.26, 95% CI: 0.87-1.81; p=0.224; p for interaction=0.015). The risk of MI associated with 1- versus 3-month DAPT was significantly lower in patients with DM (3.3% vs 6.8%, adjHR 0.46, 95% CI: 0.26-0.84; p=0.011), whereas it did not differ in patients without DM (3.1% vs 2.1%, adjHR 1.52, 95% CI: 0.84-2.75; p=0.171; p for interaction=0.004), mainly driven by a difference in target vessel MI. Similarly, the risk of target lesion failure associated with 1- versus 3-month DAPT was reduced in DM patients (4.8% vs 8.6%, adjHR 0.54, 95% CI: 0.33-0.89; p=0.016) but not in non-DM patients (5.8% vs 3.6%, adjHR 1.57, 95% CI: 1.01-2.45; p=0.045; p for interaction<0.001). Rates of stroke and stent thrombosis were generally low and were not statistically different between 1- and 3-month DAPT regimens in both patients with and without DM; the incidence of ischaemic stroke was significantly lower in DM patients receiving 1-month DAPT (0.8% vs 2.2%, adjHR 0.31, 95% CI: 0.10-0.98; p=0.045), compared to those receiving 3-month DAPT.

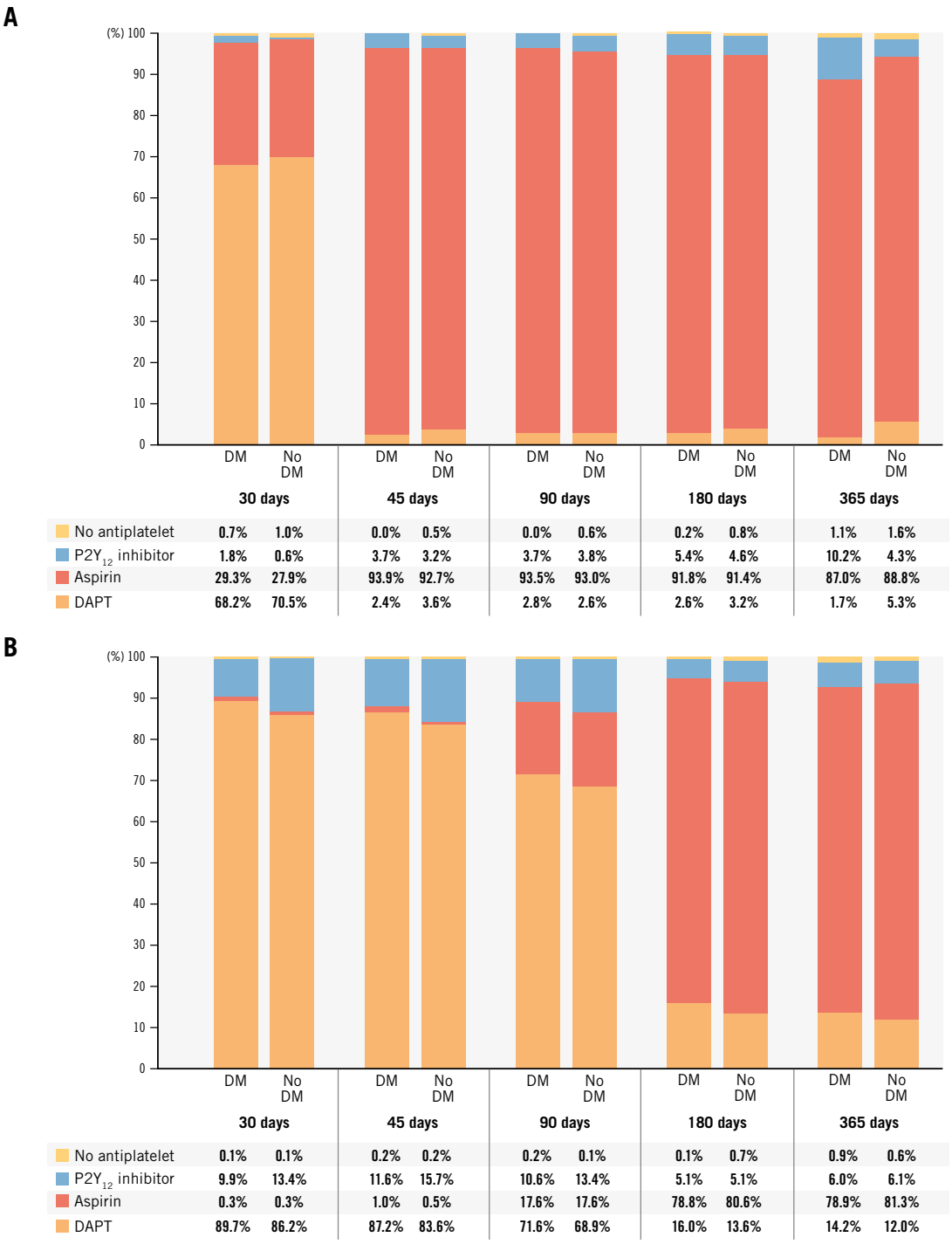


Figure 2. *Antiplatelet regimens during the study. A) Antiplatelet regimens in patients enrolled in XIENCE 28, stratified by diabetes status. B) Antiplatelet regimens in patients enrolled in XIENCE 90, stratified by diabetes status. DAPT discontinuation was mandated at 1 month after percutaneous coronary intervention (PCI) in XIENCE 28 and at 3 months after PCI in XIENCE 90. DAPT: dual antiplatelet therapy; DM: diabetes mellitus*

Between 1 and 12 months, the risk of BARC Type 2-5 bleeding tended to be lower with 1- versus 3-month DAPT in both DM (8.1% vs 10.4%; adjHR 0.67, 95% CI: 0.45-1.01; p=0.057) and non-DM patients (8.1% vs 10.1%; adjHR 0.78, 95% CI: 0.56-1.07; p=0.125; p for interaction=0.973). There was no difference in the risk of BARC 3-5 bleeding between 1- and 3-month DAPT in patients with (4.5% vs 4.7%, adjHR 0.77, 95% CI: 0.44-1.37; p=0.381) or without DM (3.5% vs 4.7%, adjHR 0.72, 95% CI: 0.44-1.16; p=0.178; p for interaction=0.538). Finally, 1-month DAPT significantly reduced the incidence of NACE in DM patients (11.0% vs 15.4%, adjHR 0.64, 95% CI: 0.46-0.90; p=0.010) but not

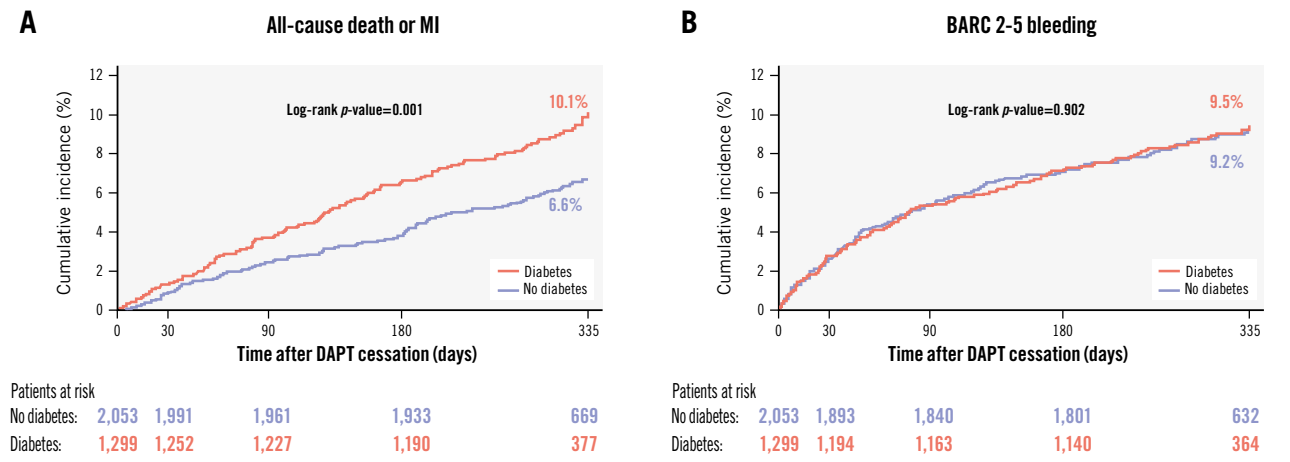


Figure 3. *Cumulative incidence of the composite of all-cause death or MI and of BARC Type 2 to 5 bleeding in patients with and without diabetes mellitus. A) Cumulative incidence of all-cause death or MI. B) Cumulative incidence of BARC 2-5 bleeding. BARC: Bleeding Academic Research Consortium; DAPT: dual antiplatelet therapy; MI: myocardial infarction*

Table 3. One-year clinical outcomes of HBR patients with and without diabetes receiving 1- versus 3-month DAPT.

