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ORIGINAL RESEARCH

One- versus three-month dual antiplatelet therapy in high bleeding risk patients undergoing percutaneous coronary intervention for non-ST-segment elevation acute coronary syndromes

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ABSTRACT

BACKGROUND: A short dual antiplatelet therapy (DAPT) duration has been proposed for patients at high bleeding risk (HBR) undergoing drug-eluting coronary stent (DES) implantation. Whether this strategy is safe and effective after a non-ST-segment elevation acute coronary syndrome (NSTE-ACS) remains uncertain.

AIMS: We aimed to compare the impact of 1-month versus 3-month DAPT on clinical outcomes after DES implantation among HBR patients with or without NSTE-ACS.

METHODS: This is a prespecified analysis from the XIENCE Short DAPT programme involving three prospective, international, single-arm studies evaluating the safety and efficacy of 1-month (XIENCE 28 USA and Global) or 3-month (XIENCE 90) DAPT among HBR patients after implantation of a cobalt-chromium everolimus-eluting stent. Ischaemic and bleeding outcomes associated with 1- versus 3-month DAPT were assessed according to clinical presentation using propensity score stratification.

RESULTS: Of 3,364 HBR patients (1,392 on 1-month DAPT and 1,972 on 3-month DAPT), 1,164 (34.6%) underwent DES implantation for NSTE-ACS. At 12 months, the risk of the primary endpoint of death or myocardial infarction was similar between 1- and 3-month DAPT in patients with (hazard ratio [HR] 1.09, 95% confidence interval [CI]: 0.71-1.65) and without NSTE-ACS (HR 0.88, 95% CI: 0.63-1.23; p-interaction=0.34). The key secondary endpoint of Bleeding Academic Research Consortium (BARC) Type 2-5 bleeding was consistently reduced in both NSTE-ACS (HR 0.57, 95% CI: 0.37-0.88) and stable patients (HR 0.84, 95% CI: 0.61-1.15; p-interaction=0.15) with 1-month DAPT.

CONCLUSIONS: Among HBR patients undergoing implantation of an everolimus-eluting stent, 1-month, compared to 3-month DAPT, was associated with similar ischaemic risk and reduced bleeding at 1 year, irrespective of clinical presentation.

KEYWORDS: ACS/NSTE-ACS; adjunctive pharmacotherapy; bleeding; drug-eluting stent; myocardial infarction

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Dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ receptor inhibitor is recommended for up to 12 months after percutaneous coronary intervention (PCI) for acute coronary syndromes (ACS) to prevent recurrent ischaemic events[1,2]. However, DAPT is encumbered by a significant risk of bleeding complications, which are proportional to the duration of treatment and negatively affect patient morbidity and mortality[3-5]. Up to 40% of patients undergoing PCI present with clinical conditions associated with a high bleeding risk (HBR) that make prolonging the duration of DAPT unattractive[6-8]. Among those patients, a DAPT duration shorter than the standard 6-month course has been proposed to mitigate the bleeding risk without compromising the antithrombotic protection[9], but evidence in support of this practice in an ACS setting is scarce[10-14].

The XIENCE Short DAPT clinical programme has previously demonstrated that among HBR patients undergoing PCI with cobalt-chromium everolimus-eluting stents for either an acute or chronic coronary syndrome, but without ST-segment elevation myocardial infarction (STEMI), DAPT for 1 or 3 months followed by aspirin monotherapy was non-inferior to a historical control of 6- or 12-month DAPT for ischaemic outcomes and superior in preventing bleeding[15-17]. Moreover, in the overall study population, the 1-month regimen, compared with the 3-month, was associated with a similar ischaemic risk and further reduced bleeding events at 1 year[17]. With the present analysis, we aimed to compare the impact of 1-month versus 3-month DAPT on the clinical outcomes of HBR patients undergoing PCI according to clinical presentation (i.e., with or without non-ST-segment elevation ACS [NSTE-ACS]).

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Impact on daily practice

Acute coronary syndrome (ACS) presentation is known to be associated with high rates of recurrent ischaemic and bleeding events. A short dual antiplatelet therapy (DAPT) duration has been proposed for high bleeding risk (HBR) patients undergoing percutaneous coronary intervention (PCI); however, there is little evidence in support of this practice after an ACS. Our analysis from the XIENCE Short DAPT programme suggests that, among HBR patients undergoing non-complex PCI for either non-ST-segment elevation ACS (NSTE-ACS) or chronic coronary syndrome, 1-month compared with 3-month DAPT is associated with a similar ischaemic risk and reduced bleeding. These findings support the safety and efficacy of a very short DAPT duration as a bleeding avoidance strategy, irrespective of clinical presentation. Future studies should explore the optimal antithrombotic agent, whether aspirin or $P2Y_{12}$ inhibitor monotherapy, for long-term secondary prevention after early DAPT discontinuation among HBR patients.

Methods

STUDY DESIGN

This is a prespecified substudy within the XIENCE Short DAPT programme, which consisted of three prospective, multicentre trials conducted at 101 sites in the USA (XIENCE 90; ClinicalTrials.gov: NCT03218787), 58 sites in the USA and Canada (XIENCE 28 USA; ClinicalTrials.gov: NCT03815175), and 52 sites in Europe and Asia (XIENCE 28 Global; ClinicalTrials.gov: NCT03355742) from July 2017 to February 2020. The study rationale, design, and principal results have been previously reported[15-17]. In brief, this clinical programme explored two different DAPT durations in patients undergoing PCI with a fluoropolymer-based cobalt-chromium everolimus-eluting stent (XIENCE [Abbott]). The XIENCE 28 and 90 studies were executed under near-identical protocols, except for the DAPT duration. It was prespecified that the USA and Global studies of XIENCE 28 were to be pooled together for data analysis. Abbott sponsored the studies. An independent data monitoring committee provided external oversight to ensure public safety. All enrolled patients provided written informed consent.

STUDY POPULATION

After successful PCI with the XIENCE stent, patients were eligible for inclusion in the study if at least one of the following HBR criteria was met: age ≥75 years, indication for chronic anticoagulant therapy, history of major bleeding within 12 months of the index procedure, history of ischaemic or haemorrhagic stroke, renal insufficiency (creatinine ≥2.0 mg/dL) or failure (maintenance dialysis), anaemia (haemoglobin <11 g/dL), and systemic conditions associated with an increased risk for bleeding, including haematological disorders such as thrombocytopaenia (platelet count <100,000/mm^3) and coagulation disorders[15-17]. All studies allowed treatment of up to 3 target lesions, with a maximum of 2 target lesions per epicardial vessel, and treatment of bifurcation lesions without 2-stent techniques during index PCI. Key exclusion criteria were presentation with STEMI, implantation of a drug-eluting stent other than a cobalt-chromium everolimus-eluting stent in the previous 12 months, target lesions that were in-stent restenosis or chronic total occlusions, those requiring overlapping stents, located in the left main stem, arterial or venous graft, or lesions containing thrombus (for XIENCE 90 only). After index PCI, all patients received open-label aspirin plus a $P2Y_{12}$ inhibitor, preferably

Abbreviations

ACS	acute coronary syndrome
BARC	Bleeding Academic Research Consortium
CCS	chronic coronary syndrome
DAPT	dual antiplatelet therapy
HBR	high bleeding risk
MI	myocardial infarction
NSTE-ACS	non-ST-segment elevation acute coronary syndrome
NSTEMI	non-ST-segment elevation myocardial infarction
PCI	percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction

clopidogrel. Eligibility to discontinue DAPT was assessed at 1 month after index PCI in XIENCE 28 and at 3 months in XIENCE 90. Patients who had been adherent to treatment and free from myocardial infarction (MI), repeat coronary revascularisation, stroke, and stent thrombosis discontinued the $P2Y_{12}$ inhibitor and continued aspirin until the end of the study. Follow-up was performed in person or via telephone at 1, 3, 6, and 12 months after index PCI in XIENCE 28, and at 3, 6, and 12 months in XIENCE 90. Per the study protocol, eligibility to discontinue DAPT was assessed at different time points in the XIENCE 28 and 90 programmes. Patients from XIENCE 90 who were event free and adherent to treatment at 1 month were retrospectively selected to match the XIENCE 28 event-free population.

