Dual antiplatelet therapy after percutaneous coronary intervention according to bleeding risk (HOST-BR): an open-label, multicentre, randomised clinical trial

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Summary

Background The optimal duration of dual antiplatelet therapy (DAPT) after coronary stenting according to bleeding risk is not well established. We aimed to evaluate the optimal duration of DAPT after coronary stenting according to bleeding risk.

Methods In this open-label, multicentre, randomised clinical trial, patients aged 19 years and older who received percutaneous coronary intervention with a drug-eluting stent at 50 high-volume cardiology centres in South Korea were stratified into high bleeding risk (HBR) or non-HBR strata, according to Academic Research Consortium for High Bleeding Risk criteria. Patients in the HBR stratum were randomly assigned (1:1) to 1-month or 3-month DAPT, and those in the non-HBR stratum were randomly assigned (1:1) to 3-month or 12-month DAPT. The three coprimary endpoints were net adverse clinical events (all-cause death, myocardial infarction, stent thrombosis, stroke, or major bleeding), major adverse cardiac or cerebral events (cardiovascular death, myocardial infarction, definite or probable stent thrombosis, or ischaemic stroke), and any actionable non-surgical bleeding at 1 year after randomisation. Primary endpoints were assessed in hierarchical order in the intention-to-treat population. This study is registered with cris.nih.go.kr, KCT0005356, and ClinicalTrials.gov, NCT05631769, and is complete.

Findings From July 24, 2020, to Sept 25, 2023, 4897 patients were enrolled (1598 in the HBR stratum and 3299 in the non-HBR stratum). In the HBR stratum, 1-month compared with 3-month DAPT did not reach non-inferiority for net adverse clinical events (144 [18·4%] of 798 *vs* 110 [14·0%] of 800 patients; hazard ratio [HR] 1·337 [95% CI 1·043–1·713]; p=0·82 for non-inferiority). Major adverse cardiac or cerebral events occurred in 74 (9·8%) patients in the 1-month DAPT group and 44 (5·8%) in the 3-month group; bleeding occurred in 105 (13·8%) patients in the 1-month group and 122 (15·8%) in the 3-month group. In the non-HBR stratum, 3-month was non-inferior to 12-month DAPT regarding net adverse clinical events (47 [2·9%] of 1649 *vs* 72 [4·4%] of 1650 patients; HR 0·657 [0·455–0·949]; p<0·0001 for non-inferiority) and major adverse cardiac or cerebral events (36 [2·2%] *vs* 37 [2·3%]; HR 0·984 [0·622–1·558]; p=0·0082 for non-inferiority), and superior for bleeding (120 [7·4%] *vs* 190 [11·7%]; HR 0·631 [0·502–0·793]; p<0·0001).

Interpretation In east Asian patients with HBR, 1-month DAPT did not reach non-inferiority to 3-month DAPT for net adverse clinical events. In patients without HBR, 3-month DAPT was non-inferior to 12-month DAPT regarding net adverse clinical events and major adverse cardiac or cerebral events, and superior for bleeding.

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Introduction

Guidelines recommend stratifying patients receiving coronary stenting according to bleeding risk.[1,2] The duration of dual antiplatelet therapy (DAPT) should balance thrombotic and bleeding risks,[3] and individuals at high bleeding risk (HBR)[4] should receive shorter DAPT. Several trials have evaluated the comparative efficacy of shorter versus longer durations of DAPT in the contemporary drug-eluting stent (DES) era, and meta-analyses have shown that a shorter duration of DAPT could reduce bleeding risk without an increase in ischaemic risk.[5,6] However, ideal DAPT durations according to bleeding risk have not been clearly established.[1,2]

Trials that exclusively enrolled patients with HBR before the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria were developed did not use a standardised definition of HBR.[7–11] We and others have shown that individuals with HBR, who are underrepresented in previous trials, are not only at a higher risk of bleeding events but also of thrombotic events,[12,13] an

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Research in context

Evidence before this study

The ideal strategy of antiplatelet therapy after percutaneous coronary intervention is directed by various factors, with bleeding risk being a major determinant. Although guidelines recommend different strategies for dual antiplatelet therapy (DAPT) stratified by bleeding risk, evidence on the duration of DAPT according to bleeding risk is scarce. We searched PubMed, Embase, and ClinicalTrials.gov from database inception to Jan 26, 2025, for randomised clinical trials published in English using the search terms "dual antiplatelet therapy", "duration", "bleeding risk", "percutaneous coronary intervention", and "randomised clinical trial". Our search identified one previous randomised study that was adequately powered to assess clinical outcomes: the MASTER DAPT study, which enrolled 4579 patients with high bleeding risk (HBR), reported that abbreviated DAPT (compared with standard therapy) was a safe strategy for these patients. However, MASTER DAPT did not use the definition of HBR proposed by the Academic Research Consortium, and the duration of DAPT was heterogeneous in the standard therapy group.

Added value of this study

The HOST-BR trial compared the effects of two different DAPT durations after percutaneous coronary intervention in participants stratified according to bleeding risk. In the HBR stratum, the 1-month DAPT group did not meet the non-inferiority criteria, as compared with the 3-month DAPT group, in regard to net adverse clinical events (a composite of all death, non-fatal myocardial infarction, stroke, or major bleeding). In the non-HBR stratum, the 3-month DAPT group was non-inferior to the 12-month DAPT group in regard to net adverse clinical events, major adverse cardiac or cerebral events (a composite of cardiovascular death, myocardial infarction, definite or probable stent thrombosis, or ischaemic stroke), and was superior for any actionable non-surgical bleeding.

Implications of all the available evidence

Our results do not support the use of 1-month DAPT after percutaneous coronary intervention in east Asian patients with HBR. For east Asian individuals without HBR, a 3-month DAPT regimen reduced bleeding risk without increasing thrombotic risk and might be preferable to a 12-month regimen.

observation that can be explained by the overlap of bleeding and thrombotic risk factors. Therefore, the optimal DAPT duration for individuals with HBR should minimise both bleeding and thrombotic complications. Current guidelines recommend DAPT durations of 1–3 months in individuals with HBR, but clinical evidence supporting this recommendation is weak, and mostly not based on randomised clinical trials.[14] Furthermore, no previous study has investigated the effect of DAPT duration on clinical outcomes in a dedicated non-HBR population. Previous trials comparing different DAPT durations after percutaneous coronary intervention (PCI) in all-comers were restricted by the inclusion of individuals with and without HBR.[15,16] To address this gap in evidence, we conducted a randomised clinical trial in which we stratified patients who received PCI with DES by bleeding risk using the ARC-HBR definition, and tested the effect of shorter versus longer DAPT durations in both strata to identify the optimal balance between thrombosis and bleeding risks.