Outcomes	Diabetes (N=1,299)				No diabetes (N=2,053)				Interaction p-value‡
	XIENCE 28 1-month DAPT (N=512)	XIENCE 90 3-month DAPT (N=787)	Adjusted hazard ratio† (95% CI)	p-value	XIENCE 28 1-month DAPT (N=870)	XIENCE 90 3-month DAPT (N=1,183)	Adjusted hazard ratio† (95% CI)	p-value	
All-cause death or MI	39 (8.4)	81 (11.3)	0.70 (0.47-1.05)	0.083	64 (7.8)	64 (5.7)	1.26 (0.87-1.81)	0.224	0.015
All-cause death	24 (5.2)	40 (5.9)	0.86 (0.51-1.46)	0.583	40 (4.8)	48 (4.2)	0.98 (0.63-1.53)	0.928	0.521
Cardiovascular death	10 (2.3)	26 (3.9)	0.57 (0.27-1.22)	0.147	22 (2.6)	23 (2.0)	1.15 (0.62-2.14)	0.655	0.094
MI	15 (3.3)	50 (6.8)	0.46 (0.26-0.84)	0.011	25 (3.1)	23 (2.1)	1.52 (0.84-2.75)	0.171	0.004
Definite or probable ST	1 (0.2)	4 (0.6)	0.48 (0.05-4.42)	0.516	3 (0.4)	2 (0.2)	2.09 (0.32-13.60)	0.442	0.245
Stroke	5 (1.0)	18 (2.5)	0.38 (0.14-1.07)	0.067	6 (0.9)	15 (1.4)	0.45 (0.17-1.22)	0.118	0.708
Ischaemic stroke	4 (0.8)	16 (2.2)	0.31 (0.10-0.98)	0.045	5 (0.8)	14 (1.3)	0.39 (0.13-1.15)	0.088	0.74
Target lesion failure	22 (4.8)	61 (8.6)	0.54 (0.33-0.89)	0.016	47 (5.8)	40 (3.6)	1.57 (1.01-2.45)	0.045	<0.001
Target lesion revascularisation	9 (2.0)	13 (1.8)	1.00 (0.41-2.43)	0.996	9 (1.1)	13 (1.2)	1.08 (0.44-2.63)	0.862	0.852
Target vessel revascularisation	13 (3.1)	26 (3.5)	0.73 (0.37-1.46)	0.371	16 (2.2)	20 (1.9)	1.28 (0.64-2.55)	0.479	0.446
Target vessel MI	12 (2.7)	40 (5.4)	0.45 (0.23-0.88)	0.02	20 (2.6)	17 (1.5)	1.68 (0.85-3.31)	0.134	0.007
BARC 2-5 bleeding	39 (8.1)	73 (10.4)	0.67 (0.45-1.01)	0.057	64 (8.1)	111 (10.1)	0.78 (0.56-1.07)	0.125	0.973
BARC 3-5 bleeding	21 (4.5)	34 (4.7)	0.77 (0.44-1.37)	0.381	28 (3.5)	52 (4.7)	0.72 (0.44-1.16)	0.178	0.538
NACE	53 (11.0)	112 (15.4)	0.64 (0.46-0.90)	0.01	91 (11.2)	114 (10.1)	1.02 (0.76-1.37)	0.889	0.047

The percentages mentioned above represent Kaplan-Meier rates at 12 months after the index procedure. †Propensity-stratified outcomes according to sex, baseline serum creatinine, anticoagulation therapy, stroke, history of major bleeding, baseline platelet, baseline haemoglobin, body mass index, hypertension, hypercholesterolaemia, prior PCI, prior CABG, prior MI, multivessel disease, diabetes, type B2/C lesion, total lesion length, mean preprocedure RVD, mean preprocedure DS, bifurcation lesion, number of lesions treated, number of vessels treated, number of stents, total stent length, $P2Y_{12}$ on discharge, PARIS risk score for major bleeding, PRECISE-DAPT risk score for bleeding. ‡*p*-value is obtained from the interaction test between the anticoagulant at discharge and DAPT after applying multiple imputation and propensity score stratification. BARC: Bleeding Academic Research Consortium; CABG: coronary artery bypass graft; CI: confidence interval; DAPT: dual antiplatelet therapy; DS: diameter stenosis; HBR: high bleeding risk; MI: myocardial infarction; NACE: net adverse clinical events; PARIS: Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients; PCI: percutaneous coronary intervention; PRECISE-DAPT: Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy; RVD: reference vessel diameter; ST: stent thrombosis

in non-DM patients (11.2% vs 10.1%, adjHR 1.02, 95% CI: 0.76-1.37; p=0.889; p for interaction=0.047).

SECONDARY ANALYSIS

The results of an exploratory analysis stratifying patients by DM status and insulin treatment are reported in **Supplementary Table 6** and were generally consistent with the primary analysis.

Discussion

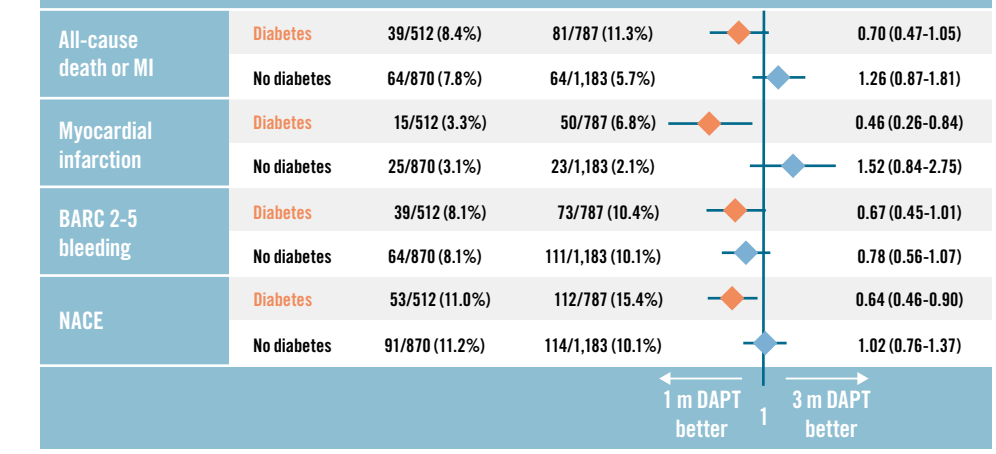
In this study, we compared the safety and efficacy of 1- versus 3-month DAPT in DM and non-DM patients with HBR

EuroIntervention — Central Illustration

One- versus three-month DAPT in diabetic patients at high bleeding risk.