CLINICAL ENDPOINTS

The primary endpoint was the composite of all-cause death or MI between 1 and 12 months after index PCI. The key secondary endpoint was Bleeding Academic Research Consortium (BARC) Type 2 to 5 bleeding[18]. Other secondary endpoints included target lesion failure (a composite of cardiovascular death, target vessel MI, or target lesion revascularisation), the individual components of the composite endpoints, stroke, definite or probable stent thrombosis, and BARC Type 3 to 5 bleeding. All clinical events were adjudicated by an independent event committee.

STATISTICAL ANALYSIS

The effects of 1- versus 3-month DAPT on ischaemic and bleeding outcomes were evaluated according to clinical presentation (NSTE-ACS vs chronic coronary syndrome [CCS]) at the time of PCI. The clinical and procedural characteristics of each group are summarised using means and standard deviations for continuous variables or counts and percentages for categorical ones. The Chi-square test and Student's t-test were used to compare groups, as appropriate. The cumulative incidence rates for both the primary and secondary endpoints were calculated with the Kaplan-Meier method. Hazard ratios (HR) and 95% confidence intervals (CI) were generated using Cox proportional hazard models. Because the treatment arms were not randomised, adjusted risks for all endpoints were estimated using propensity score stratification into quintiles. Propensity scores were derived using a logistic regression model that included the treatment group as the outcome and the selected baseline demographic, clinical, and procedural covariates as the predictors[16,17]. The Markov Chain Monte Carlo multiple imputation method was applied to handle missing data in the propensity score building with the Within approach[19]. The Rubin's combination rule was used to integrate the final analysis with each of the 10 imputed datasets. **Supplementary Figure 1** shows 10 different balance plots with standardised mean differences in baseline covariates before and after propensity score stratification. Heterogeneity of treatment effects by clinical presentation was examined with a subgroup by treatment interaction term.

As all patients in the trials were treated with single antiplatelet therapy (i.e., aspirin) after 3 months of PCI, landmark analyses at 3 months were performed to isolate the effects of actual treatment difference (1-3 months) between the two DAPT arms. In a secondary analysis, treatment effects were estimated across the spectrum of NSTE-ACS presentation, including non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina, with formal interaction testing to assess for effect modification. A sensitivity analysis was conducted by excluding patients on oral anticoagulation from the comparison between 1- versus 3-month DAPT. A 2-sided p-value of <0.05 was considered statistically significant. All analyses were performed using Stata version 16.0 (StataCorp).

Results

POPULATION CHARACTERISTICS

A total of 3,652 patients were enrolled in the XIENCE Short DAPT programme. Out of 3,364 eligible patients at 1 month **(Figure 1)**, 1,164 (34.6%) patients had undergone PCI for NSTE-ACS, and 2,200 (65.4%) for CCS. Among NSTE-ACS patients, 475 received 1-month DAPT and 689 received 3-month DAPT; in the CCS group, 917 and 1,283 were treated with 1- and 3-month DAPT, respectively **(Figure 1)**.

Baseline clinical and procedural characteristics by clinical presentation are reported in **Supplementary Table 1**. NSTE-ACS patients were more likely to be women, Asian or African American, to have a history of MI, anaemia, and higher Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy (PRECISE-DAPT) and Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients (PARIS) bleeding scores[20,21]. Radial access, complex lesions, and ticagrelor use at discharge were more frequent among NSTE-ACS patients. Baseline characteristics according to treatment arm by clinical presentation are summarised in **Table 1**, while DAPT use at different time points up to 1 year is reported in **Supplementary Figure 2**.

ISCHAEMIC OUTCOMES

As shown in **Supplementary Table 2**, NSTE-ACS patients experienced numerically higher rates of the primary endpoint of all-cause death or MI (9.0% vs 7.4%; p=0.074), primarily driven by an increased risk of MI at 1 year (5.3% vs 2.8%; p<0.001). In the NSTE-ACS cohort, the primary endpoint occurred in 9.6% of patients receiving 1-month DAPT and 8.5% of those on 3-month DAPT. After propensity score stratification, the risk of death or MI was similar between the two groups (adjusted [adj.] HR 1.09, 95% CI: 0.71-1.65) **(Figure 2)**. The adjusted risks for the secondary ischaemic endpoints were also similar among NSTE-ACS patients on 1- versus 3-month DAPT, including all-cause death (adj. HR 0.85, 95% CI: 0.41-1.37), MI (adj. HR 1.13, 95% CI: 0.65-1.96), stroke (adj. HR 0.39, 95% CI: 0.12-1.27) and target lesion failure (adj. HR 0.99, 95% CI: 0.61-1.59). Consistent treatment effects were observed in CCS patients for the primary endpoint (adj. HR 0.88, 95% CI: 0.63-1.24) as well as other secondary endpoints, with no significant interaction between clinical presentation and DAPT duration **(Figure 2, Table 2)**.

BLEEDING OUTCOMES

The 1-year incidence of the key secondary endpoint of BARC Type 2 to 5 bleeding was similar between NSTE-ACS and CCS patients (10.1% vs 8.9%; p=0.213) **(Supplementary Table 2)**.

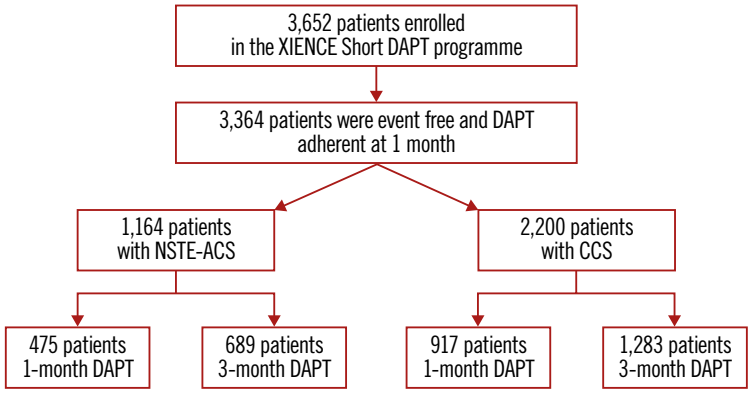


Figure 1. *Study population. CCS: chronic coronary syndrome; DAPT: dual antiplatelet therapy; NSTE-ACS: non-ST-segment elevation acute coronary syndrome*

In the NSTE-ACS cohort, BARC 2-5 bleeding occurred in 7.3% of those on 1-month DAPT versus 12.2% on 3-month DAPT, with a significant risk reduction after propensity score stratification (adj. HR 0.57, 95% CI: 0.37-0.88) **(Figure 2)**. Similar treatment effects on BARC 2-5 bleeding were observed in CCS patients for 1 versus 3 months of DAPT (adj. HR 0.84, 95% CI: 0.61-1.15; p-interaction=0.15). The risk of major BARC 3-5 bleeding did not differ between treatment arms for either NSTE-ACS (adj. HR 0.66, 95% CI: 0.36-1.19) and CCS patients (adj. HR 0.80, 95% CI: 0.50-1.27; p-interaction=0.63) **(Figure 2, Table 2)**.

EXPLORATORY ANALYSES

Landmark analyses between 1 and 3 months **(Figure 3)** showed a numerical increase in the risk of death or MI with 1- versus 3-month DAPT among NSTE-ACS (adj. HR 2.05, 95% CI: 0.74-5.66) but not CCS patients (adj. HR 0.51, 95% CI: 0.25-1.07; p-interaction=0.032). This finding was primarily driven by differences in the risk of MI (p-interaction=0.040) and to a lesser extent the risk of death (p-interaction=0.076). Conversely, between 3 and 12 months when both arms were on aspirin monotherapy, treatment effects on death or MI were consistent between CCS and NSTE-ACS patients (p-interaction=0.726).

The bleeding risk at 3 months was lower with 1- versus 3-month DAPT without evidence of heterogeneity by clinical presentation (p-interaction=0.237 for BARC 2-5; p-interaction=0.429 for BARC 3-5). No significant differences between treatment arms were observed beyond 3 months up to 1 year.

