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ORIGINAL RESEARCH

One-month dual antiplatelet therapy followed by prasugrel monotherapy at a reduced dose: the 4D-ACS randomised trial

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ABSTRACT

BACKGROUND: The efficacy and safety of a 1-month prasugrel-based dual antiplatelet therapy (DAPT) strategy followed by reduced-dose prasugrel monotherapy in acute coronary syndrome (ACS) patients treated with drug-coated stents (DCS) have not been studied.

AIMS: We aimed to evaluate the safety and efficacy of a 1-month prasugrel-based DAPT regimen followed by reduced-dose monotherapy in ACS patients receiving a DCS.

METHODS: In the multicentre, randomised, open-label trial, 656 ACS patients (age: 60.9±9.7 years; 82.6% male) receiving DCS were randomised to either 1-month DAPT with aspirin 100 mg and prasugrel 10 mg (or 5 mg in patients aged ≥75 years or body weight <60 kg) followed by prasugrel 5 mg monotherapy (1M-DAPT) or 12-month DAPT with aspirin and prasugrel 5 mg (12M-DAPT). The primary endpoint was 12-month net adverse clinical events (NACE), a composite of death, non-fatal myocardial infarction, stroke, ischaemia-driven target vessel revascularisation, and Bleeding Academic Research Consortium Type 2-5 bleeding.

RESULTS: NACE occurred in 4.9% of the 1M-DAPT group and 8.8% of the 12M-DAPT group, meeting the criteria for both non-inferiority (non-inferiority margin: 2.0%; absolute difference: –3.9%; 95% confidence interval [CI] for absolute difference: –6.7% to –0.2%; p=0.014) and superiority (hazard ratio [HR] 0.51; 95% CI: 0.27-0.95; p=0.034). Any bleeding occurred in 1.2% vs 5.2% (HR 0.23; p=0.009), and major bleeding occurred in 0.6% vs 4.6% (HR 0.13; p=0.007) in the 1M-DAPT versus 12M-DAPT group, respectively. Ischaemic outcomes were similar.

CONCLUSIONS: In ACS patients treated with DCS, a 1-month prasugrel-based DAPT strategy followed by prasugrel 5 mg monotherapy reduced NACE by 49%, mainly driven by a 77% reduction of bleeding events without compromising ischaemic safety.

KEYWORDS: acute coronary syndrome; de-escalation; dose reduction; drug-coated stent; prasugrel; 1 month

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Dual antiplatelet therapy (DAPT) has long been the standard of care following percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS). Current guidelines recommend 12 months of DAPT consisting of aspirin and a $P2Y_{12}$ inhibitor to mitigate ischaemic events[1]. While the anti-ischaemic benefit of prolonged DAPT is well established, it is also associated with increased bleeding risk. In response, alternative strategies such as a shortened DAPT duration followed by monotherapy, as well as de-escalation approaches, have been explored. Recent evidence suggests that these approaches can reduce bleeding without compromising ischaemic protection. Accordingly, recent guidelines allow for 1- or 3-month DAPT in selected ACS patients[1,2], and accumulating data now support the safety and efficacy of ultrashort regimens, including 1-month DAPT. Several trials have demonstrated that switching from DAPT (aspirin+potent $P2Y_{12}$ inhibitor) to either a less potent $P2Y_{12}$ inhibitor (e.g., clopidogrel)[3] or to a reduced dose of a potent agent[4] can preserve ischaemic protection while significantly reducing bleeding, thereby lowering overall adverse event rates. Additionally, drug-coated stents (DCS) have historically shown success with 1-month DAPT in high bleeding risk patients[5,6].

Building upon these findings, our study investigated a strategy that combined two key concepts: an ultrashort DAPT duration and pharmacological de-escalation. ACS patients undergoing PCI with a DCS were randomised to receive either 1-month DAPT, consisting of aspirin 100 mg plus standard-dose prasugrel 10 mg followed by prasugrel 5 mg monotherapy, or 12-month DAPT, consisting of aspirin and prasugrel 5 mg.

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Impact on daily practice

Our study demonstrates the benefit of a 1-month prasugrel-based dual antiplatelet therapy (DAPT) strategy followed by reduced-dose prasugrel monotherapy in acute coronary syndrome (ACS) patients implanted with a drug-coated stent (DCS). This approach significantly reduced net adverse clinical events without increasing ischaemic events, primarily by lowering major bleeding. The combination of ultrashort DAPT, prasugrel dose reduction, and DCS offers a practical and safer alternative for East Asian ACS patients.

Methods

STUDY DESIGN AND POPULATION

The effect of short Duration of DAPT followed by Dose reduction after Implantation of DCS in ACS patients (4D-ACS) trial was a multicentre, randomised, open-label trial conducted across three tertiary medical centres located in South Korea. The study protocol was reviewed and approved by the institutional review boards of all participating centres (GAIRB2021-364). The trial was registered on the Clinical Research Information Service website (https://cris.nih.go.kr/) under the identifier KCT0006992 on 10 February 2022. Written informed consent was obtained from all patients before enrolment. Patients were eligible for inclusion if they had ACS, including myocardial infarction (MI) – defined according to the Fourth Universal Definition of MI – or unstable angina, characterised by recurrent chest pain at rest or with minimal exertion, or new or worsening severe angina within 4 weeks before the index procedure, and if they underwent PCI with a biolimus-coated stent (BioFreedom Ultra [Biosensors]). Patients who required anticoagulant therapy or had a history of cerebral infarction were excluded from the study. Detailed criteria for enrolment are shown in **Supplementary Table 1**.

RANDOMISATION AND STUDY PROCEDURES

Following successful PCI, patients were randomised in a 1:1 ratio to receive either prasugrel 5 mg monotherapy (1M-DAPT) or prasugrel 5 mg plus aspirin 100 mg (12M-DAPT) following 1 month of DAPT consisting of aspirin 100 mg and prasugrel 10 mg, or 5 mg in patients aged ≥75 years or weighing <60 kg, according to dose reduction criteria **(Figure 1, Supplementary Figure 1)**[7-9]. The allocation sequence was computer generated by an independent statistician and implemented through a web-based permuted-block randomisation system. Investigators and research coordinators accessed the web-based system to ensure allocation concealment. All patients received a loading dose of aspirin (300 mg) and clopidogrel (300 mg) before PCI. Clopidogrel was switched to prasugrel within 24 hours of randomisation without a loading dose[10]. At the 1-month follow-up visit, patients in the 1M-DAPT group discontinued aspirin and continued with a reduced dose of prasugrel (5 mg once daily) for the rest of the 12-month study period. In the 12M-DAPT group, aspirin (100 mg once daily) was continued alongside prasugrel 5 mg once daily for the subsequent 11 months **(Figure 1, Supplementary Figure 1)**. The use of additional antiplatelet agents or anticoagulants was not permitted during the study. Gastroprotective medications such as proton pump inhibitors were prescribed at the discretion of the treating physician.

To ensure optimal secondary prevention, guideline-directed medical therapy was strongly recommended for all patients, including aggressive high-intensity statin-based lipid management, blood pressure control, glycaemic management in diabetic patients, smoking cessation counselling, and heart failure management when indicated.

Abbreviations

ACS	acute coronary syndrome	**ITT**	intention to treat	**PCI**	percutaneous coronary intervention
BARC	Bleeding Academic Research Consortium	**MACE**	major adverse cardiovascular events	**PP**	per protocol
DAPT	dual antiplatelet therapy	**MI**	myocardial infarction	**TVR**	target vessel revascularisation
DCS	drug-coated stent	**NACE**	net adverse clinical events		