3,352 HBR patients from the XIENCE Short DAPT programme who received everolimus-eluting stent plus 1- or 3-month DAPT were compared according to presence of diabetes

Outcomes at 1-year FU		1-month DAPT	3-month DAPT	PS-adj HR (95% CI)
All-cause death or MI	Diabetes	39/512 (8.4%)	81/787 (11.3%)	0.70 (0.47-1.05)
	No diabetes	64/870 (7.8%)	64/1,183 (5.7%)	1.26 (0.87-1.81)
Myocardial infarction	Diabetes	15/512 (3.3%)	50/787 (6.8%)	0.46 (0.26-0.84)
	No diabetes	25/870 (3.1%)	23/1,183 (2.1%)	1.52 (0.84-2.75)
BARC 2-5 bleeding	Diabetes	39/512 (8.1%)	73/787 (10.4%)	0.67 (0.45-1.01)
	No diabetes	64/870 (8.1%)	111/1,183 (10.1%)	0.78 (0.56-1.07)
NACE	Diabetes	53/512 (11.0%)	112/787 (15.4%)	0.64 (0.46-0.90)
	No diabetes	91/870 (11.2%)	114/1,183 (10.1%)	1.02 (0.76-1.37)



Diabetes was associated with increased ischaemic but not bleeding risk

Short 1-3-month DAPT was safe among HBR patients with diabetes, with no harm from 1-month DAPT

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adj: adjusted; BARC: Bleeding Academic Research Consortium; CI: confidence interval; DAPT: dual antiplatelet therapy; FU: follow-up; HBR: high bleeding risk; HR: hazard ratio; MI: myocardial infarction; NACE: net adverse clinical events; PS: propensity score

undergoing PCI with an everolimus-eluting stent within the XIENCE Short DAPT programme. The main findings are as follows: (1) HBR patients with diabetes incurred a significantly higher risk of ischaemic but not bleeding events; (2) HBR patients with DM did not derive ischaemic harm from 1-month DAPT compared with the 3-month regimen, in the presence of a significant interaction across comparisons with the non-DM group; (3) clinically relevant BARC Type 2-5 bleeding tended to be numerically lower in both DM and non-DM patients on 1-month DAPT, without heterogeneity between groups.

DM affects up to 40% of patients undergoing PCI. It is associated with a prothrombotic and proinflammatory state and increases the risk of ischaemic complications after myocardial revascularisation[17]. In the FREEDOM trial, DM patients with multivessel disease undergoing PCI had significantly higher rates of death or MI at 5-year follow-up, compared with those receiving coronary artery bypass graft[18]. The worse outcomes of DM patients were partly driven by higher rates of both spontaneous as well as stent-related adverse events[19]. The introduction of new-generation DES has substantially reduced the need for repeat revascularisation after PCI in the general population; yet, this benefit appears to be less pronounced among patients with DM[20-22]. Moreover, owing to the established association of DM with thrombotic complications, prolonged DAPT is often considered after PCI in these patients[13]. Such an approach has shown some benefit in patients at very high ischaemic risk (e.g., those with acute coronary syndrome [ACS]) despite resulting in an increased incidence of bleeding events. In the PEGASUS-TIMI 54 trial, an extended course of aspirin and ticagrelor reduced the risk of the composite of cardiovascular death, MI, or stroke while increasing the risk of major bleeding in patients with a prior MI and additional risk factors including diabetes[23]. However, when a similar strategy was tested in diabetic patients with stable coronary artery disease in the THEMIS trial, the observed benefit in the overall population was modest, though larger in those with a history of PCI[10,24]. Interestingly, in the DAPT Study, extended treatment with either clopidogrel or prasugrel plus aspirin beyond 12 months after stent implantation in the DM subgroup was associated with an attenuation of major adverse cardiovascular events reduction originally observed in the overall study population[25].

Haemorrhagic complications may mitigate the benefit provided by a more intense or prolonged antithrombotic regimen, resulting in a null effect on overall survival[1]. Thus, when a thrombotic risk enhancer like diabetes coexists with high bleeding risk status, the scenario is even more complex. Among HBR patients undergoing PCI, our study confirmed a high prevalence of DM, which was associated with a worse ischaemic risk profile. Diabetic patients exhibited more comorbidities, a greater extent of coronary artery disease, and had twice the risk of suffering an MI at 1-year follow-up. Of note, despite patients with DM having higher rates of revascularisation, the incidence of stent thrombosis was reassuringly low – below 0.5% at 1 year – without any significant interaction for diabetes status and DAPT regimen. This is noteworthy as most of the advancements in stent technologies have allowed a reduction in the duration of DAPT while maintaining efficacy in preventing thrombotic events, especially in HBR patients[26-29].

When patients were stratified according to DAPT regimen, we found a significant heterogeneity for the effects of 1- versus 3-month DAPT for the incidence of the primary endpoint, MI, and target lesion failure, which were overall lower in diabetic patients receiving 1-month DAPT. Moreover, 1-month DAPT was also associated with a numerically greater bleeding risk reduction in DM patients, and it is well recognised that bleeding itself can trigger ischaemic complications by precipitating type 2 MI or leading to DAPT disruption[30,31]. A recent large meta-analysis showed that a longer DAPT regimen is effective in reducing major adverse cardiovascular events after complex PCI only when HBR features are not present, with an incremental effect in ACS patients[32]. Similarly, in our cohort of DM patients, we might speculate that the coexistence of HBR status shifted the balance of clinical benefit in favour of the shorter 1-month DAPT. Of note, DM patients presented with a slightly higher number of HBR criteria, mainly due to a higher prevalence of anaemia and renal insufficiency. Moreover, a higher number (14%) of diabetic patients assigned to the 3-month regimen were still on DAPT at 1 year, thus being exposed to a relatively more prolonged risk of bleeding. However, we interpret the reduced ischaemic risk observed with 1-month DAPT in diabetic patients as a signal of safety rather than a definitive sign of superiority. The interplay between competing risks may partly explain the observed MI patterns, though this remains speculative. Indeed, the recent MASTER DAPT trial, which randomised HBR patients undergoing PCI with a biodegradable-polymer sirolimus-eluting stent implantation to abbreviated or standard (≥3 months) DAPT, did not show any significant impact of diabetic status on the abbreviated treatment effects[33]. Our study was not powered to evaluate single ischaemic endpoints such as MI, and this finding may be attributed to chance. While propensity score matching was applied to balance baseline characteristics, the possibility of residual confounders cannot be entirely excluded, including differences in geographical representation. The 1-month DAPT arm included patients from two studies (XIENCE 28 USA and XIENCE 28 Global) conducted across the USA, Europe, and Asia, whereas the 3-month DAPT arm comprised exclusively US patients (XIENCE 90). For instance, Asian patients – who were predominantly represented in the 1-month DAPT arm and exhibited significant imbalances between diabetic and non-diabetic groups – are known to have a higher bleeding rather than ischaemic risk, and their characteristics may have contributed to the observed results. Additionally, most patients in this cohort received only a single stent, and the overall complexity of the PCI procedures was low; consequently, the applicability of these findings to the broader population of diabetic patients undergoing PCI – many of whom undergo more complex interventions, often in the setting of ACS – may be limited. The difference in target vessel MI, which was higher in diabetic patients – in the absence of any difference in stent thrombosis – may be attributed to the higher risk of restenosis and disease progression; however, the same limitations discussed above should be considered for the comparison between 1- and 3-month DAPT.

Finally, in XIENCE Short DAPT, most of the included patients received aspirin monotherapy after DAPT discontinuation. However, a strategy of short DAPT followed by the use of $P2Y_{12}$ inhibitor monotherapy after early aspirin withdrawal has recently emerged as an alternative antithrombotic strategy for secondary prevention[34,35]. In DM patients receiving everolimus-eluting stents, both clopidogrel and ticagrelor monotherapy after 1 to 3 months of DAPT have been proven effective in reducing bleeding without increasing ischaemic events, as compared to standard DAPT[36-38]. Thus, $P2Y_{12}$ inhibitor monotherapy can play a key role, especially in patients with HBR undergoing PCI[3,39].