In the analysis by NSTE-ACS subtypes **(Table 3)**, there was no signal of treatment effect modification according to presentation for NSTEMI, unstable angina, or CCS, with respect to both ischaemic and bleeding events.

In the sensitivity analysis excluding patients on oral anticoagulation **(Table 4)**, the risk of the primary and key secondary endpoints with 1- versus 3-month DAPT according to clinical presentation remained consistent with the primary analysis. A significant interaction between clinical presentation and DAPT duration was observed for MI (p-interaction=0.012), with a lower risk associated with 1-month DAPT in CCS but not NSTE-ACS patients.

Discussion

In a large cohort of HBR patients undergoing successful, non-complex PCI with a cobalt-chromium everolimus-eluting stent, who had been adherent to treatment and free from ischaemic events while on DAPT, discontinuation of the $P2Y_{12}$ inhibitor after 1 month compared with 3 months was associated with a similar ischaemic risk and reduced actionable bleeding events, irrespective of clinical presentation at the time of PCI. Although NSTE-ACS compared with CCS presentation was associated with a 2-fold higher risk of MI at 12-month follow-up, extending DAPT to 3 months did not appear to confer an extra ischaemic protection across the spectrum of HBR patients. Conversely, the incidence of BARC Type 2-5 bleeding was comparable between NSTE-ACS and CCS patients, with both subgroups deriving consistent benefit from 1-month DAPT **(Central illustration)**.

The XIENCE Short DAPT programme was designed to assess the safety and efficacy of two abbreviated DAPT regimens (1 month in XIENCE 28 and 3 months in XIENCE 90) which have previously been shown to be non-inferior to a historical cohort of patients receiving 6 to 12 months of DAPT for the primary endpoint of death or MI[16]. Other stent platforms have proven similar safety with a DAPT duration as short as 3 months but, at variance with our study, failed to include ACS patients[22]. In a more recent analysis from XIENCE Short DAPT involving the overall study population, DAPT for 1 month compared with 3 months was associated with a similar ischaemic risk and lower bleeding complications at 1-year follow-up[17]. The present substudy extends these observations to HBR patients presenting with NSTE-ACS, in whom bleeding avoidance strategies that do not compromise antithrombotic efficacy are most challenging.

Real-world registries have reported on the prevalence and prognostic impact of HBR conditions in relation to clinical presentation at the time of PCI[23,24]. Advanced age, oral anticoagulation, and anaemia were the most frequent HBR conditions, the latter being more prevalent among NSTE-ACS than CCS patients in our study, together with higher PRECISE-DAPT and PARIS bleeding risk scores. ACS presentation, *per se*, has previously been found to be an independent predictor of bleeding, with a graded relationship across ACS subtypes:

Table 1. Baseline characteristics.

	NSTE-ACS (N=1,164)			CCS (N=2,200)		
	1-month DAPT N=475 (40.8)	3-month DAPT N=689 (59.2)	*p*-value	1-month DAPT N=917 (41.7)	3-month DAPT N=1,283 (58.3)	*p*-value
High bleeding risk criteria						
Age ≥75 years	308 (64.8)	447 (64.9)	0.990	641 (69.9)	845 (65.9)	0.046
Chronic anticoagulant therapy	201 (42.3)	280 (40.6)	0.568	416 (45.4)	525 (40.9)	0.036
Anaemia	90 (18.9)	119 (17.3)	0.464	111 (12.1)	194 (15.1)	0.045
History of stroke	54 (11.4)	86 (12.5)	0.566	91 (9.9)	137 (10.7)	0.573
Renal insufficiency	51 (10.7)	47 (6.8)	0.018	65 (7.1)	110 (8.6)	0.207
Thrombocytopaenia	15 (3.2)	14 (2.1)	0.235	16 (1.8)	24 (1.9)	0.900
History of major bleeding	19 (4.0)	25 (3.6)	0.744	27 (2.9)	32 (2.5)	0.517
Number of HBR criteria	1.6±0.7	1.5±0.7	0.074	1.5±0.7	1.5±0.7	0.246
Clinical characteristics						
Age, years	75.6±9.3	74.9±9.4	0.191	76.2±7.8	75.2±9.4	0.010
Female	170 (35.8)	260 (37.7)	0.499	283 (30.9)	441 (34.4)	0.084
Race						
American Indian or Alaskan native	2 (0.6)	4 (0.6)	1.000	0 (0.0)	7 (0.5)	0.103
Asian	56 (17.8)	18 (2.6)	<0.001	70 (10.7)	27 (2.1)	<0.001
Black or African American	18 (5.7)	47 (6.8)	0.516	18 (2.7)	70 (5.5)	0.007
Native Hawaiian or Pacific Islander	0 (0.0)	0 (0.0)	N/A	0 (0.0)	5 (0.4)	0.174
White	238 (75.8)	597 (86.6)	<0.001	569 (86.6)	1,142 (89.0)	0.120
Hispanic or Latino ethnicity	55 (12.2)	18 (2.6)	<0.001	83 (9.6)	38 (3.0)	<0.001
Hypertension	405 (85.3)	626 (90.9)	0.003	774 (84.4)	1,145 (89.2)	<0.001
Dyslipidaemia	309 (65.1)	580 (84.2)	<0.001	630 (68.7)	1,042 (81.2)	<0.001
Diabetes mellitus	179 (37.8)	282 (40.9)	0.291	333 (36.6)	505 (39.4)	0.186
Chronic kidney disease	232 (50.2)	277 (40.6)	0.001	399 (46.0)	524 (41.1)	0.026
Prior PCI	120 (25.3)	231 (33.5)	0.003	270 (29.4)	376 (29.3)	0.944
Prior CABG	37 (7.8)	77 (11.2)	0.056	75 (8.2)	169 (13.2)	<0.001
Prior MI	93 (19.7)	131 (19.4)	0.891	134 (14.7)	186 (14.7)	0.983
Multivessel disease	184 (38.7)	321 (46.6)	0.008	389 (42.4)	597 (46.5)	0.056
NSTEMI	245 (51.6)	141 (20.5)	<0.001	-	-	-
Unstable angina	230 (48.4)	548 (79.5)	<0.001	-	-	-
PARIS bleeding risk score	6.5±2.3	6.1±2.3	0.001	5.9±2.3	6.0±2.3	0.381
PARIS bleeding risk score	6.0 [5.0-8.0]	6.0 [4.0-8.0]	<0.001	6.0 [4.0-8.0]	6.0 [4.0-8.0]	0.472
PRECISE-DAPT bleeding risk score	29.4±12.3	26.7±11.6	<0.001	26.8±10.6	25.9±11.7	0.101
PRECISE-DAPT bleeding risk score	28.0 [22.0-37.0]	26.0 [19.0-33.0]	<0.001	26.0 [19.0-32.0]	25.0 [18.0-32.0]	0.058
Procedural characteristics						
Number of lesions treated	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.945	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.972
Number of vessels treated	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.144	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.408
B2/C lesion	197 (41.5)	257 (37.3)	0.151	301 (32.8)	430 (33.5)	0.735
Bifurcation lesion	51 (10.7)	57 (8.3)	0.154	110 (12.0)	96 (7.5)	<0.001
Radial access	371 (78.1)	414 (60.1)	<0.001	615 (67.1)	614 (47.9)	<0.001
Number of stents per subject	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.844	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.653
Total stent length, mm	28.6±15.3	26.5±14.5	0.021	26.5±13.9	25.0±13.4	0.013
Preprocedural RVD, mm	3.0±0.5	3.0±0.5	0.856	3.0±0.5	3.0±0.5	0.190
Preprocedural %DS	85.0±10.8	84.4±9.9	0.363	81.3±9.9	83.7±9.4	<0.001
Antiplatelet therapy at discharge						
Aspirin	424 (89.3)	644 (93.5)	0.010	708 (77.2)	1,157 (90.2)	<0.001
Clopidogrel	368 (77.5)	551 (80.0)	0.304	836 (91.2)	1,061 (82.7)	<0.001
Prasugrel	4 (0.8)	19 (2.8)	0.021	10 (1.1)	27 (2.1)	0.068
Ticagrelor	103 (21.7)	120 (17.4)	0.069	71 (7.7)	197 (15.4)	<0.001