See Online for appendix

Methods

Study design and participants

The Harmonizing Optimal Strategy for Treatment of coronary artery diseases—DAPT duration according to the Bleeding Risk (HOST-BR) trial was an investigator-initiated, open-label, multicentre, randomised clinical trial conducted at 50 high-volume cardiology centres in South Korea. Patients were eligible for enrolment if they were aged 19 years or older and had undergone successful PCI with a DES, regardless of PCI indication. Enrolled patients were stratified into the HBR or non-HBR stratum, according to the ARC-HBR definition,[4] after PCI. Baseline characteristics, including self-reported sex, were collected at enrolment. Patients enrolled into the HBR stratum were randomly allocated (1:1) to 1-month or 3-month DAPT after PCI and before discharge. Patients enrolled into the non-HBR stratum were randomly allocated (1:1) to 3-month or 12-month DAPT after PCI and before discharge. Detailed inclusion and exclusion criteria are shown in the appendix (p 10).

This study was conducted in accordance with the standards of the International Council for Harmonization Guidelines for Good Clinical Practice and the principles of the Declaration of Helsinki. The trial protocol was approved by the institutional review board of Seoul National University Hospital (H-2002-150-1106, approved on April 9, 2020), and by the ethics committees of all participating institutions (appendix pp 5–8). All participants provided written informed consent before randomisation. The executive committee and all authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol (appendix pp 4–8). This study is registered with cris.nih.go.kr, KCT0005356, and ClinicalTrials.gov, NCT05631769, and is complete.

Randomisation

Randomisation was done using a web-based randomisation programme (IIS 8.0, ASP.NET 4.0, and Oracle 12) developed by an independent organisation (T&W Software, Seoul, South Korea), and was run by an independent research nurse or clinical nurse coordinator, who was not involved in the trial. Randomisation was performed without any further stratification, and patients

and study investigators were not masked to the assigned group.

Procedures

As per protocol, patients in the HBR stratum underwent PCI with the XIENCE or XIENCE Skypoint stents (Abbott, Chicago, IL, USA). Patients in the non-HBR stratum underwent PCI with the Onyx or Onyx Frontier stents (Medtronic, Minneapolis, MN, USA). After PCI, all patients received aspirin 100 mg daily and a P2Y12 inhibitor at the treating physician's discretion. The antiplatelet monotherapy agent after the designated DAPT duration was left to the treating physician's discretion. Clinical follow-up was scheduled at 1, 3, 6, and 12 months after the index PCI via an office visit or telephone interview. Clinical status, medication adherence, and the occurrence of any clinical events were assessed at each follow-up visit.

Outcomes

This trial had three coprimary endpoints, tested in a hierarchical order. The first coprimary endpoint was net adverse clinical events, defined as a composite of any-cause death, non-fatal myocardial infarction, definite and probable stent thrombosis, stroke, or major bleeding defined by the Bleeding Academic Research Consortium (BARC) criteria (type 3 or 5).[17] The second coprimary endpoint was major adverse cardiac and cerebrovascular events, defined as a composite of cardiac death, non-fatal myocardial infarction, definite and probable stent thrombosis, or ischaemic stroke. The third coprimary endpoint was any actionable non-surgical bleeding defined by the BARC criteria (type 2, 3, and 5). The secondary endpoints were the individual components of the primary endpoints, medication compliance, revascularisation (target vessel and non-target vessel), bleeding according to the International Society on Thrombosis and Haemostasis classification, and stent procedure success.

The main analysis of the primary endpoints was done on all randomly assigned patients (intention-to-treat population) at 1 year after randomisation. A per-protocol analysis was also performed. A post-hoc subgroup analysis was performed on subgroups according to sex, age (<65 years or ≥65 years), diabetes, chronic kidney disease, acute coronary syndrome, potent P2Y12 inhibitor usage, and oral anticoagulant usage, using the Cox proportional hazards regression model. A landmark analysis was performed after the timepoint at which the two groups had identical antiplatelet strategies, to exclude the period when the treatment effect was null. To evaluate patients who had both HBR and high thrombotic risk, clinical outcomes were analysed according to thrombotic risk using the Patterns of Non-Adherence to Anti-Platelet Regimen in Stented Patients thrombotic risk score.[18] Detailed definitions of each endpoint and the study population are given in the appendix (pp 17–22). The vital status of all patients was cross-checked through the National Health Insurance Service system of South Korea and Statistics Korea. Causes of death were confirmed by the recorded data classified by ICD-10 Clinical Modification codes. All clinical outcomes were adjudicated by an independent clinical event committee, which was masked to the treatment assignment, and patient safety was overseen by the data and safety monitoring board.

Statistical analysis

The primary objective of this study was to compare the effect of a shorter versus a longer DAPT strategy, according to patient bleeding risk (HBR or non-HBR). We tested whether the shorter DAPT strategy (1-month DAPT for the HBR stratum and 3-month DAPT for the non-HBR stratum) would be non-inferior to the longer DAPT strategy (3-month DAPT for the HBR stratum and 12-month DAPT for the non-HBR stratum) for net adverse clinical events and major adverse cardiac or cerebral events, and whether the shorter DAPT strategy would be superior to the longer DAPT strategy for any actionable non-surgical bleeding during the 1-year follow-up. The three coprimary endpoints were tested in hierarchical order. The cumulative incidence of each group was calculated at 1 year after randomisation.

The sample size calculation of the HBR stratum was based on the assumption that the event rates of net adverse clinical events would be 7·0% in the 1-month DAPT group and 9·0% in the 3-month DAPT group. The non-inferiority margin was 2·7%, which corresponds to a hazard ratio (HR) of 1·3. With a sampling ratio of 1:1 and an estimated rate of loss to follow-up of 2·0%, 1600 patients were needed to ensure a power of 90% with a two-sided α of 5% (one-sided 2·5%) to prove the first hypothesis. With this sample size, the power for the second and third hypotheses was estimated at a two-sided α of 5% in sequential hierarchical order. The expected annual major adverse cardiac or cerebral event rate was 5·6% in the 1-month DAPT group and 7·2% in the 3-month DAPT group, and the non-inferiority margin was 1·5%, which corresponds to an HR of 1·3, yielding a power of 80% to detect non-inferiority of 1-month DAPT. For the third hypothesis, assuming a 33% relative risk (RR) reduction in the 1-month DAPT group compared with the 3-month DAPT group (expected annual rate of bleeding 8% in the shorter DAPT group and 12% in the longer DAPT group), the power to detect superiority of 1-month DAPT was 80%.