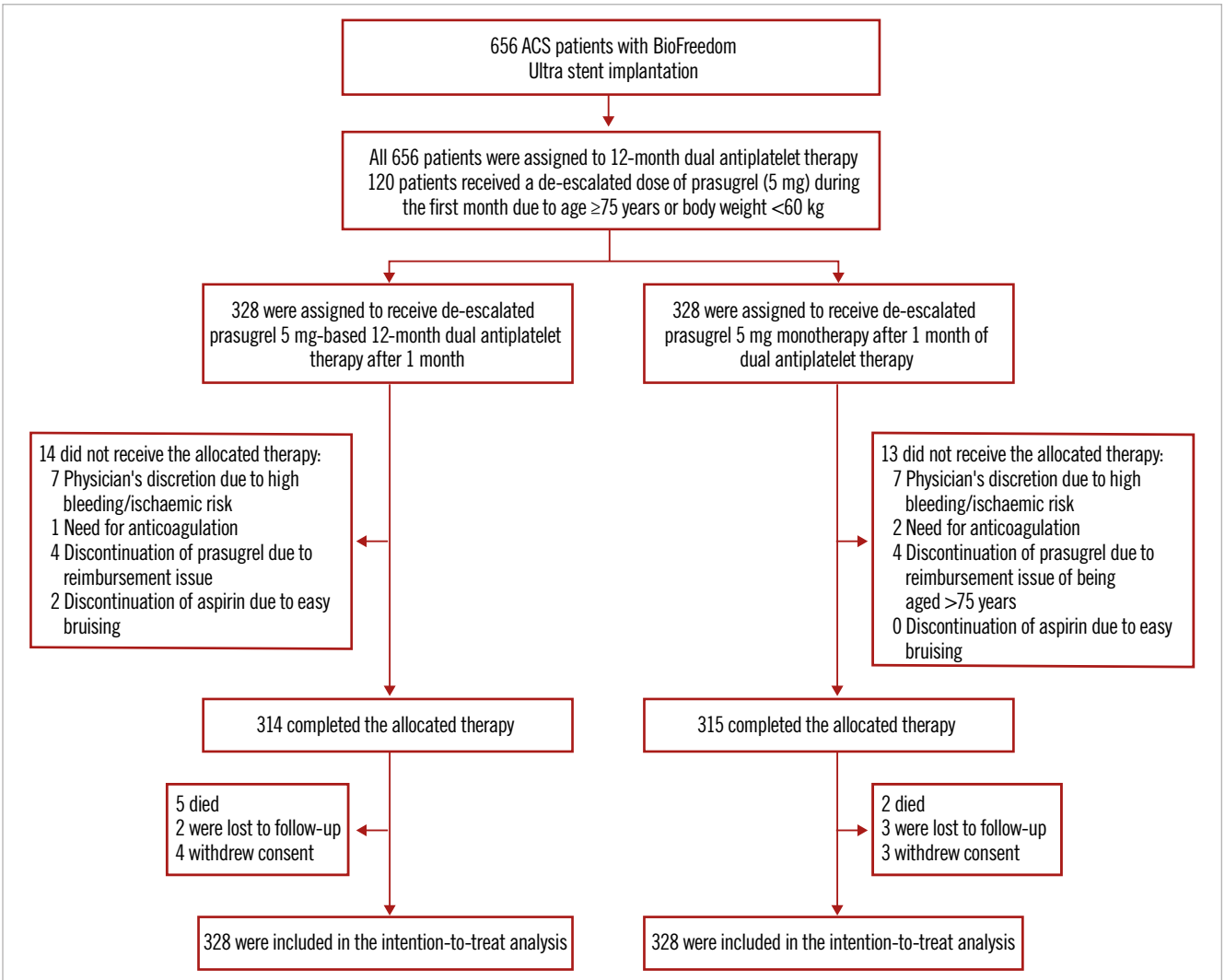


Figure 1. *Study flow diagram. A total of 656 patients with ACS undergoing PCI with drug-coated stents were randomised to either 12-month DAPT or 1-month DAPT followed by prasugrel 5 mg monotherapy. ACS: acute coronary syndrome; DAPT: dual antiplatelet therapy; PCI: percutaneous coronary intervention*

Follow-up visits were scheduled for 1 month, 6 months, and 12 months after the index procedure. At each visit, information on clinical status, medication adherence, adverse events, and the occurrence of any clinical endpoints was collected. Standardised case report forms were used to document data, and source documents were centrally collected for monitoring. Routine follow-up coronary angiography was not mandated unless clinically indicated by recurrent ischaemic symptoms or suspected stent-related complications.

STUDY ENDPOINTS

The primary endpoint of the study was the incidence of 1-year net adverse clinical events (NACE), defined as a composite of all-cause death, non-fatal MI, ischaemia-driven target vessel revascularisation (TVR), stroke, and Bleeding Academic Research Consortium (BARC) Type 2 to 5 bleeding[11]. Secondary endpoints included all-cause death, cardiovascular death, non-fatal MI, ischaemia-driven TVR, stent thrombosis, stroke, major bleeding (BARC 3 to 5), minor or major bleeding (BARC 2 to 5), and major adverse cardiovascular events (MACE), which comprised cardiovascular death, non-fatal MI, stroke, and ischaemia-driven TVR.

Clinical endpoints and safety events were defined according to established international criteria as follows. Major bleeding was classified as BARC Type 3 to 5, whereas minor or major bleeding was defined as BARC Type 2 to 5[11]. Cardiovascular death encompassed fatalities resulting from MI, sudden cardiac death (including unwitnessed death), heart failure, stroke, cardiovascular procedure-related complications, cardiovascular haemorrhage, and any death where a cardiac cause could not be ruled out. Stent thrombosis was categorised based on standard criteria. Stroke was defined as an acute cerebrovascular event leading to a neurological deficit lasting at least 24 hours or the presence of acute infarction confirmed by imaging. Ischaemia-driven TVR was defined as repeat PCI or coronary artery bypass grafting of the target vessel with a stenosis of at least 50% and additional evidence of ischaemia, including recurrent angina, abnormal ischaemia testing, invasive functional diagnostic results, or a stenosis of at least 70% in the absence of overt ischaemic symptoms.

Routine angiographic follow-up in asymptomatic patients was not mandated. Patients were classified as having high bleeding risk based on the criteria proposed by the Academic Research Consortium[12].

All suspected adverse events, including bleeding and ischaemic outcomes, were promptly documented in an electronic case report form, with source documents collected centrally. The study coordination centre and local institutional review boards conducted ongoing monitoring to identify unreported adverse events. Upon central collection, any information that could unblind the treatment assignment was redacted before submission to the independent clinical event adjudication committee, which remained blinded to treatment allocation and trial results throughout the adjudication process.

STATISTICAL ANALYSIS

The study was designed as a non-inferiority trial comparing 1M-DAPT with 12M-DAPT in terms of NACE. Based on previous data, the expected event rates were estimated at 6% in the 12-month DAPT group and 4% in the monotherapy group[13]. A non-inferiority margin of 2.0%, 90% power, and a 1-sided alpha of 0.025 were used for the sample size estimation. Considering a 10% loss to follow-up, the calculated sample size was 623 patients per group, leading to a total target enrolment of 1,370 patients. However, after approximately 2 years of enrolment, a preplanned interim analysis in January 2024 revealed a higher-than-expected event rate in the 12M-DAPT group (≥8%), compared to the originally anticipated rate of approximately 6%. At that time, the primary endpoint event rates were 8.2% in the 12M-DAPT (N=282) group and 4.2% in the 1M-DAPT group (N=283). On 29 January 2024, the Data Safety Monitoring Board recommended adjusting the sample size from the initially planned 1,370 patients to 654 patients (327 per group), maintaining the same non-inferiority framework and statistical assumptions but adjusting the control group's expected event rate from 6% to 8%. The 4D-ACS Investigator Steering Committee approved the protocol revision accordingly. Consequently, the study was completed with 328 patients in each group, for a total of 656 enrolled participants.

The primary analysis was performed in the intention-to-treat (ITT) population. Event rate differences between groups were analysed using a two-proportion z-test with a 1-sided significance level of 0.025. The 95% confidence interval (CI) for the absolute difference in NACE rates was calculated using the Wald method. Non-inferiority was confirmed if the upper bound of the 95% CI did not exceed the predefined margin of 2.0%. If non-inferiority was established, a subsequent test for superiority was conducted using a 2-sided significance level of 0.05.

Secondary endpoints were analysed using Cox proportional hazards models and Kaplan-Meier survival curves, with comparisons performed using log-rank tests. Subgroup analyses were conducted to evaluate the consistency of treatment effects across key clinical characteristics. All statistical analyses were performed using R, version 4.3.0 (R Foundation for Statistical Computing), with statistical significance set at a p-value of less than 0.05.

Results

Between 17 November 2021 and 2 September 2024, a total of 656 patients were enrolled across three tertiary centres. Of these, 328 patients were randomly assigned to 12M-DAPT, and 328 patients were assigned to the 1M-DAPT group **(Figure 1)**. Over 99.8% of patients were randomised within 1 day after PCI. In the 12M-DAPT group, 314 patients (95.7%) completed the allocated therapy, while in the 1M-DAPT group, 315 patients (96.0%) fulfilled the designated regimen **(Figure 1)**. Aspirin was discontinued at a median of 31.0 days (interquartile range 25.0 to 37.0 days). Details regarding the reasons for discontinuation are provided in **Figure 1** and **Supplementary Table 2**. Most patients adhered to their assigned treatment, with only a small percentage discontinuing prasugrel or aspirin due to administrative or clinical considerations **(Supplementary Table 2)**. The use of discharge medications was similar between the two groups, with proton pump inhibitors or potassium-competitive acid blockers prescribed in 22.5% and 25.3% of patients in the 1M-DAPT and 12M-DAPT groups, respectively **(Supplementary Table 3)**. At the time of database lock (September 2024), 7 patients had died, and clinical follow-up had been completed for all but 12 patients **(Figure 1)**.

In the ITT analysis, clinical, lesion, and procedural characteristics were well balanced between the treatment groups **(Table 1)**. The mean age of the study population was 60.9±9.7 years. Male patients accounted for 82.7% of patients, and 31.7% had diabetes. Among all the enrolled participants, 32.8% had ST-segment elevation MI (STEMI), 30.8% had non-STEMI, and 36.7% had unstable angina. Angiographic and procedural characteristics of the patients and treated lesions at the index procedure are provided in **Table 2**, with no significant differences noted between the groups.

At 12 months, the primary outcome of NACE occurred in 8.8% (29 patients) in the 12M-DAPT group and 4.9% (16 patients) in the 1M-DAPT group in the ITT analysis. The absolute risk difference was –3.9% (95% CI: –6.7% to –0.2%), and the upper bound of the 95% CI did not exceed the prespecified non-inferiority margin of 2.0%, confirming non-inferiority (p for non-inferiority=0.014). While the 1M-DAPT strategy also met statistical criteria for superiority over 12M-DAPT, with a hazard ratio (HR) of 0.51 (95% CI: 0.27-0.95; p=0.034), this difference was primarily driven by a lower incidence of bleeding events in the 1M-DAPT group, as shown in **Table 3** and **Figure 2A**. In a landmark analysis beyond day 30, the incidence of NACE remained lower in the 1M-DAPT group (7.1% vs 1.9%; HR 0.27, 95% CI: 0.11-0.66; p=0.004), as shown in **Table 3** and **Figure 2B**.