Values are n (%), mean±SD or n [IQR]. CABG: coronary artery bypass grafting; CCS: chronic coronary syndrome; DAPT: dual antiplatelet therapy; DS: diameter stenosis; HBR: high bleeding risk; IQR: interquartile range; MI: myocardial infarction; N/A: not applicable; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; 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; RVD: reference vessel diameter; SD: standard deviation

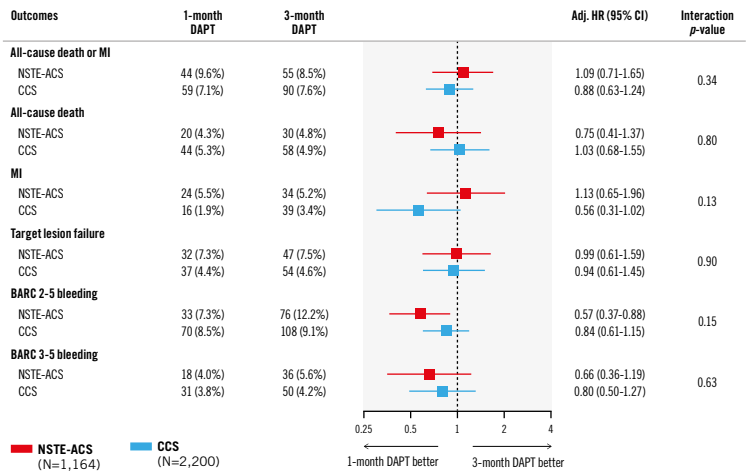


Figure 2. *Clinical outcomes with 1-month versus 3-month DAPT by clinical presentation. Adj. HR: adjusted hazard ratio; BARC: Bleeding Academic Research Consortium; CCS: chronic coronary syndrome; CI: confidence interval; DAPT: dual antiplatelet therapy; MI: myocardial infarction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome*

Table 2. Primary and secondary outcomes with 1-month versus 3-month DAPT by clinical presentation.

Outcomes	NSTE-ACS (N=1,164)				CCS (N=2,200)				Interaction *p*-value‡
	1-month DAPT (N=475)	3-month DAPT (N=689)	Adjusted hazard ratio† (95% CI)	*p*-value	1-month DAPT (N=917)	3-month DAPT (N=1,283)	Adjusted hazard ratio† (95% CI)	*p*-value	
All-cause death or MI	44 (9.6)	55 (8.5)	1.09 (0.71-1.65)	0.703	59 (7.1)	90 (7.6)	0.88 (0.63-1.24)	0.479	0.337
All-cause death	20 (4.3)	30 (4.8)	0.75 (0.41-1.37)	0.352	44 (5.3)	58 (4.9)	1.03 (0.68-1.55)	0.885	0.803
Cardiovascular death	13 (2.8)	19 (3.1)	0.90 (0.43-1.90)	0.783	19 (2.3)	30 (2.6)	0.84 (0.46-1.54)	0.580	0.798
MI	24 (5.5)	34 (5.2)	1.13 (0.65-1.96)	0.658	16 (1.9)	39 (3.4)	0.56 (0.31-1.02)	0.059	0.134
Definite or probable ST	0 (0.0)	3 (0.5)	N/A	N/A	4 (0.5)	3 (0.3)	2.32 (0.50-10.81)	0.282	0.992
Stroke	4 (0.9)	12 (1.9)	0.39 (0.12-1.27)	0.118	7 (1.0)	21 (1.8)	0.43 (0.18-1.05)	0.064	0.959
Ischaemic stroke	3 (0.7)	10 (1.6)	0.32 (0.08-1.22)	0.095	6 (0.9)	20 (1.7)	0.37 (0.14-0.95)	0.040	0.964
Target lesion failure	32 (7.3)	47 (7.5)	0.99 (0.61-1.59)	0.957	37 (4.4)	54 (4.6)	0.94 (0.61-1.45)	0.775	0.897
Target lesion revascularisation	6 (1.4)	16 (2.6)	0.56 (0.21-1.50)	0.250	12 (1.5)	10 (0.8)	1.77 (0.74-4.23)	0.198	0.079
Target vessel revascularisation	9 (2.3)	23 (3.7)	0.56 (0.25-1.26)	0.162	20 (2.6)	23 (1.9)	1.35 (0.72-2.51)	0.347	0.123
BARC 2-5 bleeding	33 (7.3)	76 (12.2)	0.57 (0.37-0.88)	0.011	70 (8.5)	108 (9.1)	0.84 (0.61-1.15)	0.270	0.150
BARC 3-5 bleeding	18 (4.0)	36 (5.6)	0.66 (0.36-1.19)	0.166	31 (3.8)	50 (4.2)	0.80 (0.50-1.27)	0.341	0.632

Data are presented as number of events (%). The percentages represent Kaplan-Meier rates between 1 and 12 months after the index procedure. †Propensity-stratified outcomes according to sex, baseline serum creatinine, anticoagulation therapy, history of stroke, history of major bleeding, baseline platelet, baseline haemoglobin, BMI, hypertension, hypercholesterolaemia, prior PCI, prior CABG, prior MI, multivessel disease, diabetes, B2/C lesion, total lesion length, mean preprocedural RVD, mean preprocedural %DS, bifurcation lesion, number of lesions treated, number of vessels treated, number of stents, total stent length, $P2Y_{12}$ inhibitor at discharge, PARIS risk score for major bleeding, and PRECISE-DAPT risk score for bleeding. ‡P-value is obtained from the interaction test between clinical presentation and DAPT treatment. BARC: Bleeding Academic Research Consortium; BMI: body mass index; CABG: coronary artery bypass grafting; CI: confidence interval; CCS: chronic coronary syndrome; DAPT: dual antiplatelet therapy; DS: diameter stenosis; MI: myocardial infarction; N/A: not applicable; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; 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

highest risk after a STEMI and lowest in case of unstable angina[23]. Although we observed a similar incidence of BARC 2-5 bleeding among NSTE-ACS and CCS patients (10.1% vs 8.9%), the analysis by NSTE-ACS subtypes highlighted a numerical trend towards a higher bleeding risk in those with an NSTEMI. Therefore, the finding of a proportionally larger bleeding risk reduction with 1- versus 3-month DAPT among NSTEMI patients relative to those with unstable angina or CCS is of high clinical relevance and warrants prospective confirmation from dedicated studies.

Overall, our findings are in keeping with those from the MASTER DAPT trial, which randomised HBR patients undergoing PCI with a biodegradable-polymer sirolimus-eluting stent between 1-month versus standard (≥3-month) DAPT. In line with the main trial results, the subgroups presenting with and without an acute or recent MI (i.e., within

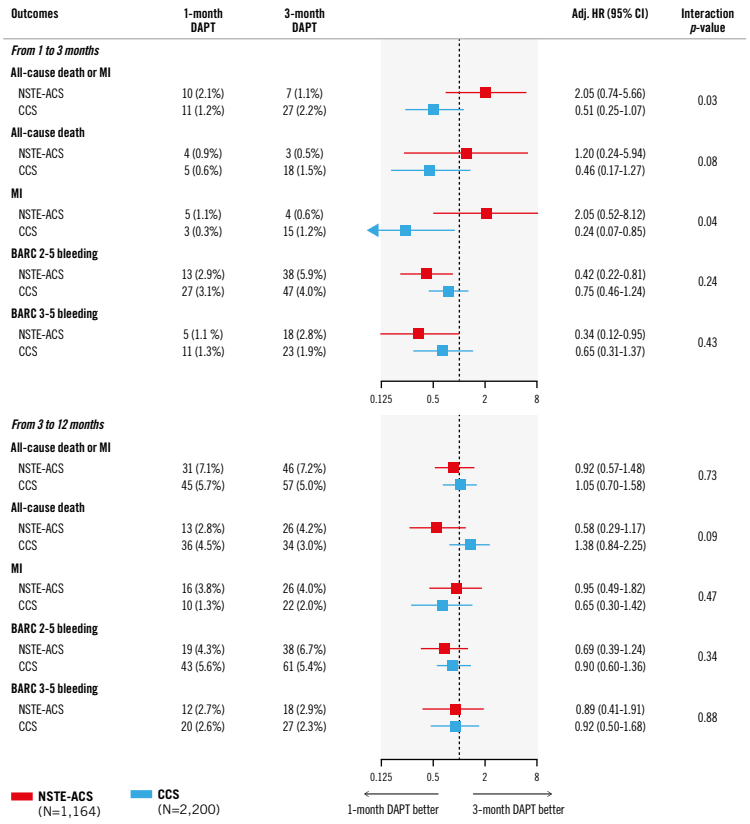


Figure 3. *Landmark analysis at 3 months. Adj. HR: adjusted hazard ratio; BARC: Bleeding Academic Research Consortium; CCS: chronic coronary syndrome; CI: confidence interval; DAPT: dual antiplatelet therapy; MI: myocardial infarction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome*