The sample size calculation of the non-HBR stratum assumed that the rate of net adverse clinical events would be 4·0% for 3-month DAPT and 5·0% for 12-month DAPT. The non-inferiority margin was 1·5%, corresponding to an HR of 1·3. With a sampling ratio of 1:1 and an estimated rate of loss to follow-up of 5·0%, 3300 patients were needed to ensure a power of 90% with a two-sided α of 5% (one-sided 2·5%) to test the first hypothesis. With this sample size, the power for the

second and third hypotheses was estimated at a two-sided α of 5% in sequential hierarchical order. The expected annual major adverse cardiac or cerebral event rate in the non-HBR stratum was 3·2% for 3-month DAPT and 4·0% for 12-month DAPT, and the non-inferiority margin was 1·2%, corresponding to an HR of 1·3, yielding a power of 79% to detect non-inferiority of 3-month DAPT. For the third hypothesis, assuming a 37·5% RR reduction in the 3-month DAPT group compared with the 12-month DAPT group (expected annual rate of any actionable non-surgical bleeding 5% in the 3-month DAPT group and 8% in the 12-month DAPT group), the power to detect superiority of 3-month DAPT was 95%. On the basis of these calculations, the required sample size was 4900 patients (1600 with HBR and 3300 without HBR; appendix pp 13–17, 24).

Continuous variables are reported as mean (SD) and categorical variables as n (%). Differences between continuous variables were compared by Student's *t* test for independent data. All primary and secondary endpoints were analysed in both the intention-to-treat and per-protocol sets. The primary endpoints were analysed by a time-to-event analysis using the time to the first occurrence of the event. A Cox proportional hazards model and Kaplan–Meier survival curves were used to estimate the risk of clinical events according to the type of antiplatelet agent with no covariate adjustment. Patients lost to follow-up, and subsequently lost to assessment of the primary endpoint, were considered to be censored in the estimation of Kaplan–Meier event rates. Detailed description of the statistical analysis is provided in the appendix (pp 17–18). Statistical tests were performed using SPSS (version 25) and R (version 4.2.4).

Role of the funding source

The study funders had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication.

Results

From July 24, 2020, to Sept 25, 2023, 4900 patients were screened and 4897 patients (1598 in the HBR stratum

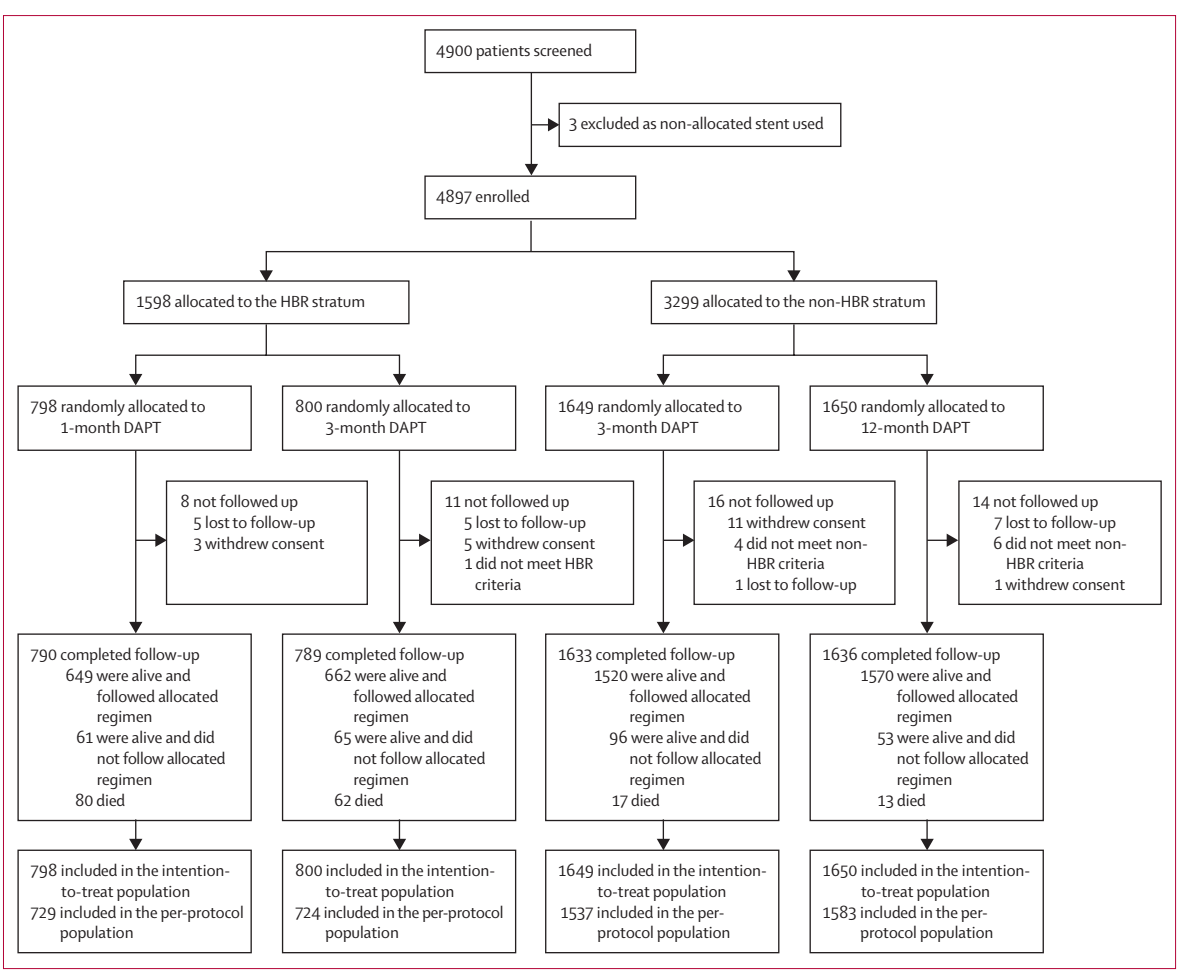

Figure 1: **Trial profile**
DAPT=dual antiplatelet therapy. HBR=high bleeding risk.

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and 3299 in the non-HBR stratum) were randomly allocated to either shorter or longer DAPT duration (figure 1). 19 (1·2%) patients in the HBR stratum and 30 (0·9%) patients in the non-HBR stratum were lost to follow-up, withdrew consent, or did not meet bleeding risk criteria. Vital status data were obtained in 4856 (99·2%) patients and clinical status data were confirmed for all patients who completed follow-up. Data on race or ethnicity were not collected for this study. Demographic and clinical characteristics and laboratory data are shown in table 1, and lesion characteristics in table 2. In the HBR stratum, the median age was 76 years (IQR 68–81), and 535 (33·5%) patients were female and 1063 (66·5%) male (table 1). The distribution of the ARC-HBR criteria is shown in the appendix (pp 38–39). Anaemia (642 [40·2%] patients) and chronic kidney disease (313 [19·6%] patients) were the most common among the ARC-HBR criteria (appendix pp 38–39). The median duration of DAPT was 31 days (IQR 28–37) in the 1-month DAPT group and 91 days (85–102) in the