Analysis of the key secondary endpoints are shown in **Table 3**. All bleeding (BARC Type 2-5) occurred in 5.2% of patients in the 12M-DAPT group and 1.2% in the 1M-DAPT group (HR 0.23, 95% CI: 0.08-0.69; p=0.009). This was mainly driven by the reduction in major bleeding (4.6% vs 0.6%; HR 0.13, 95% CI: 0.03-0.58; p=0.007), as shown in **Figure 2C**. Type 3b bleeding (defined as overt bleeding with a haemoglobin drop ≥5 g/dL, cardiac tamponade, bleeding requiring surgical intervention, or necessitating intravenous vasoactive agents)[11] was the most frequent major bleeding subtype. It occurred in 3.0% of patients in the 12M-DAPT

Table 1. Baseline characteristics of the intention-to-treat analysis.

	Prasugrel-based 12-month DAPT (N=328)	Prasugrel 5 mg monotherapy after 1 month of DAPT (N=328)	*p*-value
Demographics			
Age, years			
Mean	61.3±9.6	60.4±9.8	0.228
≥75	20 (6.1)	19 (5.8)	1.000
Male sex	273 (83.2)	269 (82.0)	0.757
Dose reduction of prasugrel during 1st month of DAPT	66 (20.1)	54 (16.5)	0.267
Weight, kg			
Mean	69.2±12.0	70.7±12.2	0.128
<60	67 (90.5)	51 (83.6)	0.343
Body mass index, kg/m^2	25.0±3.1	25.2±3.4	0.424
High bleeding risk	44 (13.5)	37 (11.3)	0.476
Hypertension	197 (60.1)	179 (54.6)	0.180
Diabetes	104 (31.7)	104 (31.7)	1.000
Dyslipidaemia	278 (84.8)	270 (82.3)	0.461
Chronic kidney disease	12 (3.7)	9 (2.7)	0.657
Smoking			0.352
Current	138 (42.1)	120 (36.6)	
Former	45 (13.7)	48 (14.6)	
Never	145 (44.2)	160 (48.8)	
Previous myocardial infarction	7 (2.1)	9 (2.7)	0.800
Previous PCI	23 (7.0)	23 (7.0)	1.000
Previous CABG	0 (0)	3 (0.9)	0.249
Family history of CAD	19 (5.8)	16 (4.9)	0.728
Left ventricular ejection fraction, %	55.0±11.9	54.3±13.2	0.487
Clinical presentation			0.355
ST-segment elevation myocardial infarction	99 (30.2)	116 (35.4)	
Non-ST-segment elevation myocardial infarction	103 (31.4)	98 (29.9)	
Unstable angina	126 (38.4)	114 (34.8)	
Laboratory findings			
Haemoglobin, g/dL	14.1±1.7	14.6±7.9	0.225
Platelets, x10^3 per mL	232.6±60.2	234.4±63.2	0.71
Blood urea nitrogen, mg/dL	18.6±9.8	18.3±13.9	0.736
Creatinine, mg/dL	1.1±1.2	1.0±0.9	0.431
Total cholesterol, mg/dL	170.6±50.4	170.6±45.4	0.983
LDL cholesterol, mg/dL	96.6±45.7	97.4±42.3	0.816
HDL cholesterol, mg/dL	43.7±11.6	42.7±10.9	0.242
Triglyceride, mg/dL	151.1±130.2	151.4±117.9	0.979
Remnant cholesterol, mg/dL	31.8±32.6	31.1±28.4	0.781

Data are presented as mean±SD or n (%). CABG: coronary artery bypass grafting; CAD: coronary artery disease; DAPT: dual antiplatelet therapy; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PCI: percutaneous coronary intervention; SD: standard deviation

group compared to 0.3% in the 1M-DAPT group (HR 0.10, 95% CI: 0.01-0.77; p=0.027). Between day 30 and day 360, the difference in major bleeding remained significant (3.5% vs 0%; p=0.002), further supporting the safety advantage of 1M-DAPT **(Table 3)**. Gastrointestinal (GI) bleeding was the major cause of bleeding, accounting for over 70% of all bleeding cases. There was no difference in MACE between groups (3.7% vs 2.4%; HR 0.66, 95% CI: 0.27-1.61;

Table 2. Procedural and angiographic findings of the intention-to-treat analysis.

	Prasugrel-based 12-month DAPT (N=328)	Prasugrel 5 mg monotherapy after 1 month of DAPT (N=328)	*p*-value
Transradial access	279 (85.1)	276 (84.1)	0.829
Multivessel coronary artery disease	200 (61.0)	186 (56.7)	0.302
Left main disease	6 (1.8)	1 (0.3)	0.123
Bifurcation lesion	8 (2.4)	15 (4.6)	0.200
In-stent restenosis lesion	1 (0.3)	3 (0.9)	0.624
Number of lesions	1.9±1.0	1.8±1.0	0.641
Multilesion intervention	174 (62.4)	186 (66.4)	0.360
Multivessel intervention	200 (61.0)	186 (56.7)	0.302
Disease extent			0.368
1VD	128 (39.0)	142 (43.3)	
2VD	116 (35.4)	116 (35.4)	
3VD	84 (25.6)	70 (21.3)	
Treated lesion			0.390
Left main coronary artery	7 (2.1)	4 (1.2)	
Left anterior descending artery	228 (69.5)	217 (66.2)	
Left circumflex artery	31 (9.5)	43 (13.1)	
Right coronary artery	62 (18.9)	64 (19.5)	
Ramus intermedius artery	0 (0)	1 (0.3)	
Total stent length, mm	26.9±10.9	26.5±9.2	
Stent diameter, mm	3.07±0.44	3.09±0.45	0.612
Stent length, mm	24.67±6.69	24.18±6.44	0.337
Diameter stenosis, %	88.3±13.9	89.2±13.2	0.386
Intra-aortic balloon pump	0 (0)	1 (0.3)	1.000
Percutaneous cardiopulmonary support	0 (0)	1 (0.3)	1.000
Unfractionated heparin	254 (77.4)	252 (76.8)	0.926
Low-molecular-weight heparin	53 (2.1)	5 (1.5)	0.771
Use of glycoprotein IIb/IIIa inhibitors	1 (0.3)	1 (0.3)	1.000
Use of intravascular ultrasound	41 (12.5)	46 (14.1)	0.634

Data are presented as mean±SD or n (%). 1VD: single-vessel disease; 2VD: two-vessel disease; 3VD: three-vessel disease; DAPT: dual antiplatelet therapy

p=0.360), as shown in **Figure 2D**. There were no significant differences between groups for all-cause death, cardiovascular death, MI, ischaemia-driven TVR, stent thrombosis, or stroke. No stent thrombosis events were observed among the total 656 patients during the study follow-up period. Two deaths occurred in the 12M-DAPT group. In contrast, all five deaths in the 1M-DAPT group occurred during the first month of therapy. Details of the death and stroke cases are described in **Supplementary Table 4**.

In the per-protocol (PP) analysis, baseline clinical, procedural, and angiographic characteristics were well balanced between the two treatment groups **(Supplementary Table 5, Supplementary Table 6)**. During the 12 months, NACE occurred in 9.2% (29 patients) in the 12M-DAPT group and 4.5% (14 patients) in the 1M-DAPT group **(Supplementary Table 7)**. The absolute risk difference was –4.7% (95% CI: –7.8% to –1.5%), confirming non-inferiority (p for non-inferiority=0.0094) and consistent with the findings of the ITT analysis **(Figure 3A)**. Furthermore, 1M-DAPT showed superiority in reducing NACE (HR 0.48, 95% CI: 0.25-0.91; p=0.024), primarily driven by a lower incidence of bleeding events. In the landmark analysis beyond 30 days, the event rate of NACE remained lower in the 1M-DAPT group (7.1% vs 2.0%; HR 0.27, 95% CI: 0.11-0.66; p=0.004) as shown in **Figure 3B**. The incidence of all bleeding (BARC Type 2-5) and major bleeding (BARC Type 3-5) was consistently lower in the 1M-DAPT group throughout the study period **(Table 3, Figure 3C)**. There were no significant differences between the groups with regard to all-cause death, cardiovascular death, MI, ischaemia-driven target vessel revascularisation, stent thrombosis, stroke, or MACE **(Supplementary Table 7, Figure 3D)**.

Figure 4 shows the results of the subgroup analyses for the primary endpoint across key clinical characteristics. The treatment effect of 1-month DAPT followed by reduced-dose prasugrel monotherapy was consistent across all subgroups, including ACS subtypes (unstable angina, non-STEMI, and STEMI). The effect was also consistent among patients who required prasugrel dose reduction from the beginning, due to age or body weight, suggesting that early heterogeneity in prasugrel

Table 3. Outcomes of the intention-to-treat analysis.