Limitations

This analysis should be interpreted in light of some limitations. First, as previously mentioned, due to the non-randomised design, we cannot exclude the presence of residual confounders, and the study was not powered to detect differences in individual ischaemic endpoints. Second, the observed findings should be interpreted in the context of the inclusion criteria and procedural characteristics of the patients enrolled in the XIENCE Short DAPT programme, which may limit generalisability to a larger population of DM patients undergoing PCI. Third, for patients enrolled in XIENCE 90, eligibility was retrospectively evaluated given the lack of 1-month follow-up. Finally, it is important to note that most of the enrolled patients were treated with clopidogrel (>80%) and mainly in the setting of chronic coronary syndrome; additionally, the findings may not be applicable to individuals who received different DAPT regimens and/or a stent different from the study stent.

Conclusions

In HBR patients undergoing PCI with the cobalt-chromium everolimus-eluting XIENCE stent, those with DM, although at a higher risk, did not experience ischaemic harm from 1-month DAPT compared with 3-month DAPT, and a numerical reduction of bleeding was observed at the 1-year follow-up. These findings should be interpreted in the context of a study population consisting predominantly of patients with chronic coronary syndrome and low procedural complexity and may not be generalisable to higher-risk cases.

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Conflict of interest statement

D.J. Angiolillo declares that he has received consulting fees or honoraria from Abbott, Amgen, Anthos, AstraZeneca, Bayer, Biosensors, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, CSL Behring, Daiichi Sankyo, Eli Lilly, Faraday, Haemonetics, Janssen, Merck, Novartis, PhaseBio, PLx Pharma, Pfizer, and Sanofi; and institution research grants from Amgen, AstraZeneca, Bayer, Biosensors, CeloNova, CSL Behring, Daiichi Sankyo, Eisai, Eli Lilly, Faraday, Gilead, Idorsia, Janssen, Matsutani Chemical Industry Co., Merck, Novartis, and the Scott R. MacKenzie Foundation. M. Valgimigli reports grants and personal fees from Terumo, AstraZeneca, Alvimedica/CID, Abbott, Daiichi Sankyo, Bayer, CoreFlow, Idorsia Pharmaceuticals Ltd, Universität Basel - Departement Klinische Forschung, Vifor, Bristol-Myers Squibb, Biotronik, Boston Scientific, Medtronic, Vesalio, Novartis, Chiesi, and PhaseBio. D. Cao reports consulting fees from Terumo. D.L. Bhatt discloses the following relationships – advisory board: Angiowave, Bayer, Boehringer Ingelheim, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, High Enroll, Janssen, Level Ex, McKinsey, Medscape Cardiology, Merck, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, and Stasys; board of directors: American Heart Association New York City; Angiowave (stock options), Bristol-Myers Squibb (stock), DRS.LINQ (stock options), and High Enroll (stock); consultant: Broadview Ventures, GlaxoSmithKline, Hims, SFJ, and Youngene; data monitoring committees: Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (Chair, PEITHO trial), Cleveland Clinic, Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo; for the ABILITY-DM trial, funded by Concept Medical; for ALLAY-HF, funded by Alleviant Medical), Novartis, Population Health Research Institute, and Rutgers University (for the NIH-funded MINT Trial); honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Chair, ACC Accreditation Oversight Committee), Arnold and Porter law firm (work related to Sanofi/Bristol-Myers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor-in-Chief, Harvard Heart Letter), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering committees), CSL Behring (AHA lecture), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor-in-Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), K2P (Co-Chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Oakstone CME (Course Director, Comprehensive Review of Interventional Cardiology), Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), WebMD (CME steering committees), and Wiley (steering committee); other: Clinical Cardiology (Deputy Editor); patent: sotagliflozin (named on a patent for sotagliflozin assigned to Brigham and Women's Hospital who assigned to Lexicon; neither he nor Brigham and Women's Hospital receive any income from this patent); research funding: Abbott, Acesion Pharma, Afimmune, Aker BioMarine, Alnylam, Amarin, Amgen, AstraZeneca, Bayer, Beren, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CinCor, Cleerly, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin,

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Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria of XIENCE 90 and XIENCE 28 studies.

Supplementary Table 2. Study endpoint definitions.

Supplementary Table 3. Baseline clinical characteristics of patients with and without diabetes mellitus.

Supplementary Table 4. Procedural characteristics and therapy at discharge of patients with and without diabetes mellitus.

Supplementary Table 5. Association between diabetes status and adverse events.

Supplementary Table 6. Effect of 1- versus 3-month DAPT on outcomes between 1 and 12 months after PCI in patients stratified according to presence of diabetes and insulin treatment.

Data availability statement

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00897

Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria of XIENCE 90 and XIENCE 28 studies.

XIENCE 90	XIENCE 28 Global	XIENCE 28 USA
General Inclusion Criteria: 1. Subject is considered at high risk for bleeding (HBR), defined as meeting one or more of the following criteria at the time of registration and in the opinion of the referring physician, the risk of major bleeding with > 3-month DAPT outweighs the benefit: a) ≥ 75 years of age. b) Clinical indication for chronic (at least 6 months) or lifelong anticoagulation therapy. c) History of major bleeding which required medical attention within 12 months of the index procedure. d) History of stroke (ischemic or hemorrhagic). e) Renal insufficiency (creatinine ≥ 2.0 mg/dl) or failure (dialysis dependent). f) Systemic conditions associated with an increased bleeding risk (e.g. hematological disorders, including a history of or current thrombocytopenia defined as a platelet count <100,000/mm^3, or any known coagulation disorder associated with increased bleeding risk). g) Anemia with hemoglobin < 11g/dl. 2. Subject must be at least 18 years of age. 3. *Subject or a legally authorized representative must provide written informed consent as approved by the Institutional Review Board (IRB)/Ethics Committee (EC) of the respective clinical site prior to any study related procedure*.	**General Inclusion Criteria:** 1. Subject is considered at high risk for bleeding (HBR), defined as meeting one or more of the following criteria at the time of registration and in the opinion of the referring physician, the risk of major bleeding with > 1-month DAPT outweighs the benefit: a) ≥ 75 years of age. b) Clinical indication for chronic (at least 6 months) or lifelong anticoagulation therapy. c) History of major bleeding which required medical attention within 12 months of the index procedure. d) History of stroke (ischemic or hemorrhagic). e) Renal insufficiency (creatinine ≥ 2.0 mg/dl) or failure (dialysis dependent). f) Systemic conditions associated with an increased bleeding risk (e.g. hematological disorders, including a history of or current thrombocytopenia defined as a platelet count <100,000/mm^3, or any known coagulation disorder associated with increased bleeding risk). g) Anemia with hemoglobin < 11g/dl. 2. Subject must be at least 18 years of age. 3. *Subject must provide written informed consent as approved by the Ethics Committee (EC) of the respective clinical site prior to any trial related procedure*. 4. Subject is willing to comply with all protocol requirements, including agreement to stop	**General Inclusion Criteria:** 1. Subject is considered at high risk for bleeding (HBR), defined as meeting one or more of the following criteria at the time of registration and in the opinion of the referring physician, the risk of major bleeding with > 1-month DAPT outweighs the benefit: a) ≥ 75 years of age. b) Clinical indication for chronic (at least 6 months) or lifelong anticoagulation therapy. c) History of major bleeding which required medical attention within 12 months of the index procedure. d) History of stroke (ischemic or hemorrhagic). e) Renal insufficiency (creatinine ≥ 2.0 mg/dl) or failure (dialysis dependent). f) Systemic conditions associated with an increased bleeding risk (e.g. hematological disorders, including a history of or current thrombocytopenia defined as a platelet count <100,000/mm3, or any known coagulation disorder associated with increased bleeding risk). g) Anemia with hemoglobin < 11g/dl. 2. Subject must be at least 18 years of age. 3. *Subject must provide written informed consent as approved by the Institutional Review Board (IRB) of the respective clinical site prior to any trial related procedure.* 4. Subject is willing to comply with all protocol requirements, including agreement to stop