	High bleeding risk stratum		Non-high bleeding risk stratum	
	1-month DAPT (n=798)	3-month DAPT (n=800)	3-month DAPT (n=1649)	12-month DAPT (n=1650)
Age, years	76 (67–81)	76 (68–81)	64 (58–70)	64 (57–70)
Sex				
Male	533 (66·8%)	530 (66·2%)	1302 (79·0%)	1308 (79·3%)
Female	265 (33·2%)	270 (33·8%)	347 (21·0%)	342 (20·7%)
BMI, kg/m²	24·1 (3·6)	24·3 (3·6)	25·2 (3·1)	25·2 (3·2)
Body surface area, m²	1·66 (0·18)	1·67 (0·18)	1·76 (0·17)	1·77 (0·17)
Clinical diagnosis				
Stable angina	328 (41·1%)	321 (40·1%)	625 (37·9%)	602 (36·5%)
Unstable angina	218 (27·3%)	226 (28·3%)	508 (30·8%)	508 (30·8%)
Non-ST segment elevation myocardial infarction	200 (25·1%)	196 (24·5%)	312 (18·9%)	328 (19·9%)
ST segment elevation myocardial infarction	44 (5·5%)	42 (5·3%)	177 (10·7%)	186 (11·3%)
Other	8 (1·0%)	14 (1·8%)	26 (1·6%)	27 (1·6%)
Clinical risk factors				
Hypertension	646 (81·0%)	604 (75·5%)	1010 (61·2%)	1025 (62·1%)
Diabetes	440 (55·1%)	409 (51·1%)	531 (32·2%)	535 (32·4%)
Insulin-dependent diabetes	86 (10·8%)	63 (7·9%)	43 (2·6%)	43 (2·6%)
Dyslipidaemia	583 (73·1%)	555 (69·4%)	1189 (72·1%)	1153 (69·9%)
Congestive heart failure	52 (6·5%)	45 (5·6%)	16 (1·0%)	11 (0·7%)
Peripheral artery disease	18 (2·3%)	16 (2·0%)	9 (0·5%)	13 (0·8%)
Smoking status				
Ex-smoker	109 (13·7%)	94 (11·8%)	233 (14·1%)	248 (15·0%)
Current smoker	107 (13·4%)	95 (11·9%)	479 (29·0%)	457 (27·7%)
Chronic kidney disease	265 (33·2%)	237 (29·6%)	27 (1·6%)	31 (1·9%)
Previous myocardial infarction	66 (8·3%)	60 (7·5%)	87 (5·3%)	78 (4·7%)
Previous percutaneous coronary intervention	160 (20·1%)	167 (20·9%)	221 (13·4%)	204 (12·4%)
Previous coronary artery bypass graft surgery	14 (1·8%)	12 (1·5%)	10 (0·6%)	13 (0·8%)
Previous cerebrovascular accident	134 (16·8%)	114 (14·3%)	41 (2·5%)	46 (2·8%)
Left ventricular ejection fraction	53·8 (12·1)	54·7 (11·5)	58·9 (9·0)	58·7 (8·7)
Atrial fibrillation	151 (18·9%)	172 (21·5%)	11 (0·7%)	17 (1·0%)
Laboratory data				
White blood cells, cells/μL	7·34 (2·94)	7·47 (2·98)	7·42 (2·60)	7·49 (2·67)
Haemoglobin, g/dL	11·4 (2·0)	11·7 (2·0)	14·2 (3·2)	14·1 (1·4)
Platelet count, 10³/μL	211·9 (77·1)	213·1 (78·1)	228·8 (56·2)	229·7 (58·1)
Creatinine, mg/dL	2·08 (2·57)	1·87 (2·31)	0·88 (0·44)	0·89 (0·48)
Estimated glomerular filtration rate, mL/min per 1·73 m²	59·4 (33·6)	61·9 (32·8)	87·6 (20·4)	87·9 (21·1)
Total cholesterol, mg/dL	140·0 (57·9)	140·5 (38·7)	160·0 (46·1)	161·9 (47·9)
Triglyceride, mg/dL	112·9 (63·6)	111·4 (58·2)	143·8 (106·7)	145·2 (119·8)
HDL cholesterol, mg/dL	41·7 (12·9)	42·4 (14·2)	45·2 (14·9)	44·8 (11·4)
LDL cholesterol, mg/dL	76·4 (54·9)	76·3 (32·4)	87·2 (39·8)	89·1 (39·9)

(Table 1 continues on next page)

	High bleeding risk stratum		Non-high bleeding risk stratum	
	1-month DAPT (n=798)	3-month DAPT (n=800)	3-month DAPT (n=1649)	12-month DAPT (n=1650)
(Continued from previous page)				
Discharge medication				
Aspirin	780 (97·7%)	780 (97·5%)	1641 (99·5%)	1644 (99·6%)
P2Y12 inhibitor (non-specified)	789 (98·9%)	788 (98·5%)	1642 (99·6%)	1648 (99·9%)
P2Y12 inhibitor (clopidogrel)	730 (91·5%)	728 (91·0%)	1238 (75·1%)	1271 (77·0%)
P2Y12 inhibitor (prasugrel)	11 (1·4%)	9 (1·1%)	178 (10·8%)	175 (10·6%)
P2Y12 inhibitor (ticagrelor)	48 (6·0%)	51 (6·4%)	226 (13·7%)	202 (12·2%)
DAPT	777 (97·4%)	776 (97·0%)	1640 (99·5%)	1644 (99·6%)
Oral anticoagulant	123 (15·4%)	152 (19·0%)	..	..
Renin–angiotensin–aldosterone system inhibitor	474 (59·4%)	487 (60·9%)	905 (54·9%)	919 (55·7%)
Beta blocker	430 (53·9%)	406 (50·8%)	753 (45·7%)	776 (47·0%)
Statin	733 (91·9%)	722 (90·3%)	1567 (95·0%)	1572 (95·3%)
Calcium channel blocker	259 (32·5%)	259 (32·4%)	493 (29·9%)	430 (26·1%)

Data are median (IQR), mean (SD), or n (%). DAPT=dual antiplatelet therapy.