Clinical outcomes	Total duration				Day 30-360			
	Prasugrel-based 12-month DAPT (N=328)	Prasugrel 5 mg monotherapy after 1 month of DAPT (N=328)	HR (95% CI)	p-value	Prasugrel-based 12-month DAPT (N=328)	Prasugrel 5 mg monotherapy after 1 month of DAPT (N=328)	HR (95% CI)	p-value
Net adverse clinical events (a composite of all-cause death, myocardial infarction, stroke, ischaemia-driven TVR, and BARC Type 2-5 bleeding)	29 (8.8)	16 (4.9)	0.51 (0.27-0.95)	0.034	22 (7.1)	6 (1.9)	0.27 (0.11-0.66)	0.004
All bleeding (BARC Type 2-5)	17 (5.2)	4 (1.2)	0.23 (0.08-0.69)	0.009	13 (4.2)	1 (0.3)	0.07 (0.01-0.57)	<0.001
Type 2	2 (0.6)	2 (0.6)	0.98 (0.14-6.98)	0.986	2 (0.6)	1 (0.3)	0.48 (0.04-5.35)	0.554
Major bleeding (BARC Type 3-5)	15 (4.6)	2 (0.6)	0.13 (0.03-0.58)	0.007	11 (3.5)	0 (0)	-	0.002
Type 3a	3 (0.9)	1 (0.3)	0.33 (0.03-3.19)	0.340	2 (0.6)	0 (0)	-	0.499
Type 3b	10 (3.0)	1 (0.3)	0.10 (0.01-0.77)	0.027	7 (2.2)	0 (0)	-	0.015
Type 3c	2 (0.6)	0 (0)	-	-	2 (0.6)	0 (0)	-	0.499
Type 5	0 (0)	0 (0)	-	-	0 (0)	0 (0)	-	-
Gastrointestinal bleeding	13 (4.0)	2 (0.6)	0.15 (0.03-0.67)	0.013	9 (2.9)	1 (0.3)	0.11 (0.01-0.86)	0.035
All-cause death	2 (0.6)	5 (1.5)	2.48 (0.48-12.78)	0.278	2 (0.6)	0 (0)	-	-
Cardiovascular death	1 (0.3)	2 (0.6)	1.99 (0.18-21.94)	0.574	1 (0.3)	0 (0)	-	-
Myocardial infarction	3 (0.9)	1 (0.3)	0.33 (0.03-3.14)	0.332	2 (0.6)	1 (0.3)	0.49 (0.04-5.38)	0.558
Ischaemia-driven TVR	7 (2.1)	6 (1.8)	0.84 (0.28-2.50)	0.755	6 (1.9)	4 (1.3)	0.65 (0.18-2.31)	0.508
Stent thrombosis	0 (0)	0 (0)	-	-	0 (0)	0 (0)	-	-
Stroke	4 (1.2)	0 (0)	-	-	2 (0.6)	0 (0)	-	-
Ischaemic	4 (1.2)	0 (0)	-	-	2 (0.6)	0 (0)	-	-
Haemorrhagic	0 (0)	0 (0)	-	-	0 (0)	0 (0)	-	-
Major adverse cardiovascular events (a composite of cardiovascular death, myocardial infarction, stroke, and ischaemia-driven TVR)	12 (3.7)	8 (2.4)	0.66 (0.27-1.61)	0.360	9 (2.9)	4 (1.3)	0.44 (0.13-1.41)	0.166

Data are n (%), unless otherwise indicated. BARC: Bleeding Academic Research Consortium; CI: confidence interval; DAPT: dual antiplatelet therapy; HR: hazard ratio; TVR: target vessel revascularisation

dosing did not modify the overall treatment effect. Notably, in patients with high bleeding risk, there was a potential signal suggesting greater benefit with 1M-DAPT, showing a lower HR for NACE (HR 0.44, 95% CI: 0.21-0.89), although the p-value for interaction was not statistically significant.

Discussion

To our knowledge, the 4D-ACS trial is the first to demonstrate the benefit of a 1-month prasugrel-based DAPT strategy compared to 12-month DAPT in ACS patients. Additionally, our study uniquely integrates both an ultrashort DAPT duration, prasugrel dose reduction, and DCS implantation. The results show that this strategy enhances safety while preserving ischaemic protection for ACS patients **(Central illustration)**.

The optimal duration of DAPT in ACS patients has been progressively shortened based on accumulating evidence. Previous trials have demonstrated the feasibility

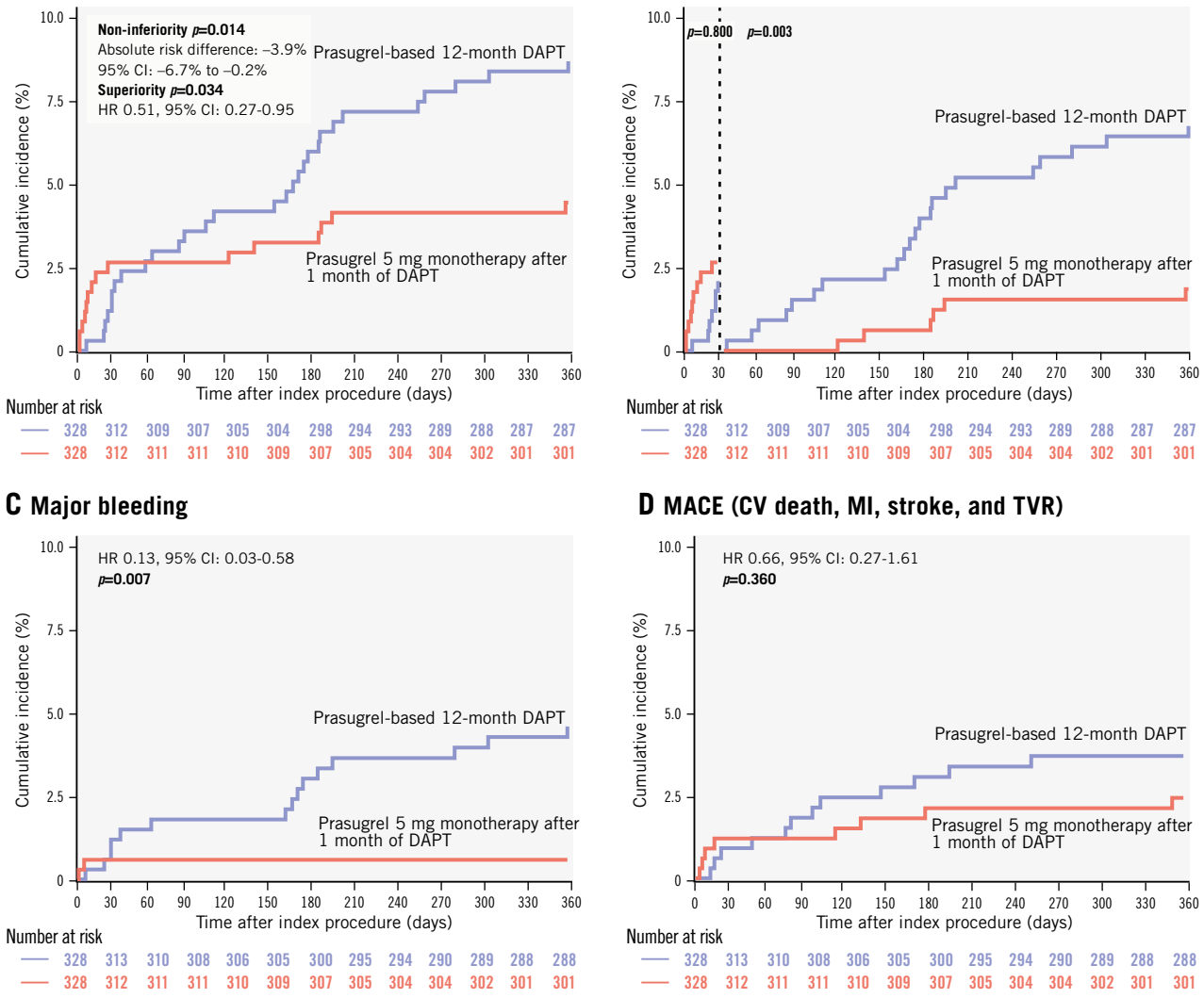


Figure 2. *Primary and secondary outcomes of the intention-to-treat analysis. A) Primary outcome of NACE up to 12 months. B) Landmark analysis of NACE between day 30 and day 360. C) Major bleeding (BARC Type 3-5). D) MACE incidence. BARC: Bleeding Academic Research Consortium; CI: confidence interval; CV: cardiovascular; DAPT: dual antiplatelet therapy; HR: hazard ratio; MACE: major adverse cardiovascular events; MI: myocardial infarction; NACE: net adverse clinical events; ST: stent thrombosis; TVR: target vessel revascularisation*

of 1- or 3-month DAPT followed by non-prasugrel-based mono antiplatelet therapy[13-17]. More recently, the ShorT and OPtimal duration of Dual AntiPlatelet Therapy-3 (STOPDAPT-3)[18] trial evaluated an even more aggressive approach, comparing the 1-month outcome of initiating prasugrel 3.75 mg monotherapy (without aspirin) versus a standard 1-month DAPT regimen. During the evaluated 30 days, however, the aspirin-free prasugrel-only group had a 1.8-fold higher ischaemic event rate and a 3.8-fold higher stent thrombosis risk, raising concerns that complete DAPT omission may be premature in ACS patients. Notably, prasugrel monotherapy following a short DAPT regimen compared to conventional prasugrel-based DAPT has not been previously evaluated in this setting. The 4D-ACS trial addresses this gap by demonstrating that 1-month DAPT followed by prasugrel 5 mg monotherapy provides a safer yet effective alternative to both prolonged 12-month DAPT and immediate aspirin-free strategies.