Table 3. Outcomes with 1-month versus 3-month DAPT by NSTE-ACS subtypes.

Outcomes	CCS (N=2,200)				UA (N=778)				NSTEMI (N=386)				Interaction *p*-value‡
	1-month DAPT (N=917)	3-month DAPT (N=1,283)	Adjusted hazard ratio† (95% CI)	*p*-value	1-month DAPT (N=230)	3-month DAPT (N=548)	Adjusted hazard ratio† (95% CI)	*p*-value	1-month DAPT (N=245)	3-month DAPT (N=141)	Adjusted hazard ratio† (95% CI)	*p*-value	
All-cause death or MI	59 (7.1)	90 (7.6)	0.88 (0.63-1.24)	0.479	15 (7.4)	41 (8.1)	0.78 (0.42-1.44)	0.421	29 (11.9)	14 (10.2)	1.19 (0.61-2.33)	0.607	0.895
All-cause death	44 (5.3)	58 (4.9)	1.03 (0.68-1.55)	0.885	10 (4.5)	21 (4.3)	0.95 (0.43-2.11)	0.909	10 (4.1)	9 (6.6)	0.46 (0.18-1.18)	0.106	0.851
MI	16 (1.9)	39 (3.4)	0.56 (0.31-1.02)	0.059	5 (3.0)	27 (5.1)	0.43 (0.16-1.16)	0.097	19 (8.0)	7 (5.2)	2.00 (0.81-4.93)	0.133	0.654
BARC 2-5 bleeding	70 (8.5)	108 (9.1)	0.84 (0.61-1.15)	0.269	15 (6.9)	58 (11.8)	0.54 (0.30-0.98)	0.042	18 (7.6)	18 (13.7)	0.56 (0.28-1.13)	0.104	0.253
BARC 3-5 bleeding	31 (3.8)	50 (4.2)	0.80 (0.50-1.27)	0.341	10 (4.6)	24 (4.7)	0.81 (0.37-1.76)	0.593	8 (3.4)	12 (9.2)	0.40 (0.16-1.03)	0.059	0.716

Data are presented as number of events (%) unless otherwise specified. The percentages represent Kaplan-Meier rates between 1 and 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, BMI, hypertension, hypercholesterolaemia, prior PCI, prior CABG, prior MI, multivessel disease, diabetes, B2/C lesion, total lesion length, mean preprocedural RVD, mean preprocedural %DS, bifurcation lesion, number of lesions treated, number of vessels treated, number of stents, total stent length, $P2Y_{12}$ inhibitor at discharge, PARIS risk score for major bleeding, and PRECISE-DAPT risk score for bleeding. ‡P-value is for the interaction test between DAPT treatment and clinical presentation. BARC: Bleeding Academic Research Consortium; BMI: body mass index; CABG: coronary artery bypass grafting; CCS: chronic coronary syndrome; CI: confidence interval; DAPT: dual antiplatelet therapy; DS: diameter stenosis; MI: myocardial infarction; N/A: not applicable; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; 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; RVD: reference vessel diameter; UA: unstable angina

the past 12 months), including STEMI, derived a consistent net benefit from 1-month DAPT, with similar cardiovascular events (prior MI: 7.6% vs 8.7% and no prior MI: 5.0 vs 4.5%) and reduced BARC 2, 3, or 5 bleeding (prior MI: 6.2% vs 9.3% and no prior MI: 6.7 vs 9.4%)[11]. Notably, the study designs of XIENCE Short DAPT and MASTER DAPT

Table 4. Sensitivity analysis excluding patients on oral anticoagulation.

Outcomes	NSTE-ACS (N=668)				CCS (N=1,234)				Interaction *p*-value‡
	1-month DAPT (N=261)	3-month DAPT (N=407)	Adjusted hazard ratio† (95% CI)	*p*-value	1-month DAPT (N=487)	3-month DAPT (N=747)	Adjusted hazard ratio† (95% CI)	*p*-value	
All-cause death or MI	28 (11.3)	28 (7.1)	1.59 (0.90-2.79)	0.107	32 (6.8)	51 (7.4)	0.92 (0.58-1.45)	0.723	0.149
All-cause death	12 (4.7)	13 (3.3)	1.10 (0.47-2.57)	0.821	28 (6.0)	31 (4.5)	1.30 (0.77-2.21)	0.325	0.923
Cardiovascular death	8 (3.2)	9 (2.3)	1.05 (0.38-2.95)	0.921	13 (2.7)	15 (2.2)	1.24 (0.58-2.67)	0.583	0.928
MI	16 (6.8)	21 (5.4)	1.48 (0.74-2.97)	0.270	4 (0.8)	25 (3.7)	0.25 (0.09-0.73)	0.011	0.012
Definite or probable ST	0 (0.0)	1 (0.3)	N/A	N/A	1 (0.2)	3 (0.5)	0.69 (0.07-6.70)	0.745	N/A
Stroke	3 (1.2)	7 (1.8)	0.90 (0.21-3.78)	0.883	4 (0.9)	13 (1.9)	0.42 (0.13-1.33)	0.140	0.686
Ischaemic stroke	2 (0.8)	6 (1.6)	0.62 (0.11-3.36)	0.577	4 (0.9)	13 (1.9)	0.42 (0.13-1.33)	0.140	0.911
Target lesion failure	20 (8.3)	28 (7.3)	1.13 (0.61-2.10)	0.697	20 (4.2)	30 (4.3)	1.00 (0.56-1.79)	0.997	0.812
Target lesion revascularisation	2 (0.8)	10 (2.8)	0.33 (0.07-1.61)	0.171	7 (1.5)	7 (1.0)	1.52 (0.52-4.47)	0.445	0.091
Target vessel revascularisation	5 (2.3)	15 (4.1)	0.53 (0.18-1.54)	0.240	13 (2.9)	16 (2.3)	1.36 (0.64-2.87)	0.425	0.167
BARC 2-5 bleeding	14 (5.7)	33 (8.6)	0.61 (0.31-1.19)	0.145	27 (5.8)	48 (6.9)	0.78 (0.48-1.28)	0.327	0.542
BARC 3-5 bleeding	6 (2.4)	14 (3.6)	0.61 (0.22-1.68)	0.336	11 (2.4)	22 (3.2)	0.70 (0.33-1.48)	0.346	0.845

Data are presented as number of events (%) unless otherwise specified. The percentages represent Kaplan-Meier rates between 1 and 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, BMI, hypertension, hypercholesterolaemia, prior PCI, prior CABG, prior MI, multivessel disease, diabetes, B2/C lesion, total lesion length, mean preprocedural RVD, mean preprocedural %DS, bifurcation lesion, number of lesions treated, number of vessels treated, number of stents, total stent length, $P2Y_{12}$ inhibitor at discharge, PARIS risk score for major bleeding, PRECISE-DAPT risk score for bleeding. ‡P-value is obtained from the interaction test between clinical presentation and DAPT after applying multiple imputation and propensity score stratification. BARC: Bleeding Academic Research Consortium; BMI: body mass index; CABG: coronary artery bypass grafting; CCS: chronic coronary syndrome; CI: confidence interval; DAPT: dual antiplatelet therapy; DS: diameter stenosis; MI: myocardial infarction; N/A: not applicable; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; 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; RVD: reference vessel diameter; ST: stent thrombosis

were different with respect to stent platform, ACS subgroup definition, and single antiplatelet regimen following DAPT (75% of patients in MASTER DAPT received $P2Y_{12}$ inhibitor monotherapy). Moreover, in our landmark analysis, the effects of 1- versus 3-month DAPT on the risk of death or MI was inconsistent among NSTE-ACS and CCS patients between 1 and 3 months. It is remarkable, however, that this finding was driven by a relatively small number of events, and there was no such signal of heterogeneity on the 1-year outcomes. These differences notwithstanding, taken together, both trials provide encouraging data on the safety of 1 month compared with ≥3 months of DAPT after PCI, regardless of clinical presentation.