Table 1: **Baseline clinical characteristics**

	High bleeding risk stratum		Non-high bleeding risk stratum	
	1-month DAPT	3-month DAPT	3-month DAPT	12-month DAPT
Participants in patient-level analysis	798	800	1649	1650
Angiographic disease extent				
One-vessel disease	276 (34·6%)	284 (35·5%)	745 (45·2%)	767 (46·5%)
Two-vessel disease	265 (33·2%)	253 (31·6%)	578 (35·1%)	532 (32·2%)
Three-vessel disease	257 (32·2%)	263 (32·9%)	326 (19·8%)	351 (21·3%)
Total number of vessels treated	1·31 (0·52)	1·27 (0·52)	1·26 (0·49)	1·27 (0·52)
Total number of lesions treated	1·83 (0·81)	1·78 (0·79)	1·74 (0·80)	1·78 (0·81)
Total stent length, mm	43·8 (56·9)	42·4 (43·8)	38·3 (27·6)	39·9 (30·1)
Total number of stents	1·56 (0·96)	1·55 (0·93)	1·51 (0·92)	1·57 (0·99)
Usage of intravascular imaging	322 (40·4%)	330 (41·3%)	736 (44·6%)	738 (44·7%)
SYNTAX score at baseline	12·6 (9·5)	12·0 (8·5)	10·6 (7·8)	10·9 (8·0)
SYNTAX score after percutaneous coronary intervention	0·5 (2·3)	0·4 (1·6)	0·3 (1·4)	0·3 (1·6)
Participants in lesion-level analysis	898	892	1843	1946
Target vessel location				
Left main coronary artery	75 (8·4%)	59 (6·6%)	103 (5·6%)	106 (5·4%)
Left anterior descending coronary artery	400 (44·5%)	422 (47·3%)	860 (46·7%)	888 (45·6%)
Left circumflex coronary artery	160 (17·8%)	154 (17·3%)	360 (19·5%)	357 (18·3%)
Right coronary artery	263 (29·3%)	257 (28·8%)	520 (28·2%)	595 (30·6%)
Lesion length, mm	25·4 (14·4)	25·4 (14·3)	22·7 (15·7)	22·2 (12·9)
Reference vessel diameter, mm	3·05 (0·44)	3·07 (1·02)	3·08 (0·52)	3·12 (0·75)
Minimum lumen diameter, mm	0·87 (0·33)	0·84 (0·31)	0·79 (0·36)	0·79 (0·37)
Diameter stenosis, %	74·9% (13·1%)	75·6% (12·6%)	78·3% (13·5%)	78·5% (13·5%)
Chronic total occlusion	53 (5·9%)	52 (5·8%)	143 (7·8%)	162 (8·3%)
Bifurcation lesions	204 (22·7%)	203 (22·8%)	517 (28·1%)	527 (27·1%)
Stent diameter, mm	3·06 (0·43)	3·06 (0·46)	3·18 (0·52)	3·19 (0·53)
Stent length, mm	31·8 (17·4)	31·8 (16·9)	30·9 (20·3)	31·7 (22·0)

Data are n, n (%), or mean (SD). DAPT=dual antiplatelet therapy. SYNTAX=Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Table 2: **Baseline lesion characteristics**

3-month DAPT group. In the non-HBR stratum, the median age was 64 years (IQR 57–70), and 689 (20·9%) patients were female and 2610 (79·1%) male (table 1). The median duration of DAPT was 90 days (IQR 89–99) in the 3-month DAPT group and 365 days (356–365) in the 12-month DAPT group. After the DAPT duration, 681 (22·3%) of 3062 patients received aspirin, 2084 (68·2%) received clopidogrel, and 270 (8·8%) received a potent P2Y12 inhibitor (prasugrel or ticagrelor) as a single antiplatelet agent (appendix p 41). The clinical characteristics and lesion characteristics were well balanced in both treatment groups within the HBR and non-HBR strata.

In the HBR stratum, net adverse clinical events (first coprimary endpoint) occurred in 144 (18·4%) patients (Kaplan–Meier estimate at 1 year) in the 1-month DAPT group and in 110 (14·0%) patients (Kaplan–Meier estimate at 1 year) in the 3-month DAPT group (absolute risk difference [ARD] 4·39% [95% CI 1·33–7·46]; HR 1·337 [95% CI 1·043–1·713]; p=0·818 for non-inferiority; figure 2, table 3). The non-inferiority criteria were not met for the first primary endpoint; therefore, statistical testing was not done for the second and third primary endpoints. Major adverse cardiac or cerebral events (second coprimary endpoint) occurred in 74 (9·8%) patients in the 1-month DAPT group and 44 (5·8%) patients in the 3-month DAPT group (ARD 3·98% [1·72–6·23]; HR 1·724 [1·187–2·504]). The third coprimary endpoint of any actionable non-surgical bleeding occurred in 105 (13·8%) patients in the 1-month DAPT group and 122 (15·8%) patients in the 3-month DAPT group (ARD –2·03% [–5·02 to 0·96]; HR 0·853 [0·657 to 1·107]).

In the non-HBR stratum, net adverse clinical events (first coprimary endpoint) occurred in 47 (2·9%) patients in the 3-month DAPT group and in 72 (4·4%) patients in the 12-month DAPT group (ARD –1·53% [95% CI –2·62 to –0·45]; HR 0·657 [95% CI 0·455 to 0·949]; p<0·0001 for non-inferiority). Major adverse cardiac or