De-escalating strategies, such as dose reduction of potent $P2Y_{12}$ inhibitors or switching to less potent $P2Y_{12}$ inhibitors, have been investigated in previous trials. The Harmonizing Optimal Strategy for Treatment of coronary artery diseases – comparison of REDUCtion of prasugrEl dose or POLYmer TECHnology in ACS patients (HOST-REDUCE-POLYTECH-ACS) trial demonstrated that de-escalating prasugrel from 10 mg to 5 mg after the first month reduced bleeding without increasing ischaemic events in Korean patients with ACS[4]. The Timing of Platelet Inhibition after ACS (TOPIC) trial showed that switching from aspirin plus a potent $P2Y_{12}$ inhibitor to aspirin plus a less potent

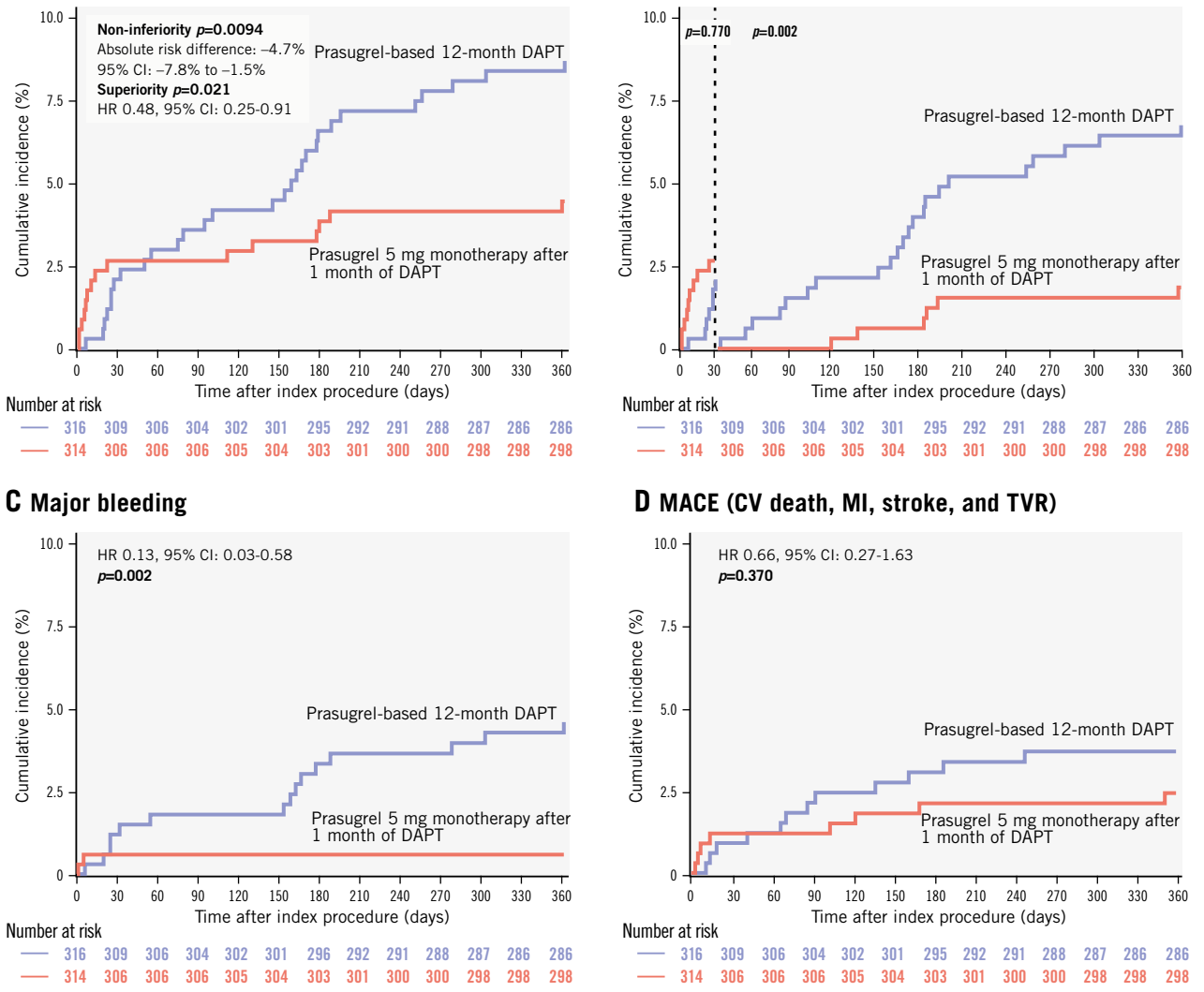


Figure 3. *Primary and secondary outcomes of the per-protocol population. A) Primary outcome of NACE up to 12 months. B) Landmark analysis of NACE between day 30 and day 360. C) Major bleeding (BARC Type 3-5). D) MACE incidence. BARC: Bleeding Academic Research Consortium; CI: confidence interval; CV: cardiovascular; DAPT: dual antiplatelet therapy; HR: hazard ratio; MACE: major adverse cardiovascular events; MI: myocardial infarction; NACE: net adverse clinical events; ST: stent thrombosis; TVR: target vessel revascularisation*

$P2Y_{12}$ inhibitor – clopidogrel – 1 month after ACS reduced NACE[19]. Building upon these findings, the 4D-ACS trial extended the concept of de-escalation by discontinuing aspirin – unlike HOST-REDUCE-POLYTECH-ACS – and maintaining prasugrel monotherapy at a reduced dose, rather than switching to a less potent agent, as in the TOPIC trial. The favourable outcomes in the 1M-DAPT group might suggest that continued aspirin beyond 1 month may contribute to bleeding without additional ischaemic benefit. Moreover, our results demonstrate that prasugrel dose reduction alone, without switching to clopidogrel, can provide a superior net clinical benefit. This may be particularly relevant in East Asian patients, in whom clopidogrel metabolism is variable and associated with a higher risk of ischaemic events[20].

A growing body of evidence has supported the clinical use of low-dose prasugrel, particularly in East Asia. In Japan and Taiwan, prasugrel 3.75 mg is the standard approved maintenance dose. The PRASugrel compared with clopidogrel For Japanese patIenTs with ACS undergoing PCI (PRASFIT ACS) study demonstrated the pharmacodynamics and clinical feasibility of low-dose prasugrel monotherapy in Japanese patients[21,22]. Outside of Japan and Taiwan, prasugrel 10 mg remains the standard dose – even in South Korea. Prasugrel 5 mg has shown platelet inhibition comparable to prasugrel 10 mg in pharmacodynamic studies of Korean patients[23,24] and is now widely used in real-world clinical practice together with prasugrel 10 mg in South Korea[4,10]. Notably, unlike clopidogrel, which is metabolically activated via cytochrome P450 2C19 (CYP2C19), prasugrel is primarily activated