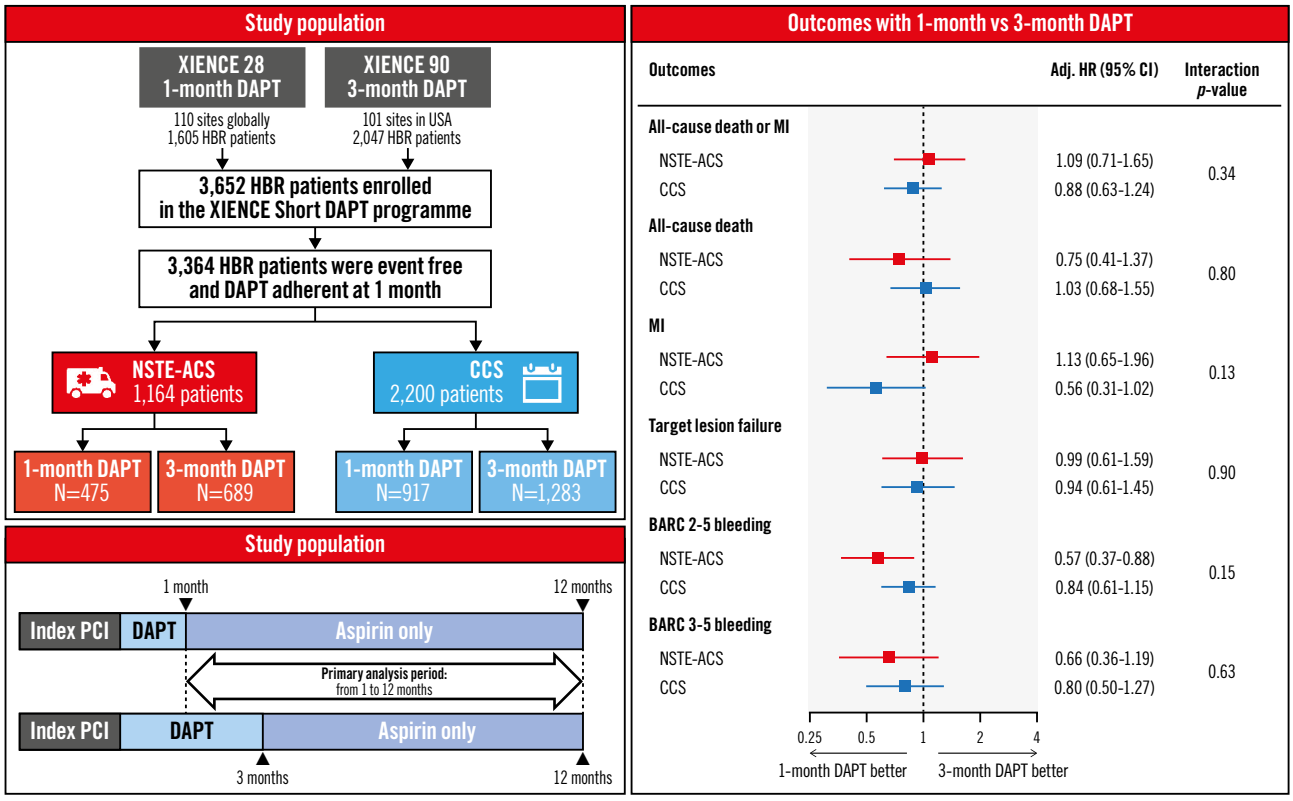
An important caveat of all short DAPT studies relates to the monotherapy regimen based on either aspirin or $P2Y_{12}$ inhibitors following DAPT discontinuation. The XIENCE Short DAPT protocol required the use of aspirin monotherapy after the initial DAPT course. However, recent evidence supports the superiority of $P2Y_{12}$ inhibitor monotherapy over aspirin for long-term secondary prevention in subjects with established coronary artery disease[25]. This observation may partly explain the heterogeneity in treatment effects seen in our landmark and sensitivity analyses where 1-month DAPT (followed by aspirin) was associated with less favourable outcomes, especially MI, after an NSTE-ACS. In fact, a growing body of evidence suggests a potential role of early aspirin withdrawal followed by potent $P2Y_{12}$ inhibitor monotherapy among those subjects in whom both bleeding and ischaemic risks are of concern[26,27]. Owing to their double-sided risk, HBR-ACS patients may be ideal candidates for such an approach. In the TWILIGHT trial, subjects at high risk for ischaemic and bleeding events who had completed a 3-month course of aspirin plus ticagrelor post-PCI were randomised to ticagrelor monotherapy or ticagrelor plus aspirin for an additional 12 months[28]. Surprisingly, the NSTE-ACS subgroup derived the greatest net benefit from this monotherapy regimen[10]. To be enrolled in the trial, however, patients had to be deemed eligible for a long-term DAPT with ticagrelor, which resulted in only 17% of them being classified as HBR[29]. Other trials on short DAPT followed by potent $P2Y_{12}$ inhibitor monotherapy have yielded consistent results[12]. However, controversies persist with regard to clopidogrel monotherapy, especially in an ACS setting. In the STOPDAPT-2 ACS Study, which enrolled 4,196 patients mostly at low-to-intermediate bleeding risk who underwent PCI for an ACS using the same cobalt-chromium everolimus-eluting stent, 1-month DAPT followed by clopidogrel monotherapy failed to attest non-inferiority to 12-month DAPT for the primary endpoint of net clinical benefit, with a numerical increase in cardiovascular events despite less bleeding[13]. Whether a strategy of $P2Y_{12}$ inhibitor monotherapy holds the promise of preserving ischaemic protection while effectively reducing bleeding after only 1 month of DAPT, or even omitting DAPT, among HBR patients is yet to be proven in large-scale studies[30-32].

Limitations

The non-randomised design introduces the risk for residual unmeasured confounding despite efforts to adjust through propensity score stratification using rigorous statistical methodology.

The present subgroup analysis as well as the comparison between 1 and 3 months of DAPT were prespecified, but the propensity score analysis of the pooled XIENCE 28

Outcomes of 1- versus 3-month DAPT in high bleeding risk patients undergoing PCI according to clinical presentation.



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High bleeding risk patients who underwent successful, non-complex PCI with a cobalt-chromium everolimus-eluting stent were enrolled in the XIENCE Short DAPT programme and received 1-month DAPT (XIENCE 28 Global and 28 USA) or 3-month DAPT (XIENCE 90) followed by aspirin monotherapy. Patients who had been adherent to treatment and free from MI, repeat coronary revascularisation, stroke, or stent thrombosis at 1 month post-PCI were included. In this subgroup analysis, the effects of 1- versus 3-month DAPT were evaluated using propensity score stratification according to clinical presentation (NSTE-ACS or CCS). Adj. HR: adjusted hazard ratio; BARC: Bleeding Academic Research Consortium; CCS: chronic coronary syndrome; CI: confidence interval; DAPT: dual antiplatelet therapy; HBR: high bleeding risk; MI: myocardial infarction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention

and 90 population was not. In XIENCE 90, there was no scheduled follow-up at 1 month, and event-free patients were derived retrospectively to match the corresponding cohort of patients on 1-month DAPT from XIENCE 28. The XIENCE Short DAPT programme included only patients who had undergone successful PCI of non-complex target lesion anatomy, with exclusive use of the same cobalt-chromium everolimus-eluting stent platform. Those with STEMI were excluded, and therefore, our findings do not apply to patients who did not meet the study enrolment criteria nor those who were not event free at the predefined time points. Moreover, the HBR criteria used in XIENCE Short DAPT partially differ from those proposed by the Academic Research Consortium consensus, which became available after both XIENCE 28 and 90 had started enrolling[15,33]. Lastly, our findings must be considered hypothesis-generating. As with most subgroup analyses, the present study was likely underpowered to detect clinically relevant differences in ischaemic and bleeding outcomes, and the wide CIs do not conclusively rule out a potential for harm with either of the two DAPT strategies.