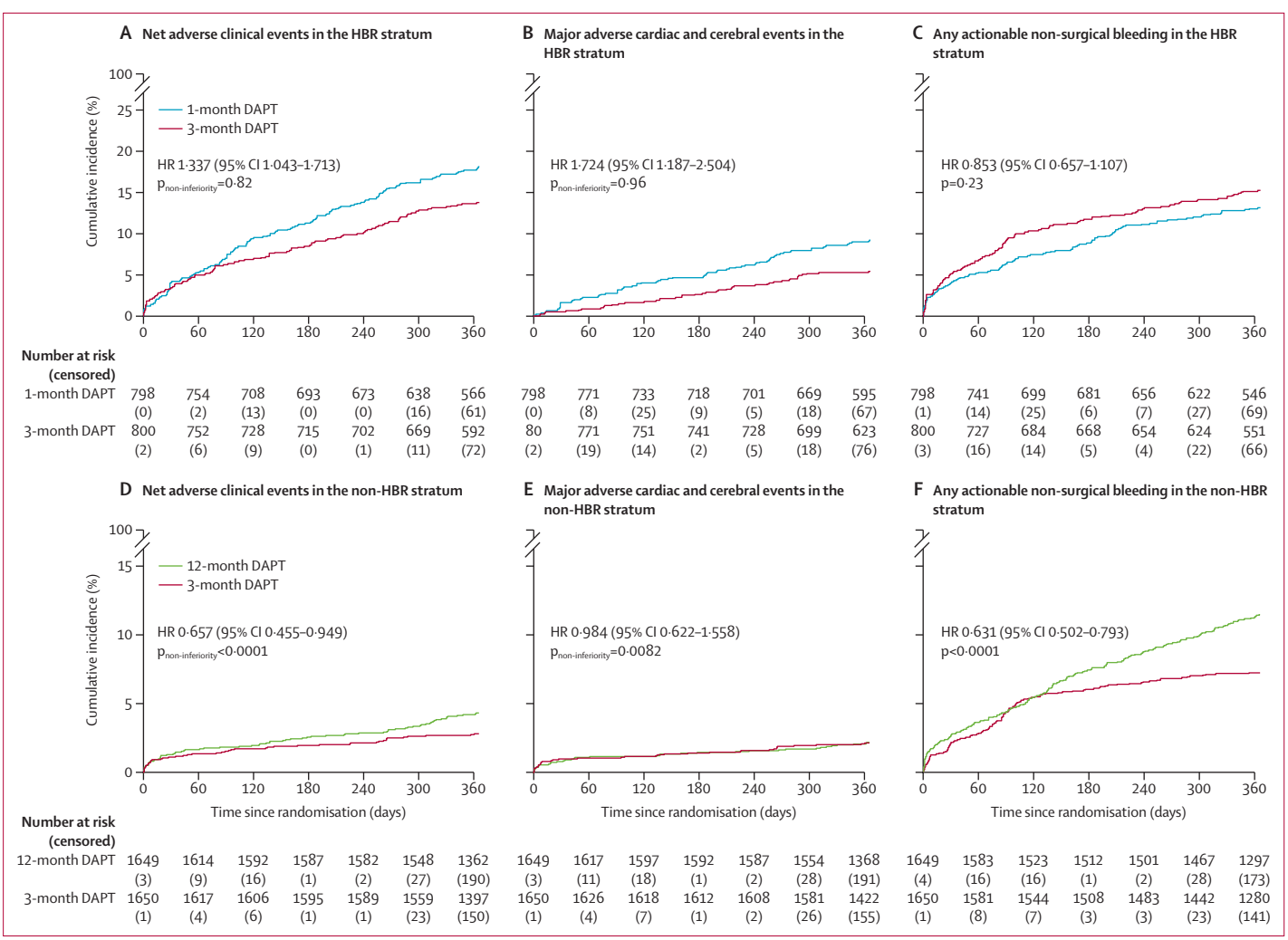

Figure 2: **Cumulative incidence of the primary endpoints at 1 year after randomisation**
Kaplan–Meier event curves of the HBR stratum (A–C) and the non-HBR stratum (D–F). DAPT=dual antiplatelet therapy. HBR=high bleeding risk. HR=hazard ratio.

cerebral events (second coprimary endpoint) occurred in 36 (2·2%) patients in the 3-month DAPT group and in 37 (2·3%) patients in the 12-month DAPT group (ARD –0·05% [–0·92 to 0·81]; HR 0·984 [0·622 to 1·558]; p=0·0082 for non-inferiority). The third coprimary endpoint of any actionable non-surgical bleeding occurred in 120 (7·4%) patients in the 3-month DAPT group and in 190 (11·7%) patients in the 12-month DAPT

	High bleeding risk stratum					Non-high bleeding risk stratum				
	1-month DAPT (n=798)	3-month DAPT (n=800)	ARD (95% CI)	HR (95% CI)*	p value†	3-month DAPT (n=1649)	12-month DAPT (n=1650)	ARD (95% CI)	HR (95% CI)*	p value
Net adverse clinical events	144 (18·4%)	110 (14·0%)	4·39 (1·33 to 7·46)	1·337 (1·043–1·713)	0·82 for non-inferiority based on ARD, 0·59 for non-inferiority based on HR	47 (2·9%)	72 (4·4%)	–1·53 (–2·62 to –0·45)	0·657 (0·455–0·949)	<0·0001 for non-inferiority based on ARD, 0·0001 for non-inferiority based on HR
Major adverse cardiac or cerebral events	74 (9·8%)	44 (5·8%)	3·98 (1·72 to 6·23)	1·723 (1·186–2·502)	..	36 (2·2%)	37 (2·3%)	–0·05 (–0·92 to 0·81)	0·984 (0·622–1·558)	0·0082 for non-inferiority based on ARD, 0·12 for non-inferiority based on HR
Any actionable non-surgical bleeding	105 (13·8%)	122 (15·8%)	–2·03 (–5·02 to 0·96)	0·853 (0·657–1·107)	..	120 (7·4%)	190 (11·7%)	–4·32 (–6·02 to –2·62)	0·631 (0·502–0·793)	<0·0001
All-cause death	81 (10·2%)	62 (7·8%)	2·47 (–0·07 to 4·86)	1·319 (0·948–1·838)	..	17 (1·0%)	14 (0·8%)	0·18 (–0·37 to 0·74)	1·229 (0·606–2·493)	..
Cardiovascular death	42 (5·2%)	28 (3·5%)	1·91 (0·13 to 3·69)	1·518 (0·941–2·449)	..	11 (0·7%)	8 (0·5%)	0·19 (–0·25 to 0·63)	1·389 (0·559–3·454)	..
Myocardial infarction	10 (1·3%)	10 (1·3%)	0·01 (–0·97 to 0·99)	1·013 (0·422–2·433)	..	11 (0·7%)	13 (0·8%)	–0·11 (–0·62 to 0·39)	0·859 (0·385–1·918)	..
Target vessel myocardial infarction	6 (0·8%)	8 (1·0%)	–0·27 (–1·08 to 0·55)	0·757 (0·263–2·181)	..	8 (0·5%)	11 (0·7%)	–0·18 (–0·63 to 0·27)	0·738 (0·297–1·834)	..
Non-target vessel myocardial infarction	4 (0·5%)	2 (0·3%)	0·28 (–0·27 to 0·83)	2·039 (0·373–11·130)	..	3 (0·2%)	2 (0·1%)	0·07 (–0·17 to 0·30)	1·526 (0·255–9·134)	..
Stent thrombosis	2 (0·3%)	2 (0·3%)	0·03 (–0·41 to 0·47)	1·009 (0·142–7·163)	..	2 (0·1%)	3 (0·2%)	–0·08 (–0·31 to 0·16)	0·679 (0·114–4·069)	..
Definite	1 (0·1%)	2 (0·3%)	–0·11 (–0·49 to 0·27)	0·503 (0·046–5·547)	..	2 (0·1)	2 (0·1)	–0·01 (–0·21 to 0·20)	0·987 (0·139–7·004)	..
Probable	1 (0·1%)	0	0·13 (–0·08 to 0·33)	..	..	0	1 (0·1)	–0·06 (–0·16 to 0·04)	..	..
Coronary thrombotic event	11 (1·4%)	11 (1·4%)	–0·03 (–1·05 to 1·00)	0·987 (0·428–2·277)	..	11 (0·7%)	13 (0·8%)	–0·11 (–0·62 to 0·39)	0·859 (0·385–1·918)	..
Stroke	30 (3·8%)	14 (1·8%)	2·11 (0·68 to 3·55)	2·182 (1·157–4·115)	..	17 (1·0%)	24 (1·5%)	–0·44 (–1·09 to 0·20)	0·716 (0·385–1·332)	..
Ischaemic stroke	25 (3·1%)	9 (1·1%)	2·12 (0·85 to 3·38)	2·824 (1·318–6·050)	..	16 (1·0%)	18 (1·1%)	–0·13 (–0·72 to 0·46)	0·899 (0·459–1·763)	..
Haemorrhagic stroke	5 (0·6%)	5 (0·6%)	–0·01 (–0·70 to 0·69)	1·009 (0·292–3·487)	..	1 (0·1%)	6 (0·4%)	–0·31 (–0·58 to –0·04)	0·168 (0·02–1·402)	..
Bleeding										
BARC 2	48 (6·0%)	71 (8·9%)	–3·00 (–5·33 to –0·68)	0·670 (0·465–0·966)	..	110 (6·7%)	159 (9·7%)	–3·08 (–4·68 to –1·48)	0·691 (0·542–0·882)	..
BARC 3	53 (6·6%)	49 (6·1%)	0·53 (–1·67 to 2·74)	1·072 (0·727–1·518)	..	8 (0·5%)	30 (1·8%)	–1·46 (–2·11 to –0·80)	0·266 (0·122–0·579)	..
BARC 5	4 (0·5%)	2 (0·3%)	0·31 (–0·25 to 0·87)	1·983 (0·363–10·830)	..	2 (0·1%)	1 (0·1%)	0·06 (–0·13 to 0·25)	1·997 (0·181–22·030)	..
ISTH clinically relevant non-major bleeding	53 (7·0%)	62 (7·9%)	–1·13 (–3·42 to 1·15)	0·895 (0·623–1·284)	..	81 (5·4%)	120 (7·8%)	–2·47 (–3·88 to –1·06)	0·674 (0·510–0·890)	..
ISTH major bleeding	49 (6·2%)	59 (7·4%)	–1·37 (–3·64 to 0·89)	0·845 (0·584–1·224)	..	33 (2·0%)	66 (4·0%)	–2·21 (–3·25 to –1·17)	0·511 (0·344–0·759)	..