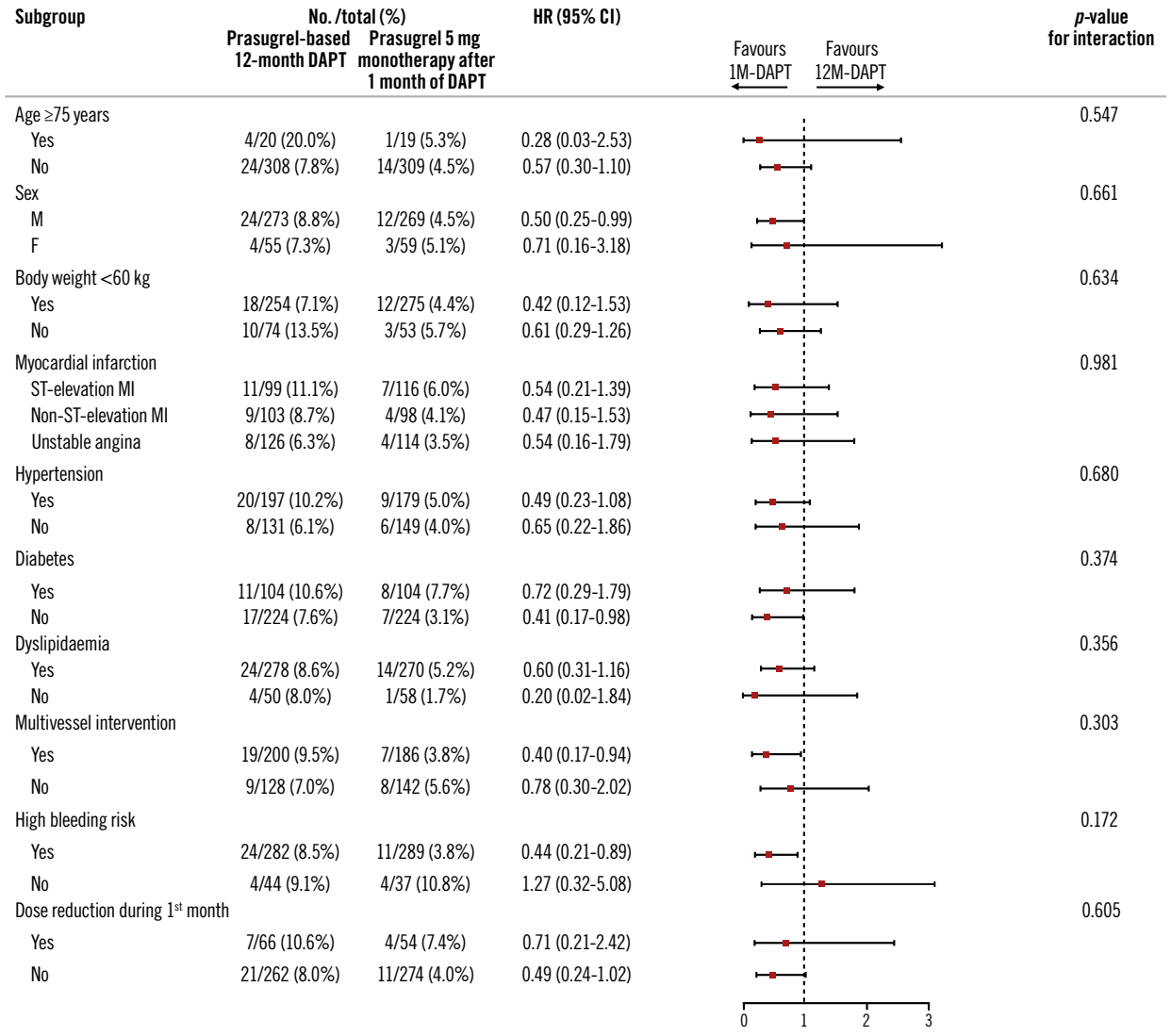
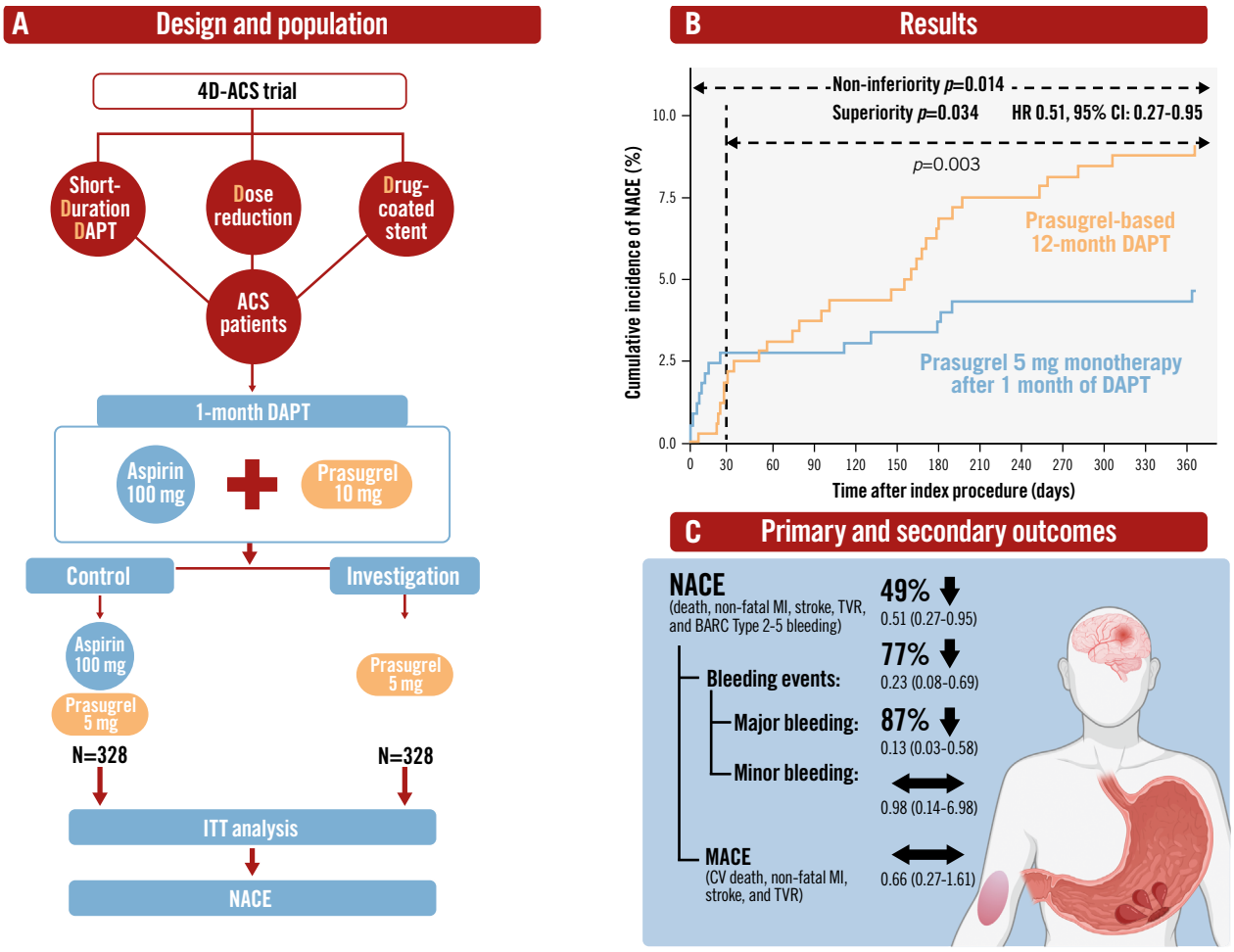


Figure 4. *Forest plot of the primary outcome across clinical subgroups. HRs and 95% CIs for NACE comparing 1M-DAPT and 12M-DAPT are shown across predefined subgroups. 1M-DAPT: 1-month DAPT followed by prasugrel 5 mg monotherapy; 12M-DAPT: 12-month DAPT; CI: confidence interval; DAPT: dual antiplatelet therapy; F: female; HR: hazard ratio; M: male; MI: myocardial infarction; NACE: net adverse clinical events*

through cytochrome P450 3A4 and 2B6. The PRASFIT-ACS pharmacogenomic subanalysis showed that low-dose prasugrel provided consistent platelet inhibition and clinical efficacy irrespective of the CYP2C19 genotype, in contrast to clopidogrel, which showed significantly reduced effectiveness in intermediate or poor metabolisers[21]. Given the high prevalence of CYP2C19 loss-of-function alleles among East Asians, this metabolic stability of prasugrel may be particularly advantageous in this population.

The pharmacological rationale for prasugrel 5 mg has also been explored in Western populations[25]. The Comparison of Prasugrel and Clopidogrel in Low Body Weight Versus Higher Body Weight With Coronary Artery Disease (FEATHER)[9] and Comparison of Prasugrel and Clopidogrel in Very Elderly and Non-Elderly Patients With Stable Coronary Artery Disease (GENERATIONS)[8] trials showed that prasugrel 5 mg achieved platelet inhibition that was non-inferior to prasugrel 10 mg in low-body-weight and elderly patients, respectively, while maintaining a bleeding profile comparable to clopidogrel. Furthermore, the Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment (ISAR-REACT 5)[26] and TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes (TRILOGY ACS)[27] trials applied the same dose-reduction criteria, albeit in a minority of patients, and demonstrated the feasibility of prasugrel 5 mg in selected Westerners. Although the results of the 4D-ACS trial may be most applicable to East Asian patients – given the East Asian paradox, which describes the distinct phenotype of lower ischaemic but higher bleeding risk in this population[28] – they may also be appropriate for selected Western patients with high bleeding risk or those meeting dose-reduction criteria. Nonetheless, broader validation in diverse populations is warranted to confirm the generalisability of this approach.

Summary of the 4D-ACS trial.



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A) Trial details; (B) NACE incidence according to a 1-month or 12-month DAPT strategy; (C) primary and secondary outcomes with HRs and 95% CIs. 4D-ACS: The Effect of Short Duration of Dual-Antiplatelet Therapy Followed by Dose Reduction After Implantation of Drug-Coated Stent in Acute Coronary Syndrome; ACS: acute coronary syndrome; BARC: Bleeding Academic Research Consortium; CI: confidence interval; CV: cardiovascular; DAPT: dual antiplatelet therapy; HR: hazard ratio; ITT: intention-to-treat; MACE: major adverse cardiovascular events; MI: myocardial infarction; NACE: net adverse clinical events; TVR: target vessel revascularisation

Aspirin is well established as an essential agent in the secondary prevention of cardiovascular diseases; however, its role in cardiovascular prevention has become increasingly limited because of concerns about bleeding. Recent guidelines have restricted its use for primary prevention in patients with low to moderate cardiovascular risk[29], and alternative strategies using non-aspirin agents are being explored[30]. Even in secondary prevention settings, prolonged aspirin use may elevate bleeding risk – particularly GI bleeding. In our study, GI bleeding was significantly more common in the 12M-DAPT group, occurring nearly 7 times more frequently than in the 1M-DAPT group, and accounted for the majority of bleeding events (88%, 15 of 17 events). Notably, between day 30 and day 360, following the discontinuation of DAPT in the 1M-DAPT group, only one minor bleeding event occurred in the 1M-DAPT group, whereas the 12M-DAPT group experienced 13 BARC Type 2-5 bleeding events (including 11 [84.6%] major bleeding events). This corresponds to an 11- to 13-fold increase in bleeding risk – including a nearly 9-fold increase in GI bleeding – associated with the continuation of aspirin beyond the first month. These findings underscore the importance of re-evaluating the optimal duration of aspirin therapy, especially beyond the early phase of treatment.

Another important factor that may have contributed to the favourable outcomes observed in our strategy is the

use of a DCS, specifically the polymer-free biolimus-eluting BioFreedom Ultra stent. Previous real-world data[31] and randomised trials, such as the Prospective, Randomized Comparison of BioFreedom Biolimus A9 Drug Coated Stent Versus the Gazelle Bare Metal Stent in Patients With High Risk of Bleeding (LEADERS FREE)[5] trial and A Clinical Study Comparing Two Forms of Anti-platelet Therapy After Stent Implantation (GLOBAL LEADERS)[32] trial, have demonstrated that DCS perform well even with only 1 month of DAPT. Polymer-free drug-eluting stents are designed to mitigate the chronic inflammatory response associated with both durable and biodegradable polymers, which can impair endothelial healing and increase the risk of stent thrombosis[33]. This may partly explain the absence of stent thrombosis among the 656 patients in our study. However, the favourable outcomes observed in this trial may not be directly extrapolable to drug-eluting stents that incorporate durable or biodegradable polymers, which differ in terms of vascular healing kinetics, drug release profiles, and long-term biocompatibility. Whether similarly abbreviated DAPT strategies would yield comparable safety and efficacy with such stents remains uncertain and requires further investigation.