Conclusions

Among HBR patients undergoing non-complex PCI with an everolimus-eluting stent and enrolled in the XIENCE Short DAPT programme, about one in three presented with NSTE-ACS. DAPT for 1 month, compared with DAPT for 3 months followed by aspirin monotherapy, was associated with a similar 1-year risk of death or MI and lower bleeding risk, irrespective of clinical presentation.

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Conflict of interest statement

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Supplementary data

Supplementary Table 1. Baseline characteristics by clinical presentation.

Supplementary Table 2. Clinical outcomes in patients with NSTE-ACS versus CCS between 1 and 12 months.

Supplementary Figure 1. Balance plots with standardised mean differences in baseline covariates before and after propensity score stratification.

Supplementary Figure 2. DAPT use during follow-up.

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Supplementary data

Supplementary Table 1. Baseline characteristics by clinical presentation.

	NSTE-ACS N=1164 (34.6%)	CCS N=2200 (65.4%)	P-Value
High bleeding risk criteria			
Age ≥ 75 years	755 (64.9%)	1486 (67.5%)	0.116
Chronic anticoagulant therapy	481 (41.3%)	941 (42.8%)	0.412
Anemia	209 (18.0%)	305 (13.9%)	0.002
History of stroke	140 (12.0%)	228 (10.4%)	0.143
Renal insufficiency	98 (8.4%)	175 (8.0%)	0.641
Thrombocytopenia	29 (2.5%)	40 (1.9%)	0.218
History of major bleeding	44 (3.8%)	59 (2.7%)	0.079
Number of HBR criteria	1.5±0.7	1.5±0.7	0.132
Clinical characteristics			
Age, years	75.2±9.4	75.6±8.8	0.208
Female sex	430 (36.9%)	724 (32.9%)	0.019
Race			
American Indian or Alaskan Native	6 (0.6%)	7 (0.4%)	0.386
Asian	74 (7.4%)	97 (5.0%)	0.009
Black or African American	65 (6.5%)	88 (4.5%)	0.024
Native Hawaiian or Pacific Islander	0 (0.0%)	5 (0.3%)	0.173
White	835 (83.3%)	1711 (88.2%)	<.001
Hispanic or Latino ethnicity	73 (6.4%)	121 (5.6%)	0.371
Hypertension	1031 (88.6%)	1919 (87.2%)	0.258
Dyslipidemia	889 (76.4%)	1672 (76.0%)	0.808
Diabetes mellitus	461 (39.7%)	838 (38.3%)	0.426
Chronic kidney disease	509 (44.5%)	923 (43.1%)	0.440
Prior PCI	351 (30.2%)	646 (29.4%)	0.633
Prior CABG	114 (9.8%)	244 (11.1%)	0.246
Prior MI	224 (19.5%)	320 (14.7%)	<.001
Multivessel disease	505 (43.4%)	986 (44.8%)	0.426
NSTEMI	386 (33.2%)	0 (0.0%)	<.001
Unstable angina	778 (66.8%)	0 (0.0%)	<.001
PARIS bleeding risk score	6.2±2.3	6.0±2.3	<.001
PARIS bleeding risk score [IQR]	6.0 (5.0-8.0)	6.0 (4.0-8.0)	<.001
PRECISE-DAPT bleeding risk score	27.8±11.9	26.3±11.3	<.001
PRECISE-DAPT bleeding risk score	27.0 (20.0-35.0)	26.0 (19.0-32.0)	<.001

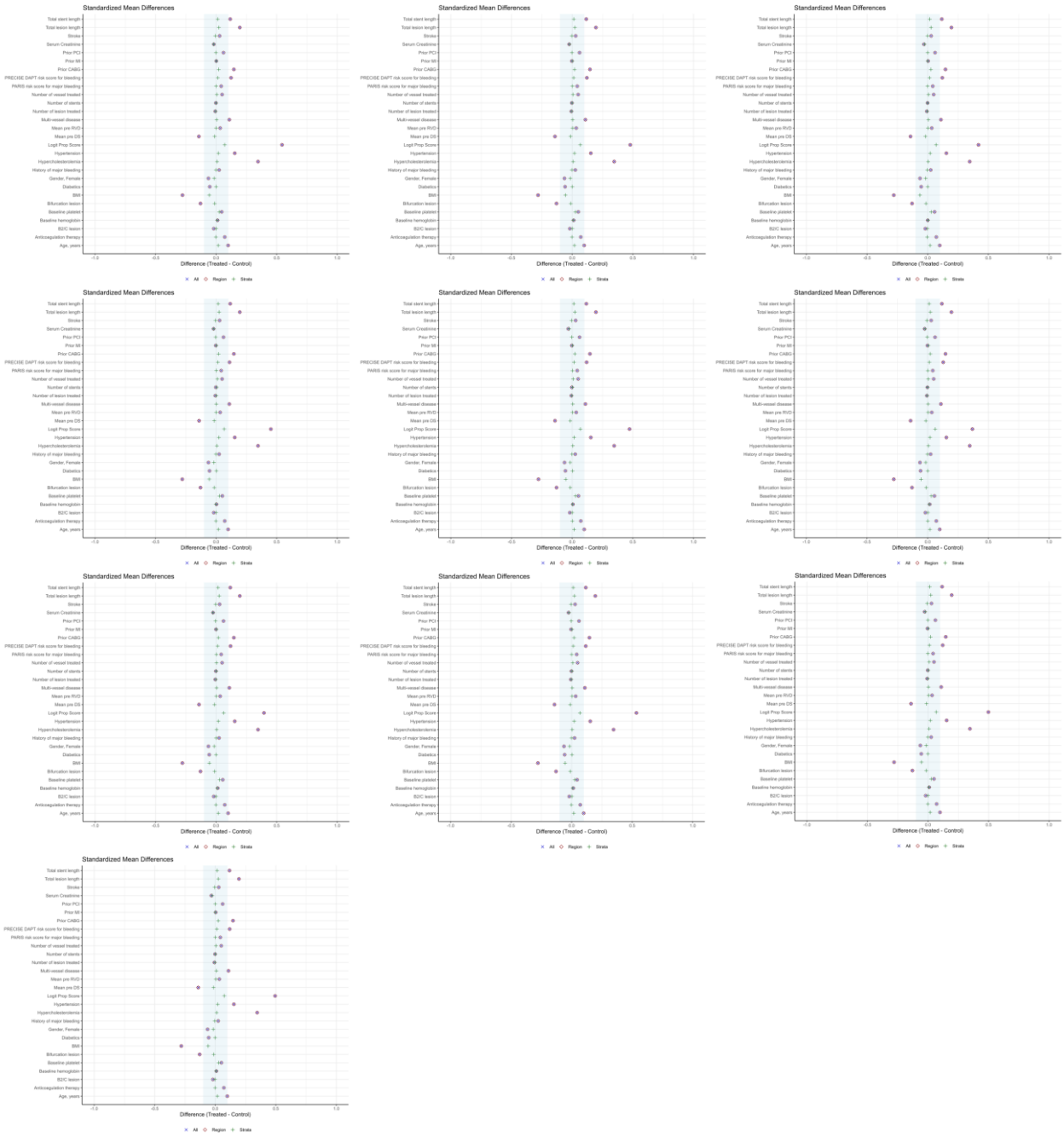
	NSTE-ACS N=1164 (34.6%)	CCS N=2200 (65.4%)	P-Value
Procedural characteristics			
Number of lesions treated [IQR]	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.011
Number of vessels treated [IQR]	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.030
B2/C lesion	454 (39.0%)	731 (33.2%)	<.001
Bifurcation	108 (9.3%)	206 (9.4%)	0.936
Radial access	785 (67.4%)	1229 (55.9%)	<.001
Number of stents per subject [IQR]	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.015
Total stent length, mm	27.3±14.9	25.7±13.7	0.001
Pre-procedure RVD, mm	3.0±0.5	3.0±0.5	0.865
Pre-procedure % DS	84.6±10.3	82.7±9.6	<.001
Antiplatelet therapy at discharge			
Aspirin	1068 (91.8%)	1865 (84.8%)	<.001
Clopidogrel	919 (79.0%)	1897 (86.2%)	<.001
Prasugrel	23 (2.0%)	37 (1.7%)	0.540
Ticagrelor	223 (19.2%)	268 (12.2%)	<.001