(Table 3 continues on next page)

	High bleeding risk stratum					Non-high bleeding risk stratum				
	1-month DAPT (n=798)	3-month DAPT (n=800)	ARD (95% CI)	HR (95% CI)*	p value†	3-month DAPT (n=1649)	12-month DAPT (n=1650)	ARD (95% CI)	HR (95% CI)*	p value
(Continued from previous page)										
Any revascularisation	41 (5·1%)	28 (3·5%)	1·89 (0·05 to 3·72)	1·499 (0·927–2·424)	..	47 (2·9%)	53 (3·2%)	−0·32 (−1·34 to 0·71)	0·905 (0·611–1·340)	..
Target lesion revascularisation	24 (3·0%)	10 (1·3%)	1·91 (0·61 to 3·22)	2·460 (1·177–5·145)	..	23 (1·4%)	23 (1·4%)	0·02 (−0·67 to 0·72)	1·021 (0·573–1·819)	..
Non-target lesion revascularisation	17 (2·1%)	18 (2·3%)	−0·03 (−1·35 to 1·30)	0·956 (0·493–1·855)	..	24 (1·5%)	30 (1·8%)	−0·34 (−1·10 to 0·42)	0·815 (0·476–1·394)	..

Data are n (%) unless otherwise stated. The percentages shown are Kaplan–Meier estimates. All primary and secondary endpoints and their associated definitions are listed in the appendix (pp 19–22). All endpoints were evaluated in the intention-to-treat population at 12 months after randomisation. ARD=absolute risk difference. HR=hazard ratio. BARC=Bleeding Academic Research Consortium. ISTH=International Society on Thrombosis and Haemostasis. *95% CIs for secondary endpoints have not been adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible. †p values were derived using calculations based on the ARD method.

Table 3: **Clinical outcomes**

group (ARD −4·32% [−6·02 to −2·62]; HR 0·631 [0·502 to 0·793]; p<0·0001).

We conducted a per-protocol analysis including 1453 (90·9%) patients in the HBR stratum and 3120 (94·6%) in the non-HBR stratum (appendix pp 25–30, 42–50). Detailed adherence rates in each group are shown in the appendix (p 40). Results were similar for all three coprimary endpoints. We also did a landmark analysis at 30 days and 120 days for the HBR stratum and at 90 days for the non-HBR stratum, considering the window period of the time of DAPT switching (appendix pp 31–32). The RR between the two groups, represented as the HR, was largest during the period in which the two groups had a different treatment strategy. A post-hoc subgroup analysis showed consistent results throughout various subgroups (appendix p 33). In the non-HBR stratum, the beneficial reduction of bleeding events by 3-month DAPT versus 12-month DAPT was larger when clopidogrel was used compared with potent P2Y12 inhibitor usage, and in patients without acute coronary syndrome (compared with those with acute coronary syndrome).

The incidences of the secondary endpoints, including the individual components of the coprimary endpoints, are shown in table 3, and the specific causes of cardiovascular death and origins of major bleeding events are shown in the appendix (p 51). In the HBR stratum, the 1-month DAPT group had a higher incidence of cardiovascular death, ischaemic stroke, or clinically driven target lesion revascularisation compared with the 3-month DAPT group. The 1-month DAPT group had a lower incidence of non-major bleeding (BARC type 2 and International Society on Thrombosis and Haemostasis clinically relevant non-major bleeding) than the 3-month DAPT group, but the incidence of major bleeding (BARC type 3 or 5 and International Society on Thrombosis and Haemostasis major bleeding) was similar. In the non-HBR stratum, the 3-month DAPT group had a lower incidence of both non-major and major bleeding compared with the 12-month DAPT group. In an additional post-hoc analysis, the effect of single antiplatelet agents after DAPT discontinuation was analysed and no difference was found for aspirin versus clopidogrel versus potent P2Y12 inhibitors (appendix pp 34–36).

Discussion

We compared two durations of DAPT after DES implantation in patients stratified by bleeding risk. Participants with HBR were randomly allocated to 1-month or 3-month DAPT, and those without HBR to 3-month or 12-month DAPT. In the HBR stratum, 1-month DAPT did not reach non-inferiority compared with 3-month DAPT for net adverse clinical events at 1 year; in fact, outcomes were worse with the shorter regimen. Because of the prespecified hierarchical statistical testing of the three coprimary outcomes, further statistical testing of the other coprimary endpoints was not performed in the HBR stratum. In the non-HBR stratum, 3-month DAPT was non-inferior to 12-month DAPT for both net adverse clinical events and major adverse cardiac or cerebral events, and was superior in reducing any actionable non-surgical bleeding. These findings indicate that shorter DAPT is beneficial for patients without HBR, reducing bleeding without increasing net adverse clinical events or major adverse cardiac or cerebral events. By contrast, in patients with HBR, 1-month DAPT did not reduce overall clinical events and was associated with more thrombotic events.