4. Subject is willing to comply with all protocol requirements, including agreement to stop taking P2Y12 inhibitor at 3 months, if eligible per protocol. 5. *Subject must agree not to participate in any other clinical trial for a period of one year following the index procedure.* **Angiographic Inclusion Criteria:** 1. Up to three target lesions with a maximum of two target lesions per epicardial vessel. Note: • The definition of epicardial vessels means left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA) and their branches. For example, the patient must not have >2 lesions requiring treatment within both the LAD and a diagonal branch in total. • If there are two target lesions within the same epicardial vessel, the two target lesions must be at least 15 mm apart per visual estimation; otherwise this is *considered as a single target lesion.* 2. *Target lesion ≤ 32 mm in length by visual estimation.* 3. Target lesion must be located in a native coronary artery with visually estimated reference vessel diameter between 2.25 mm and 4.25 mm. 4. Exclusive use of XIENCE family of stent systems during the index procedure. 5. Target lesion has been treated successfully, which is defined as achievement of a final in-stent residual diameter stenosis of <20% with final TIMI-3 flow assessed by online quantitative angiography or visual estimation, with no residual dissection NHLBI grade ≥ type B, and no transient or sustained angiographic complications (e.g., distal embolization, side branch closure), no chest pain lasting > 5	taking P2Y12 inhibitor at 1 month, if eligible per protocol. 5. *Subject must agree not to participate in any other clinical trial for a period of one year following the index procedure.* **Angiographic Inclusion Criteria:** 1. Up to three target lesions with a maximum of two target lesions per epicardial vessel. Note: • The definition of epicardial vessels means left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA) and their branches. For example, the subject must not have >2 lesions requiring treatment within both the LAD and a diagonal branch in total. • If there are two target lesions within the same epicardial vessel, the two target lesions must be at least 15 mm apart per visual estimation; otherwise this is considered as a single target lesion. 2. Target lesion must be located in a native coronary artery with visually estimated reference vessel diameter between 2.25 mm and 4.25 mm. 3. Exclusive use of XIENCE family of stent systems during the index procedure. 4. Target lesion has been treated successfully, which is defined as achievement of a final in-stent residual diameter stenosis of <20% with final TIMI-3 flow assessed by online quantitative angiography or visual estimation, with no residual dissection NHLBI grade ≥ type B, and no transient or sustained angiographic complications (e.g., distal embolization, side branch closure), no chest pain lasting > 5 minutes, and no ST segment elevation > 0.5mm or depression lasting > 5 minutes.	taking P2Y12 inhibitor at 1 month, if eligible per protocol. 5. *Subject must agree not to participate in any other clinical trial for a period of one year following the index procedure, except for cases where subject is transferred to the XIENCE 90 study after the 1-month visit assessment.* **Angiographic Inclusion Criteria:** 1. Up to three target lesions with a maximum of two target lesions per epicardial vessel. Note: • The definition of epicardial vessels means left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX) and right coronary artery (RCA) and their branches. For example, the subject must not have >2 lesions requiring treatment within both the LAD and a diagonal branch in total. • If there are two target lesions within the same epicardial vessel, the two target lesions must be at least 15 mm apart per visual estimation; otherwise this is considered as a single target lesion. 2. Target lesion must be located in a native coronary artery with visually estimated reference vessel diameter between 2.25 mm and 4.25 mm. 3. Exclusive use of XIENCE family of stent systems during the index procedure. 4. Target lesion has been treated successfully, which is defined as achievement of a final in-stent residual diameter stenosis of <20% with final TIMI-3 flow assessed by online quantitative angiography or visual estimation, with no residual dissection NHLBI grade ≥ type B, and no transient or sustained angiographic complications (e.g., distal embolization, side branch closure), no chest pain lasting > 5

minutes, and no ST segment elevation > 0.5 mm or depression lasting > 5 minutes.		minutes, and no ST segment elevation > 0.5mm or depression lasting > 5 minutes.
General Exclusion Criteria: 1. Subject with an indication for the index procedure of acute ST-segment elevation MI (STEMI). 2. Subject has a known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, P2Y12 inhibitors (clopidogrel/prasugrel/ticagrelor), everolimus, cobalt, chromium, nickel, tungsten, acrylic and fluoro polymers or contrast sensitivity that cannot be adequately pre-medicated. 3. Subject with implantation of another drug-eluting stent (other than XIENCE) within 9 months prior to index procedure. 4. Subject has a known left ventricular ejection fraction (LVEF) <30%. 5. Subject judged by physician as inappropriate for discontinuation from P2Y12 inhibitor use at 3 months, due to another condition requiring chronic P2Y12 inhibitor use. 6. Subject with planned surgery or procedure necessitating discontinuation of P2Y12 inhibitor within 3 months following index procedure. 7. Subject with a current medical condition with a life expectancy of less than 12 months 8. *Subject intends to participate in an investigational drug or device trial within 12 months following the index procedure.* 9. Pregnant or nursing subjects and those who plan pregnancy in the period up to 1 year following index procedure. Female subjects of child-bearing potential must have a negative	**General Exclusion Criteria:** 1. Subject with an indication for the index procedure of acute ST-segment elevation MI (STEMI). 2. Subject has a known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, P2Y12 inhibitors (clopidogrel/prasugrel/ticagrelor), everolimus, cobalt, chromium, nickel, tungsten, acrylic and fluoro polymers or contrast sensitivity that cannot be adequately pre-medicated. 3. Subject with implantation of another drug-eluting stent (other than XIENCE) within 12 months prior to index procedure. 4. Subject has a known left ventricular ejection fraction (LVEF) <30%. 5. Subject judged by physician as inappropriate for discontinuation from P2Y12 inhibitor use at 1 month, due to another condition requiring chronic P2Y12 inhibitor use. 6. Subject with planned surgery or procedure necessitating discontinuation of P2Y12 inhibitor within 1 month following index procedure. 7. Subject with a current medical condition with a life expectancy of less than 12 months 8. *Subject intends to participate in an investigational drug or device trial within 12 months following the index procedure.* 9. Pregnant or nursing subjects and those who plan pregnancy in the period up to 1 year following index procedure. Female subjects of child-bearing potential must have a negative	**General Exclusion Criteria:** 1. Subject with an indication for the index procedure of acute ST-segment elevation MI (STEMI). 2. Subject has a known hypersensitivity or contraindication to aspirin, heparin/bivalirudin, P2Y12 inhibitors (clopidogrel/prasugrel/ticagrelor), everolimus, cobalt, chromium, nickel, tungsten, acrylic and fluoro polymers or contrast sensitivity that cannot be adequately pre-medicated. 3. Subject with implantation of another drug-eluting stent (other than XIENCE) within 12 months prior to index procedure. 4. Subject has a known left ventricular ejection fraction (LVEF) <30%. 5. Subject judged by physician as inappropriate for discontinuation from P2Y12 inhibitor use at 1 month, due to another condition requiring chronic P2Y12 inhibitor use. 6. Subject with planned surgery or procedure necessitating discontinuation of P2Y12 inhibitor within 1 month following index procedure. 7. Subject with a current medical condition with a life expectancy of less than 12 months. 8. *Subject intends to participate in an investigational drug or device trial within 12 months following the index procedure. Transferring to the XIENCE 90 study will not be an exclusion criterion.* 9. Pregnant or nursing subjects and those who plan pregnancy in the period up to 1 year following index procedure. Female subjects of child-bearing potential must have a negative

pregnancy test done within 7 days prior to the index procedure per site standard test. **Note**: Female patients of childbearing potential should be instructed to use safe contraception (e.g., intrauterine devices, hormonal contraceptives: contraceptive pills, implants, transdermal patches, hormonal vaginal devices, injections with prolonged release.) It is accepted, in certain cases, to include subjects having a sterilized regular partner or subjects using a double barrier contraceptive method. However, this should be explicitly justified in special circumstances arising from the study design, product characteristics and/or study population. 10. *Subject is part of a vulnerable population, defined as subject whose willingness to volunteer in a clinical investigation could be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or of retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples of populations which may contain vulnerable subjects include: individuals with lack of or loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving informed consent. Other vulnerable subjects include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor**,** members of the armed forces, and persons kept in detention.*	pregnancy test done within 7 days prior to the index procedure per site standard test. **Note**: Female subjects of childbearing potential should be instructed to use safe contraception (e.g., intrauterine devices, hormonal contraceptives: contraceptive pills, implants, transdermal patches hormonal vaginal devices, injections with prolonged release.) It is accepted, in certain cases, to include subjects having a sterilized regular partner or subjects using a double barrier contraceptive method. However, this should be explicitly justified in special circumstances arising from the trial design, product characteristics and/or trial population. 10. *Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.*	pregnancy test done within 7 days prior to the index procedure per site standard test. **Note**: Female subjects of childbearing potential should be instructed to use safe contraception (e.g., intrauterine devices, hormonal contraceptives: contraceptive pills, implants, transdermal patches, hormonal vaginal devices, injections with prolonged release.) It is accepted, in certain cases, to include subjects having a sterilized regular partner or subjects using a double barrier contraceptive method. However, this should be explicitly justified in special circumstances arising from the trial design, product characteristics and/or trial population. 10. *Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the subject's ability to participate in the clinical investigation or to comply with follow-up requirements, or impact the scientific soundness of the clinical investigation results.*

11. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint.	11. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint.	11. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint.
Angiographic Exclusion Criteria: 1. Target lesion is in a left main location. 2. Target lesion is located within an arterial or saphenous vein graft. 3. Target lesion is restenotic from a previous stent implantation. 4. *Target lesion is a total occluded lesion (TIMI flow 0).* 5. *Target lesion contains thrombus as indicated in the angiographic images (per SYNTAX score thrombus definition).* 6. Target lesion is implanted with overlapping stents, whether planned or for bailout. **Note**: If there is more than one target lesion, all target lesions must satisfy the angiographic eligibility criteria. Non-target lesion (i.e., lesions that do not meet the angiographic criteria listed above) treatments are not allowed during the index procedure.	**Angiographic Exclusion Criteria:** 1. Target lesion is in a left main location. 2. Target lesion is located within an arterial or saphenous vein graft. 3. Target lesion is restenotic from a previous stent implantation. 4. *Target lesion is a chronic total occlusion (CTO, defined as lesion with TIMI flow 0 for at least 3 months).* 5. Target lesion is implanted with overlapping stents, whether planned or for bailout. **Note:** If there is more than one target lesion, all target lesions must satisfy the angiographic eligibility criteria. Non-target lesion (i.e., lesions that do not meet the angiographic criteria listed above) treatments are not allowed during the index procedure.	**Angiographic Exclusion Criteria:** 1. Target lesion is in a left main location. 2. Target lesion is located within an arterial or saphenous vein graft. 3. Target lesion is restenotic from a previous stent implantation. 4. *Target lesion is a chronic total occlusion (CTO, defined as lesion with TIMI flow 0 for at least 3 months).* 5. Target lesion is implanted with overlapping stents, whether planned or for bailout. **Note**: If there is more than one target lesion, all target lesions must satisfy the angiographic eligibility criteria. Non-target lesion (i.e., lesions that do not meet the angiographic criteria listed above) treatments are not allowed during the index procedure.

Supplementary Table 2. Study endpoint definitions.

DEATH (Per ARC Circulation 2007; 115: 2344-2351)	
All death	All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal non-cardiac disease (e.g. cancer, infection) should be classified as cardiac.
Cardiac death	Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all procedure related deaths including those related to concomitant treatment.
Vascular death	Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause
MYOCARDIAL INFARCTION (MI)	
MI (Modified ARC)	Patients present any of the following clinical or imaging evidence of ischemia: • Clinical symptoms of ischemia; • ECG changes indicative of new ischemia - new ST-T changes or new left bundle branch block (LBBB), development of pathological Q waves*; • Imaging evidence of a new loss of viable myocardium or a new regional wall motion abnormality) AND confirmed with elevated cardiac biomarkers** per ARC criteria (Circulation 2007; 115: 2344-2351): • Periprocedural MI: • Within 48h after PCI: CK-MB >3 x URL or Troponin > 3 x URL with baseline value < URL • Within 72h after CABG: CK-MB >5 x URL or Troponin > 5 x URL with baseline value < URL • Spontaneous MI (> 48h following PCI, > 72h following CABG): CK-MB > URL or Troponin > URL with baseline value < URL * Pathologic Q waves may be defined according to the Global Task Force, Minnesota code, or Novacode **The assessment of CK-MB is preferred over the assessment of troponin for the diagnosis of peri-procedural MI, if possible. Baseline biomarker value requiring before study procedure and presumes a typical rise and fall.
Electrocardiographic Classification	
Q-wave MI [QMI]	Development of new pathological Q waves in 2 or more contiguous leads with or without post- procedure CK or CK-MB levels elevated above normal.
Non Q-wave MI [NQMI]	All MIs not classified as Q waves.
STENT THROMBOSIS (Per ARC Circulation 2007; 115: 2344-2351)	
Timing	
Acute*	0 - 24 hours post stent implantation
Subacute*	>24 hours. 30 days post stent implantation
Late†	30 days - 1-year post stent implantation
Very late†	>1-year post stent implantation

** Acute/subacute can also be replaced by early stent thrombosis. Early stent thrombosis (0 - 30 days) - this definition is currently used in the community.*
† Including "primary" as well as "secondary" late stent thrombosis; "secondary" late stent thrombosis is a stent thrombosis after a target segment revascularization.

Categories

Definite

Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation.

Angiographic confirmation of stent thrombosis*
The presence of a thrombus† that originates in the stent or in the segment 5 mm proximal or distal to the stent and presence of at least 1 of the following criteria within a 48-hour time window:

- Acute onset of ischemic symptoms at rest
- New ischemic ECG changes that suggest acute ischemia
- Typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI)
- Non-occlusive thrombosis
    - Thrombus Intracoronary thrombus is defined as a (spheric, ovoid, or irregular) non-calcified filling defect or lucency surrounded by contrast material (on 3 sides or within a coronary stenosis) seen in multiple projections, or persistence of contrast material within the lumen, or a visible embolization of intraluminal material downstream.
- Occlusive thrombus
    - TIMI 0 or TIMI 1 intrastent or proximal to a stent up to the most adjacent proximal side branch or main branch (if originates from the side branch).

Pathological confirmation of stent thrombosis
Evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy.
**The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent thrombosis (silent occlusion)*
† Intracoronary thrombus.

Probable

Clinical definition of probable stent thrombosis is considered to have occurred after intracoronary stenting in the following cases:

- Any unexplained death within the first 30 days‡
- Irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause
    - ‡ For studies with ST-elevation MI population, one may consider the exclusion of unexplained death within 30 days as evidence of probable stent thrombosis.

Possible

Clinical definition of possible stent thrombosis is considered to have occurred with any unexplained death from 30 days after intracoronary stenting until end of trial follow-up.

STROKE

An acute symptomatic episode of neurological dysfunction attributed to a vascular cause lasting more than 24 hours or lasting 24 hours or less with a brain imaging study or autopsy showing new infarction. an event that last < 24 hours may be adjudicated as a stroke if the following treatments were used: Pharmacologic, i.e., thrombolytic drug administration, or non-pharmacologic, i.e., neurointerventional procedure (e.g., intracranial angioplasty)

Categories

Ischemic Stroke	An acute symptomatic episode of focal cerebral, spinal, or retinal dysfunction caused by an infarction of central nervous system tissue.
Hemorrhagic Stroke	An acute symptomatic episode of focal or global cerebral or spinal dysfunction caused by a non-traumatic intraparenchymal, intraventricular, or subarachnoid hemorrhage.
Undetermined Stroke	A stroke with insufficient information to allow categorization as ischemic or hemorrhagic.