The 2025 ACC/AHA guidelines now provide a Class I, Level of Evidence A recommendation for transitioning to ticagrelor monotherapy ≥1 month post-PCI in ACS patients who have tolerated DAPT[2]. However, no such recommendation exists for prasugrel monotherapy, reflecting an important gap in current evidence. The 4D-ACS trial provides new data in this context, demonstrating that 1-month DAPT followed by prasugrel 5 mg monotherapy may also offer similar reduction in bleeding risk while preserving ischaemic safety.

Limitations

This study has several limitations. First, while the trial was adequately powered to assess non-inferiority for NACE, it was not powered to detect differences in individual ischaemic components, which occurred infrequently in both groups. The annual incidence of MACE was 2.4% in the 1M-DAPT group and 3.7% in the 12M-DAPT group in our data, consistent with other trials in ACS populations[4,13-17]. The use of a polymer-free DCS, which is designed for rapid endothelial healing, may also have contributed to the overall low ischaemic event rates observed in both groups. Second, during the trial, we faced reimbursement restrictions related to prasugrel use in patients aged ≥75 years under the Korean National Health Insurance Review & Assessment Service. Because of concerns about increased bleeding risk in this population, institutional prescribing policies were progressively tightened, and from the midpoint of the study onward, patients aged ≥75 years could no longer be enrolled at several sites. As a result, the representation of elderly patients was limited. Third, given that this trial was conducted exclusively in East Asian patients, who generally have a lower body weight and higher susceptibility to bleeding with antiplatelet therapy, the generalisability of our findings to non-East Asian populations may be limited. Further studies in broader and more diverse populations are warranted to confirm these findings.

Conclusions

One-month DAPT followed by prasugrel 5 mg monotherapy in ACS patients with a drug-coated stent reduced NACE by 49%, primarily driven by a 77% reduction in bleeding events, compared to 12-month DAPT.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria.
Supplementary Table 2. Reasons for premature discontinuation of allocated antiplatelet therapy.
Supplementary Table 3. Discharge medications.
Supplementary Table 4. Details of mortality and stroke cases.
Supplementary Table 5. Baseline characteristics of per-protocol analysis.
Supplementary Table 6. Procedural and angiographic findings of per-protocol analysis.
Supplementary Table 7. Outcomes of per-protocol analysis.
Supplementary Figure 1. Enrolment algorithm.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-25-00331

Supplementary data

Supplementary Table 1. Inclusion and exclusion criteria.

1. Inclusion criteria
(1) Patients over the age of 19 and eligible for prasugrel use for a year in Korea
(2) Patients undergoing intervention for acute coronary syndrome
(3) Patients who underwent coronary intervention with a BioFreedom Ultra™ stent
2. Exclusion criteria
(1) Women of childbearing potential who plan to become pregnant within the study period
(2) In case of hypersensitivity to antiplatelet agents or contraindications
(3) Patients with a life expectancy of less than 1 year
(4) Patients requiring the use of anticoagulants
(5) Patients with a previous history of cerebral infarction

Supplementary Table 2. Reasons for premature discontinuation of allocated antiplatelet therapy.

	Prasugrel-based 12-month DAPT (N=14)	**Prasugrel 5mg monotherapy after 1 month of DAPT (N=13)**
Physicians' discretion due to high-bleeding risk	5 (1.5%)	3 (0.9%)
Physicians' discretion due to high-ischemic risk	2 (0.6%)	4 (1.2%)
Need of anticoagulation	1 (0.3%)	2 (0.6%)
Discontinuation of prasugrel due to reimbursement issue after becoming over 75 during study	4 (1.3%)	4 (1.3%)
Discontinuation of aspirin due to easy bruise	2 (0.6%)	0 (0.0%)

DAPT, dual-antiplatelet therapy

Supplementary Table 3. Discharge medications.

	Prasugrel-based 12-month DAPT (N=328)	Prasugrel 5mg monotherapy after 1 month of DAPT (N=328)	*P*
Discharge Medication			
Statin	322 (98.8%)	321 (98.4%)	1.000
ACE inhibitor	12 (3.7%)	10 (3%)	0.828
ARB	98 (29.9%)	81 (24.7%)	0.161
Beta-blocker	82 (25%)	85 (25.9%)	0.858
Calcium channel blocker	50 (15.2%)	34 (10.3%)	0.080
Spironolactone	14 (4.3%)	19 (5.8%)	0.475
Thiazide or loop diuretics	19 (5.8%)	24 (7.3%)	0.528
PPI or P-CAB	83 (25.3%)	74 (22.5%)	0.464

DAPT, dual-antiplatelet therapy, ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; PPI, proton pump inhibitor; P-CAB, potassium-competitive acid blocker

Supplementary Table 4. Details of mortality and stroke cases.

Type of event	Assigned group	Index presentation, other risk factors, coronary disease extent	Index PCI	Days after PCI	Medication at the event	Presentation, intervention	Prognosis
CV death	12M-DAPT	NSTEMI, HTN, DM, dyslipidemia, LVEF 54%, 3VD	1) Distal LAD (3.0 x 19mm) 2) Proximal LCX 100% (2.75 x 19 mm)	75	aspirin 100mg + prasugrel 5mg	SCD at ER	-
Non-CV death	12M-DAPT	Unstable angina, HTN, DM, current smoker LVEF 30%, 3VD	1) Mid RCA 90% (2.75 x 19 mm) 2) Proximal LCX 90% (3.0 x 29 mm)	253	aspirin 100mg + prasugrel 5mg	Biliary sepsis	-
CV death	1M-DAPT	STEMI, HTN, DM, dyslipidemia, CKD, current smoker LVEF 54%, 3VD	1) Proximal LAD 100% (2.75 x 19 mm) 2) Distal LCX 95% (3.5 x 24 mm)	40	aspirin 100mg + prasugrel 5mg	Died during initial hospitalization	-
Non-CV death	1M-DAPT	STEMI, dyslipidemia LVEF 47%, 1VD	1) Mid RCA 100% (3.0 x 19 mm)	13	aspirin 100mg + prasugrel 10mg	Died of pneumonia during initial hospitalization	-
CV death	1M-DAPT	STEMI, dyslipidemia LVEF 34%, 1VD	1) Mid LAD 100% (3.5 x 19 and 2.75 x 19 mm overlap)	22	aspirin 100mg + prasugrel 10mg	Died after surgery for post-MI infarction VSD	-
Non-CV death	1M-DAPT	Unstable angina, HTN, DM, dyslipidemia, LVEF 47%, 2VD	1) Distal LCX 90% (2.5 x 38 mm) 2) Diagonal 90% (2.5 x 19 mm)	6	aspirin 100mg + prasugrel 5mg	Died of COVID-19 infection	-
Non-CV death	1M-DAPT	STEMI, LVEF 53%, 1VD	1) Posterior descending artery 100% (2.75 x 19 mm)	10	aspirin 100mg + prasugrel 5mg	Septic shock	-

Stroke	12M-DAPT	Unstable angina, HTN, DM, dyslipidemia, current smoker LVEF 29%, 2VD	1) Diagonal 90% (2.5 x 19 mm) 2) Mid LAD (3.5 x 25 mm)	22	aspirin 100mg + prasugrel 10mg	Right side motor weakness	Alive
Stroke	12M-DAPT	STEMI, previous PCI, current smoker LVEF 65%, 3VD	1) Mid LAD 90% (2.5 x 19 mm) 2) Mid OM 100% (2.5 x 19 mm)	258	aspirin 100mg + prasugrel 5mg	Lt side motor weakness	Alive
Stroke	12M-DAPT	NSTEMI, HTN, DM, current smoker LVEF 53%, 2VD	1) Proximal LAD 90% (3.0 x 24 mm) 2) Mid LCX 80% (2.75 x 19 mm)	19	aspirin 100mg + prasugrel 10mg	Lt side motor weakness	Alive
Stroke	12M-DAPT	STEMI, current smoker LVEF 43%, 3VD	1) Proximal LAD 100% (3.0 x 24 mm) Distal LCX 80% (2.75 x 19 mm)	50	aspirin 100mg + prasugrel 10mg	Right side motor weakness	Alive

CV, cardiovascular; DAPT, dual-antiplatelet therapy; 12M-DAPT, Prasugrel-based 12-month DAPT; 1M-DAPT, Prasugrel 5mg monotherapy after 1 month of DAPT; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; HTN, hypertension; DM, diabetes mellitus; LVEF, left ventricular ejection fraction; VD, vessel disease; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; VSD, ventricular septal defect; SCD, sudden cardiac death; ER, emergency room

Supplementary Table 5. Baseline characteristics of per-protocol analysis.