Values are n/N (%) or mean ± SD, unless otherwise specified. ACS: acute coronary syndrome, PCI: percutaneous coronary intervention, CABG: coronary artery bypass grafting, MI: myocardial infarction, NSTEMI: non-ST segment elevation myocardial infarction, RVD: reference vessel diameter, DS: diameter stenosis

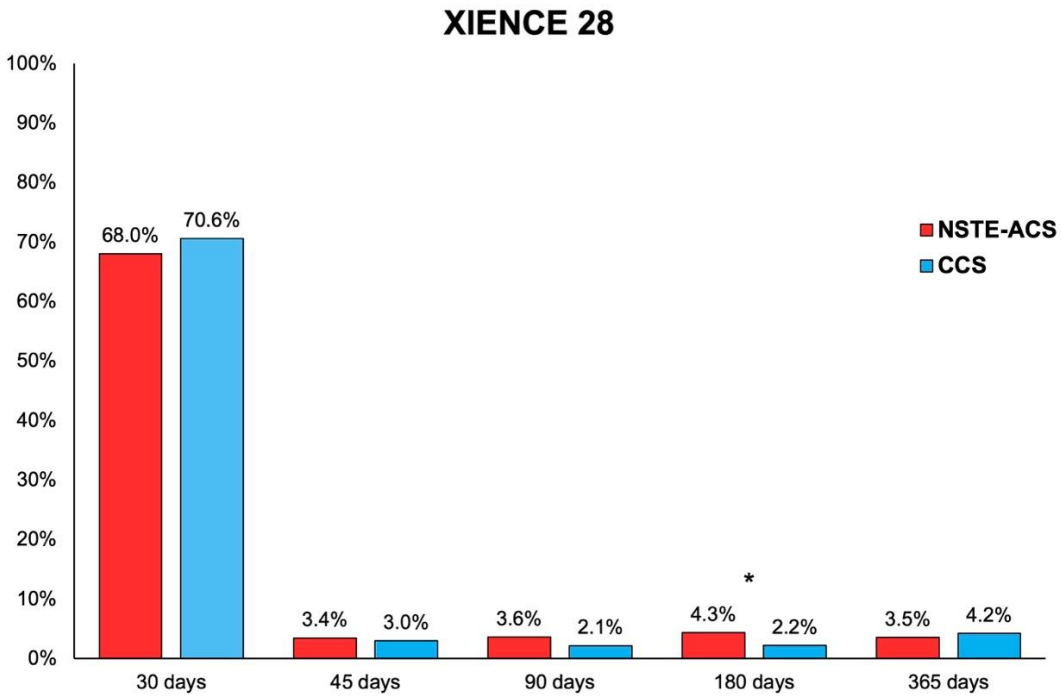
Supplementary Table 2. Clinical outcomes in patients with NSTE-ACS versus CCS between 1 and 12 months.

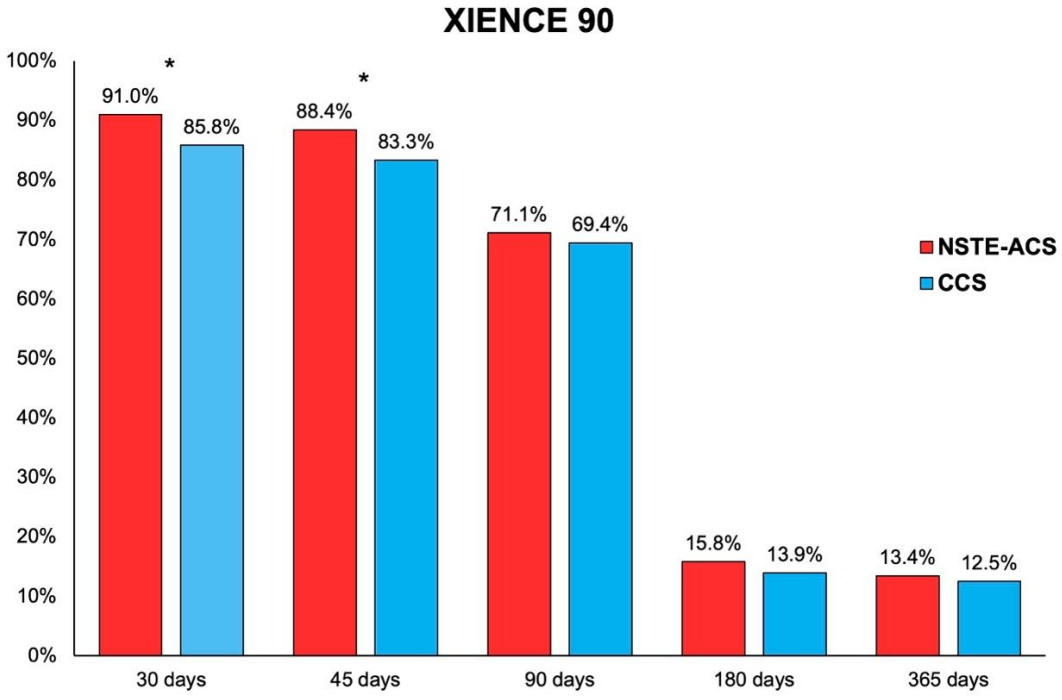
Outcomes	NSTE-ACS N=1164 (34.6%)	CCS N=2200 (65.4%)	Hazard ratio (95% CI)	p-value
	no. of events (%)			
All-cause death or MI	99 (9.0%)	149 (7.4%)	1.26 (0.98 - 1.63)	0.073
All-cause death	50 (4.5%)	102 (5.1%)	0.92 (0.66 - 1.29)	0.628
Cardiovascular death	32 (3.0%)	49 (2.5%)	1.22 (0.78 - 1.91)	0.372
MI	58 (5.3%)	55 (2.8%)	2.00 (1.38 - 2.90)	<0.001
Definite or probable ST	3 (0.3%)	7 (0.4%)	0.80 (0.21 - 3.09)	0.746
Stroke	16 (1.5%)	28 (1.5%)	1.07 (0.58 - 1.98)	0.823
Ischemic stroke	13 (1.2%)	26 (1.4%)	0.94 (0.48 - 1.83)	0.851
Target lesion failure	79 (7.4%)	91 (4.5%)	1.65 (1.22 - 2.23)	0.001
Target lesion revascularization	22 (2.1%)	22 (1.1%)	1.88 (1.04 - 3.39)	0.037
Target vessel revascularization	32 (3.1%)	43 (2.2%)	1.40 (0.88 - 2.21)	0.152
BARC 2-5 bleeding	109 (10.1%)	178 (8.9%)	1.16 (0.92 - 1.48)	0.213
BARC 3-5 bleeding	54 (4.9%)	81 (4.1%)	1.26 (0.89 - 1.78)	0.185

The percentages represent Kaplan-Meier rates between 1 and 12 months after the index procedure



Supplementary Figure 1. Balance plots with standardised mean differences in baseline covariates before and after propensity score stratification.





Supplementary Figure 2. DAPT use during follow-up.

* indicates $p<0.05$