BLEEDING (Per BARC, Circulation 2011; 123: 2736-2747)

Categories

Type 0	No bleeding
Type 1	Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional
Type 2	Any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: (1) requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation
Type 3	
Type 3a	• Overt bleeding plus hemoglobin drop of 3 to < 5 g/dL[*] (provided hemoglobin drop is related to bleed) • Any transfusion with overt bleeding
Type 3b	• Overt bleeding plus hemoglobin drop ≥ 5 g/dL[*](provided hemoglobin drop is related to bleed) • Cardiac tamponade • Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) • Bleeding requiring intravenous vasoactive agents
Type 3c	• Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal) • Subcategories confirmed by autopsy or imaging or lumbar puncture • Intraocular bleed compromising vision
Type 4: CABG-related bleeding	• Perioperative intracranial bleeding within 48 h • Reoperation after closure of sternotomy for the purpose of controlling bleeding • Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period[†] • Chest tube output ≥ 2L within a 24-h period
Type 5: fatal bleeding	
Type 5a	Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious

Type 5b	Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation
CABG related	CABG indicates coronary artery bypass graft. Platelet transfusions should be recorded and reported but are not included in these definitions until further information is obtained about the relationship to outcomes. If a CABG-related bleed is not adjudicated as at least a type 3 severity event, it will be classified as not a bleeding event. If a bleeding event occurs with a clear temporal relationship to CABG (i.e., within a 48-h time frame) but does not meet type 4 severity criteria, it will be classified as not a bleeding event. * Corrected for transfusion (1 U packed red blood cells or 1 U whole blood=1 g/dL hemoglobin). † Cell saver products are not counted.
REVASCULARIZATION (Per ARC Circulation 2007; 115: 2344-2351)	
Target Lesion Revascularization (TLR)	TLR is defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLR should be classified prospectively as clinically indicated [CI] or not clinically indicated by the investigator prior to repeat angiography. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent.
Target Vessel Revascularization (TVR)	TVR is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The target vessel is defined as the entire major coronary vessel proximal and distal to the target lesion which includes upstream and downstream branches and the target lesion itself
Clinically Indicated [CI] Revascularization (TLR/TVR)	A revascularization is considered clinically indicated if angiography at follow-up shows a percent diameter stenosis ≥ 50% and if one of the following occurs: • A positive history of recurrent angina pectoris, presumably related to the target vessel; • Objective signs of ischemia at rest (ECG changes) or during exercise test (or equivalent), presumably related to the target vessel; • Abnormal results of any invasive functional diagnostic test (e.g., Doppler flow velocity reserve, fractional flow reserve); • A TLR/TVR with a diameter stenosis ≥70% in the absence of the above-mentioned ischemic signs or symptoms.

TARGET LESION FAILURE (TLF)

TLF is defined as a composite of all cardiac death, myocardial infarction attributed to target vessel or clinically-indicated TLR.

Supplementary Table 3. Baseline clinical characteristics of patients with and without diabetes mellitus.

	Patients with DM (N=1,299)	Patients without DM (N=2,053)	p-value
Clinical characteristics			
Age, years	73.4 ± 9.5	76.8 ± 8.4	<0.001
Female sex	435 (33.5%)	715 (34.8%)	0.426
Race			
White	931 (80.7%)	1608 (90.4%)	<0.001
Hispanic or Latino ethnicity	78 (6.1%)	115 (5.7%)	0.641
Asian	97 (8.4%)	71 (4.0%)	<0.001
Black or African American	88 (7.6%)	65 (3.7%)	<0.001
Hypertension	1205 (92.8%)	1737 (84.6%)	<0.001
Dyslipidemia	1064 (81.9%)	1490 (72.6%)	<0.001
Chronic kidney disease	549 (43.0%)	878 (44.0%)	0.570
Prior PCI	420 (32.3%)	575 (28.0%)	0.008
Prior CABG	166 (12.8%)	192 (9.4%)	0.002
Prior MI	241 (18.8%)	302 (14.9%)	0.003
Multivessel disease	652 (50.2%)	836 (40.7%)	<0.001
Chronic coronary syndrome	838 (64.5%)	1352 (65.9%)	0.426
Acute coronary syndrome	461 (35.5%)	701 (34.1%)	0.426
NSTEMI	148 (11.4%)	237 (11.5%)	0.894
Unstable angina	313 (24.1%)	464 (22.6%)	0.318
PARIS bleeding score	6.1 ± 2.3	6.0 ± 2.3	0.428
PRECISE-DAPT score*	26.9 ± 12.4	26.7 ± 10.9	0.678
High Bleeding Risk Criteria			
Age >=75 years	743 (57.2%)	1489 (72.5%)	<0.001
Indication to chronic oral anticoagulation	549 (42.3%)	870 (42.4%)	0.939
Anemia	271 (20.9%)	240 (11.7%)	<0.001
History of stroke	170 (13.1%)	197 (9.6%)	0.002
Renal insufficiency	191 (14.7%)	81 (3.9%)	<0.001
Thrombocytopenia	34 (2.7%)	34 (1.7%)	0.062
History of major bleeding	37 (2.8%)	66 (3.2%)	0.548
Number of HBR criteria	1.5 ± 0.8	1.5 ± 0.7	0.012
ESC Thrombotic Risk enhancers			
Diabetes	1299 (100%)	0 (0.0%)	N/A
Prior MI	241 (18.8%)	302 (14.9%)	0.003

	Patients with DM (N=1,299)	Patients without DM (N=2,053)	p-value
Multivessel CAD	652 (50.2%)	836 (40.7%)	<0.001
eGFR 15-59 ml/min	472 (36.3%)	805 (39.2%)	0.095
Premature CAD (age < 45 years)	6 (0.5%)	5 (0.2%)	0.282
Number of risk enhancers	2.1±0.9	0.9±0.8	<0.001
High or moderate thrombotic risk	1299 (100%)	1392 (67.8%)	<0.001

Continuous variables are reported as mean ± (SD), or median [IQR]. Categorical variables are reported as n (%).
DM: diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MI: myocardial infarction; PARIS: Patterns of non-adherence to anti-platelet regimens in stented patients, HBR: High Bleeding Risk, ESC: European Society of Cardiology
*The PRECISE-DAPT (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy) score includes 5 items: age, creatinine clearance, white blood cell count, hemoglobin, and history of bleeding

Supplementary Table 4. Procedural characteristics and therapy at discharge of patients with and without diabetes mellitus.

	Patients with DM (N=1,299)	Patients without DM (N=2,053)	p-value
Procedural characteristics			
Number of lesions treated	1.0 [1.0 - 1.0]	1.0 [1.0 - 1.0]	0.770
Number of vessels treated	1.0 [1.0 - 1.0]	1.0 [1.0 - 1.0]	0.278
Type B2/C lesion	477 (36.7%)	705 (34.3%)	0.160
Bifurcation	107 (8.2%)	207 (10.1%)	0.074
Radial access	747 (57.5%)	1258 (61.3%)	0.030
Number of stents per subject	1.0 [1.0 - 1.0]	1.0 [1.0 - 1.0]	0.468
Total stent length, mm	26.5 ± 13.9	26.1 ± 14.3	0.502
Pre-procedure RVD, mm	3.0 ± 0.5	3.0 ± 0.5	0.082
Pre-procedure % DS	83.6 ± 9.7	83.2 ± 10.0	0.241
Complex PCI, any of the following:	75 (5.8%)	106 (5.2%)	0.446
• ≥3 stents implanted	49 (3.8%)	69 (3.4%)	0.529
• ≥3 lesions treated	30 (2.3%)	56 (2.7%)	0.456
• ≥3 vessel treated	1 (0.1%)	6 (0.3%)	0.183
• Total stent length > 60mm	45 (3.5%)	81 (3.9%)	0.475
Antiplatelet therapy at discharge			
Aspirin	1145 (88.1%)	1776 (86.5%)	0.168
Clopidogrel	1070 (82.4%)	1736 (84.6%)	0.095
Prasugrel	29 (2.2%)	31 (1.5%)	0.124
Ticagrelor	201 (15.5%)	288 (14.0%)	0.248

Continuous variables are reported as mean ± (SD), or median [IQR]. Categorical variables are reported as n (%).
DM: diabetes mellitus; RVD: reference vessel diameter; DS; diameter stenosis.