	Prasugrel-based 12-month DAPT (N=316)	Prasugrel 5mg monotherapy after 1 month of DAPT (N=314)	*P*
Age, years			
Mean	61.5 ± 9.6	60.9 ± 9.7	
≥75	20 (6.3)	14 (4.5)	0.388
Male sex	262 (82.9)	257 (81.8)	0.806
Dose reduction of prasugrel during 1st month of DAPT	64 (20.3)	51 (16.2)	0.230
Weight, kg			
Mean	70.0 ± 12.0	70.8 ± 12.3	
<60	65 (90.3)	50 (86.2)	0.656
Body mass index	25.0 ± 3.1	25.2 ± 3.5	0.314
High bleeding risk	43 (13.7)	34 (10.9)	0.345
Hypertension	189 (59.8)	167 (53.2)	0.110
Diabetes	101 (32.0)	98 (31.2)	0.907
Dyslipidemia	268 (84.8)	259 (82.5)	0.495
Chronic kidney disease	11 (3.5)	9 (2.9)	0.831
Smoking			0.556
Current	131 (41.5)	117 (37.3)	
Former	45 (14.2)	47 (15.0)	
Never	140 (44.3)	150 (47.8)	
Previous myocardial infarction	7 (2.2)	9 (2.9)	0.790
Previous PCI	22 (7.0)	22 (7.0)	1.000
Previous CABG	0 (0.0)	3 (1.0)	0.123
Family history of CAD	18 (5.7)	16 (5.1)	0.875
Left ventricular ejection fraction, %	55.1 ± 11.7	54.7 ± 12.9	0.670
Clinical presentation			0.355
ST-elevation myocardial infarction	95 (30.1)	111 (35.4)	
Non-ST-elevation myocardial infarction	58 (18.4)	51 (16.2)	
Unstable angina	163 (51.6)	152 (48.4)	

DAPT, dual-antiplatelet therapy; PCI, percutaneous coronary intervention; CABG, coronary artery bypass surgery; CAD, coronary artery disease

Supplementary Table 6. Procedural and angiographic findings of per-protocol analysis.

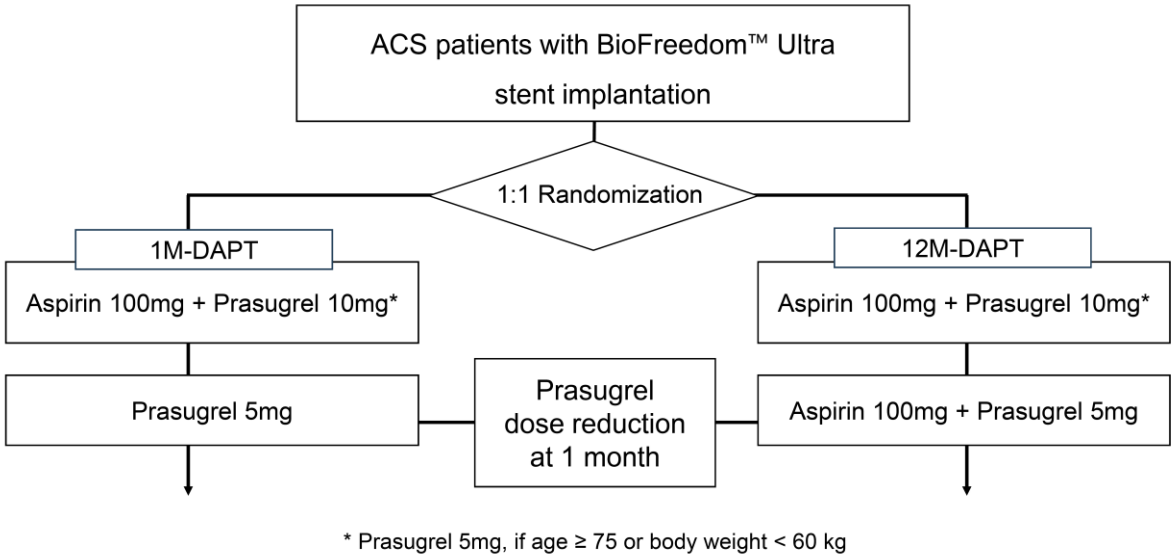
	Prasugrel-based 12-month DAPT (N=316)	Prasugrel 5mg monotherapy after 1 month of DAPT (N=314)	*P*
Transradial_access	270 (85.4)	264 (84.1)	0.714
Multivessel coronary artery disease	94 (61.4)	174 (55.4)	0.149
Left main disease	6 (1.9)	1 (0.3)	0.123
Bifurcation lesion	8 (2.5)	14 (4.5)	0.268
In-stent restenosis lesion	1 (0.3)	3 (1.0)	0.372
Number of lesions	1.9 ± 1.0	1.8 ± 1.0	0.399
Multilesion intervention (%)	170 (62.5)	180 (67.4)	0.269
Multivessel intervention (%)	194 (61.4)	174 (55.4)	0.149
Disease extent			0.274
1VD	122 (38.6)	140 (44.6)	
2VD	113 (35.8)	106 (33.8)	
3VD	81 (25.6)	68 (21.7)	
Treated lesion			0.755
Left main coronary artery	7 (2.2)	4 (1.3)	
Left anterior descending artery	220 (69.6)	214 (68.2)	
Left circumflex artery	40 (12.7)	42 (13.4)	
Right coronary artery	59 (18.7)	59 (18.8)	
Ramus intermedius artery	0 (0.0)	1 (0.3)	
Total stent length (mm)	26.52 ± 6.31	26.45 ± 7.55	0.754
Stent diameter (mm)	3.08 ± 0.44	3.10 ± 0.45	0.543
Stent length (mm)	24.63 ± 6.65	24.23 ± 6.46	0.441
Diameter stenosis (%)	88.3 ± 13.9	89.2 ± 13.2	0.386
Intra-aortic balloon pump	0 (0.0)	1 (0.3)	0.498
Percutaneous cardiopulmonary support	0 (0.0)	1 (0.3)	0.498
Unfractionated heparin	247 (78.2)	242 (77.1)	0.533
Low-molecular weight heparin	7 (2.2)	5 (1.6)	0.815
Use of glycoprotein IIb/IIIa inhibitors	1 (0.3)	1 (0.3)	1.000
Use of intravascular ultrasound	40 (12.7)	44 (14.1)	0.690

DAPT, dual-antiplatelet therapy; VD, vessel disease

Supplementary Table 7. Outcomes of per-protocol analysis.

	Total duration				Day 30 - 365			
Clinical Outcomes	**Prasugrel-based 12-month DAPT (N=316)**	**Prasugrel 5mg monotherapy after 1 month of DAPT (N=314)**	**HR (95% CI)**	***P***	**Prasugrel-based 12-month DAPT (N=316)**	**Prasugrel 5mg monotherapy after 1 month of DAPT (N=314)**	**HR (95% CI)**	***P***
Net adverse clinical events (a composite of all-cause death- myocardial infarction- stroke- ischemia-driven target vessel revascularization- and BARC type 2-5 bleeding)	29 (9.2)	14 (4.5)	0.48 (0.25-0.91)	0.024	22 (7.1)	6 (2.0)	0.27 (0.11-0.66)	0.004
All bleeding (BARC type 2-5)	17 (5.4)	3 (1.0)	0.17 (0.05-0.6)	0.005	13 (4.2)	1 (0.3)	0.08 (0.01-0.58)	0.013
Type 2	2 (0.6)	1 (0.3)	0.49 (0.04-5.37)	0.557	2 (0.6)	1 (0.3)	0.49 (0.04-5.37)	0.557
Major bleeding (BARC type 3-5)	15 (4.7)	2 (0.6)	0.13 (0.03-0.58)	0.007	11 (3.6)	0 (0.0)	-	-
Type 3a	3 (0.9)	1 (0.3)	0.33 (0.03-3.21)	0.342	2 (0.6)	0 (0.0)	-	-
Type 3b	10 (3.2)	1 (0.3)	0.10 (0.01-0.78)	0.028	7 (2.3)	0 (0.0)	-	-
Type 3c	2 (0.6)	0 (0.0)	-	-	2 (0.6)	0 (0.0)	-	-
Type 5	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
All-cause death	2 (0.6)	5 (1.5)	2.5 (0.49-12.91)	0.273	2 (0.6)	0 (0.0)	-	-
Cardiovascular death	1 (0.3)	2 (0.6)	2.01 (0.18-22.13)	0.570	1 (0.3)	0 (0.0)	-	-
Myocardial infarction	3 (0.9)	1 (0.3)	0.33 (0.03-3.16)	0.335	2 (0.6)	1 (0.3)	0.49 (0.04-5.41)	0.561
Ischemia-driven target-vessel revascularization	7 (2.2)	6 (1.9)	0.85 (0.28-2.52)	0.765	6 (1.9)	4 (1.3)	0.66 (0.19-2.32)	0.513
Stent thrombosis	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
Stroke	4 (1.3)	0 (0.0)	-	-	2 (0.6)	0 (0.0)	-	-
Ischemic	4 (1.3)	0 (0.0)	-	-	2 (0.6)	0 (0.0)	-	-
Hemorrhagic	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-
Major adverse cardiovascular event (a composite of cardiovascular death- myocardial infarction- stroke- and ischemia-driven target-vessel revascularization)	12 (3.8)	8 (2.5)	0.66 (0.27-1.63)	0.370	9 (2.9)	4 (1.3)	0.44 (0.13-1.42)	0.169

BARC, Bleeding Academic Research Consortium; DAPT, dual-antiplatelet therapy; HR, hazard ratio



Supplementary Figure 1. Enrolment algorithm.

ACS, acute coronary syndrome; 1M-DAPT, Prasugrel 5mg monotherapy after 1 month of dual-antiplatelet therapy; 12M-DAPT, Prasugrel-based 12-month DAPT