Supplementary Table 5. Association between diabetes status and adverse events.

Outcomes	Patients with DM (N=1299)	Patients without DM (N=2053)	HR (95% CI)	p-value
All-cause death, or MI	120 (10.1%)	128 (6.6%)	1.51 (1.18 - 1.94)	0.001
All-cause death	64 (5.6%)	88 (4.5%)	1.16 (0.84 - 1.60)	0.377
Cardiovascular death	36 (3.3%)	45 (2.3%)	1.27 (0.82 - 1.97)	0.282
MI	65 (5.4%)	48 (2.6%)	2.18 (1.50 - 3.17)	<0.001
Definite or probable ST	5 (0.5%)	5 (0.3%)	1.60 (0.46 - 5.52)	0.459
Stroke	23 (1.9%)	21 (1.2%)	1.74 (0.96 - 3.15)	0.066
Ischemic stroke	20 (1.7%)	19 (1.1%)	1.68 (0.89 - 3.14)	0.107
Target lesion failure	83 (7.1%)	87 (4.6%)	1.54 (1.14 - 2.08)	0.005
Target lesion revascularization	22 (1.9%)	22 (1.2%)	1.60 (0.88 - 2.89)	0.120
Target vessel revascularization	39 (3.4%)	36 (2.0%)	1.74 (1.10 - 2.73)	0.017
Target vessel MI	52 (4.3%)	37 (2.0%)	2.17 (1.42 - 3.33)	<0.001
BARC type 2-5	112 (9.5%)	175 (9.2%)	1.02 (0.80 - 1.29)	0.902
BARC type 3-5	55 (4.6%)	80 (4.2%)	1.09 (0.78 - 1.54)	0.610
NACE	165 (13.7%)	205 (10.6%)	1.30 (1.06 - 1.59)	0.013

The percentages mentioned above represent K-M rates at 12 months after index procedure
MI: myocardial infarction; ST: stent thrombosis; BARC: Bleeding Academic Research Consortium; NACE: net adverse clinical events

Supplementary Table 6. Effect of 1- versus 3-month DAPT on outcomes between 1 and 12 months after PCI in patients stratified according to presence of diabetes and insulin treatment.

	No diabetes (N=2053)				Non-insulin dependent diabetes (N= 875)				Insulin dependent diabetes (N= 424)				
	XIENCE 28 1-month DAPT (N= 870)	XIENCE 90 3-month DAPT (N=1183)	Adjusted Hazard ratio† (95% CI)	P-value (95% CI)	XIENCE 28 1-month DAPT (N= 352)	XIENCE 90 3-month DAPT (N= 523)	Adjusted Hazard ratio□† (95% CI)	P-value (95% CI)	XIENCE 28 1-month DAPT (N= 160)	XIENCE 90 3-month DAPT (N= 264)	Adjusted Hazard ratio□† (95% CI)	P-value (95% CI)	Interaction p-value‡
All-cause death, or MI	64 (7.8%)	64 (5.7%)	1.25 (0.87 - 1.81)	0.230	27 (8.6%)	52 (11.1%)	0.70 (0.43 - 1.13)	0.143	12 (7.9%)	29 (11.7%)	0.71 (0.36 - 1.40)	0.319	0.035
All-cause death	40 (4.8%)	48 (4.2%)	0.98 (0.63 - 1.53)	0.922	17 (5.4%)	25 (5.7%)	0.87 (0.46 - 1.67)	0.681	7 (4.7%)	15 (6.3%)	0.81 (0.32 - 2.02)	0.650	0.696
Cardiovascular death	22 (2.6%)	23 (2.0%)	1.15 (0.62 - 2.13)	0.660	7 (2.5%)	14 (3.2%)	0.65 (0.25 - 1.68)	0.373	3 (1.9%)	12 (5.2%)	0.45 (0.12 - 1.61)	0.216	0.281
MI	25 (3.1%)	23 (2.1%)	1.51 (0.83 - 2.75)	0.173	10 (3.3%)	30 (6.3%)	0.48 (0.23 - 1.00)	0.051	5 (3.2%)	20 (7.7%)	0.43 (0.16 - 1.17)	0.100	0.014
Definite or probable ST	3 (0.4%)	2 (0.2%)	2.08 (0.32 - 13.6)	0.443	1 (0.3%)	3 (0.8%)	0.61 (0.06 - 6.13)	0.671	0 (0.0%)	1 (0.4%)	N/A	N/A	0.325
Stroke	6 (0.9%)	15 (1.4%)	0.44 (0.16 - 1.20)	0.110	2 (0.6%)	11 (2.4%)	0.27 (0.06 - 1.26)	0.096	3 (2.0%)	7 (2.8%)	0.59 (0.15 - 2.40)	0.462	0.412
Ischemic stroke	5 (0.8%)	14 (1.3%)	0.39 (0.13 - 1.13)	0.083	2 (0.6%)	10 (2.2%)	0.28 (0.06 - 1.36)	0.115	2 (1.3%)	6 (2.4%)	0.38 (0.07 - 2.03)	0.256	0.565
TLF	47 (5.8%)	40 (3.6%)	1.57 (1.01 - 2.45)	0.046	17 (5.6%)	37 (8.0%)	0.63 (0.35 - 1.15)	0.136	5 (3.2%)	24 (9.8%)	0.36 (0.14 - 0.95)	0.040	0.013
TLR	9 (1.1%)	13 (1.2%)	1.08 (0.44 - 2.63)	0.863	8 (2.6%)	9 (1.9%)	1.31 (0.49 - 3.53)	0.592	1 (0.7%)	4 (1.5%)	0.33 (0.03 - 3.21)	0.340	0.639
TVR	16 (2.2%)	20 (1.9%)	1.28 (0.64 - 2.55)	0.483	11 (3.9%)	18 (3.7%)	0.90 (0.41 - 1.95)	0.782	2 (1.3%)	8 (3.1%)	0.38 (0.08 - 1.85)	0.229	0.658
BARC type 2-5 bleeding	64 (8.1%)	111 (10.1%)	0.78 (0.57 - 1.08)	0.134	24 (7.4%)	43 (9.1%)	0.64 (0.37 - 1.08)	0.093	15 (9.7%)	30 (12.8%)	0.74 (0.39 - 1.41)	0.363	0.987
BARC type 3-5 bleeding	28 (3.5%)	52 (4.7%)	0.72 (0.45 - 1.17)	0.187	12 (3.9%)	24 (5.1%)	0.57 (0.28 - 1.19)	0.138	9 (5.8%)	10 (4.0%)	1.32 (0.52 - 3.36)	0.556	0.902
NACE	91 (11.2%)	114 (10.1%)	1.02 (0.76 - 1.37)	0.890	33 (10.2%)	75 (15.8%)	0.55 (0.36 - 0.84)	0.006	20 (12.9%)	37 (14.7%)	0.85 (0.49 - 1.49)	0.568	0.022

DAPT: dual-antiplatelet therapy, MI: myocardial infarction, ST: stent thrombosis, TLF: target lesion failure, TLR: target lesion revascularization, TVR: target vessel revascularization, NACE: net adverse clinical events † Propensity stratified outcomes according to gender, baseline serum creatinine, anticoagulation therapy, stroke, history of major bleeding, baseline platelet, baseline hemoglobin, BMI, hypertension, hypercholesterolemia, prior PCI, prior CABG, prior MI, multi-vessel disease, diabetes, B2/C lesion, total lesion length, mean pre RVD, mean pre DS, bifurcation lesion, number of lesion treated, number of vessel treated, number of stents, total stent length, P2Y12 on discharged, PARIS risk score for major bleeding, PRECISE DAPT risk score for bleeding
‡ P value is obtained from the interaction test between diabetes statu/type and DAPT after applying multiple imputation and propensity score stratification
The percentages mentioned above represent K-M rates at 12 months after index procedure

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author with permission of Abbott.