Guidelines recommend different durations of DAPT according to bleeding risk. For example, European guidelines[1] suggest 1-month to 3-month DAPT for individuals with HBR and longer DAPT for those without HBR. This recommendation is based on studies that have evaluated the effect of short DAPT in patients with HBR (appendix p 52).[7,8,10,11,19,20] However, these studies were not direct comparisons of different DAPT durations but rather a comparison between different stents in HBR

patients who were prescribed with 1-month to 3-month DAPT. Moreover, all studies except the COMPARE 60/80 HBR trial[20] used a study-specific definition of HBR, rather than the ARC-HBR definition. Some studies compared different durations, such as the XIENCE SHORT study,[21] which was not a prospective randomised comparison but rather a retrospective comparison of 1-month versus 6-month DAPT in the XIENCE 28 registry, and of 3-month versus 12-month DAPT in the XIENCE 90 registry. Only the MASTER DAPT trial[9] compared different DAPT durations in a dedicated, large-scale HBR population (over 4500 patients from Europe, Asia, Australia, and South America, stratified by oral anticoagulation indication and history of acute myocardial infarction). Patients were randomly assigned at 1 month after PCI with a single biodegradable polymer DES. The results showed that an abbreviated DAPT strategy could reduce bleeding without increasing thrombotic events.[9] There are several differences between MASTER DAPT and our trial. First, the median duration of DAPT from index PCI in MASTER DAPT was 34 days in the abbreviated treatment group and 193 days in the standard treatment DAPT group. Thus, MASTER DAPT essentially compared 1-month versus 6-month DAPT, which is too long for patients with HBR. Second, 36% of the population had HBR due to use of an oral anticoagulant. In these patients, triple antithrombotic therapy (DAPT plus anticoagulant) was administered for 1 month, followed by dual antithrombotic therapy (single antiplatelet agent plus anticoagulant) for 5 months, and then by anticoagulant monotherapy for 6 months in the abbreviated treatment group, whereas triple antithrombotic therapy was administered for at least 3 months and switched to dual therapy for another 9 months in the standard treatment group. The strategy used in the MASTER DAPT trial for patients with an indication for oral anticoagulants was similar to that of HOST-BR, but these patients constituted a higher proportion of the MASTER DAPT study population than in our study. Third, the standardised ARC-HBR definition was not used to assess bleeding risk in the trial. Collectively, data from previous trials are insufficient to conclude that 1-month DAPT is the optimal duration for individuals with HBR. In the present trial, we used the standardised ARC-HBR criteria and compared 1-month versus 3-month DAPT, which are the durations specified in the current guidelines.[1,2,14]

The key finding in the HBR stratum was that 1-month DAPT did not meet non-inferiority to 3-month DAPT. In fact, 1-month was inferior to 3-month DAPT for net adverse clinical events. The higher incidence of adverse events with 1-month DAPT was potentially driven by a higher risk of thrombotic events, which can be inferred from the increased risk of cardiovascular death, and ischaemic stroke. According to the definitions of cardiovascular death and definite and probable stent thrombosis, an unexplained death after 30 days would not be categorised as a stent thrombosis but rather a cardiovascular death. Therefore, the cardiovascular death events could have included stent-related fatal thrombotic events that were not captured as coronary thrombotic events. The increased risk of cardiovascular death could be explained by the natural healing process after stent implantation. Preclinical and clinical studies have shown that re-endothelialisation can continue for 3 months after DES implantation.[22] A premature discontinuation of DAPT before full endothelial coverage could lead to thrombotic events.[23] This could partly explain the difference in ischaemic events beyond 120 days in the HBR stratum, as shown in the landmark analysis (appendix pp 31–32). Clinically driven target lesion revascularisation events were higher in the 1-month DAPT group, supporting this explanation. As for the rate of ischaemic stroke events, the relationship between stroke and PCI has been well defined in previous studies, and ischaemic stroke can occur more than 30 days after PCI, which might explain why ischaemic stroke was reduced in the 3-month DAPT group. Both any actionable non-surgical bleeding and BARC 3 or 5 major bleeding were similar between the two groups, suggesting that an additional 2 months of DAPT might not be associated with significant differences in bleeding even in the HBR population. Additionally, the overall event rate in the HBR stratum exceeded the estimated rate. Due to the absence of previous studies based on ARC-HBR, this outcome was unforeseen. However, the higher-than-expected event rate in ARC-defined HBR of this study might provide useful insight into the daily practice of individuals with HBR as well as future HBR study design.

The findings in the non-HBR stratum, which showed significant reduction in bleeding without an increase in net events or thrombotic events, are consistent with previous all-comer trials that suggested the safety of shorter DAPT.[15,16] We believe that these previous trials showing a benefit of shorter over longer DAPT essentially enrolled a broadly non-HBR population. Baseline patient characteristics in those studies were similar to those of the non-HBR stratum in the current trial. Unlike previous trials, we used explicit criteria to identify patients without HBR, in accordance with contemporary algorithms for antiplatelet strategy selection after PCI. In the non-HBR population of our study, a 3-month DAPT strategy was associated with a 37% lower risk of BARC type 2, 3, or 5 bleeding over the 1 year, primarily due to a reduction in minor bleeding (BARC type 2). This reduction was not offset by higher rates of thrombosis, suggesting a net benefit for shorter DAPT in the non-HBR population. Although it might be presumed that patients without HBR could benefit from longer DAPT, our results show that these patients are at low risk of both bleeding and thrombosis. In particular, in the post-hoc subgroup analysis, there was no significant interaction between presentation with acute coronary

syndrome and DAPT duration in terms of net adverse clinical events and major adverse cardiac or cerebral events. This finding is consistent with recent studies suggesting that 12-month DAPT might not be essential in acute coronary syndrome.[24] Even in patients without HBR, shortening DAPT from 12 to 3 months could be a safe strategy.

The fact that the actual event rates were higher than the estimated event rates at time of study design in the HBR stratum, and lower than the estimated event rates at time of study design in the non-HBR stratum, should be considered when interpreting our results. The higher-than-expected rates suggest sufficient power to test the original hypothesis, whereas the lower-than-expected rates suggest insufficient power. Furthermore, there could be issues raised regarding the three coprimary endpoints and the potential for increased risk of type I error from multiple testing. We minimised this risk by performing a hierarchical analysis. As such, further formal statistical testing was not performed if the hierarchical hypothesis was not met.

The results of our trial should be interpreted in light of its limitations. First, this was an open-label study, and although clinical events were adjudicated by an independent committee, the possibility of reporting or ascertainment bias remains. Second, the specific P2Y12 inhibitor during the DAPT period or as the monotherapy agent after DAPT was not specified and was left up to the treating physician. Moreover, the majority of patients received clopidogrel as a P2Y12 inhibitor, including those presenting with acute coronary syndrome. This decision was motivated by the results of previous trials in east Asia, which reported superiority of clopidogrel over potent P2Y12 inhibitors to balance ischaemic and bleeding risks.[25–27] Therefore, caution is needed when extrapolating these results to regions where other P2Y12 inhibitors, such as prasugrel or ticagrelor, are more commonly used. Third, although this was a non-inferiority study, we assumed a lower estimated event rate in the experimental group. A well designed non-inferiority study should theoretically assume equal event rates in both groups and determine an appropriate sample size accordingly. Therefore, this assumption is a limitation in the design of this trial. Fourth, our trial did not stratify patients according to the ischaemic risk, such as the presenting syndrome and complexity of PCI. Although some recent meta-analyses reported that clinical presentation and procedural complexity might not be a critical determinant of antiplatelet therapy,[28] these are important factors that should be considered in an individualised approach to DAPT duration and should be studied in future clinical trials. Fifth, our trial included patients with HBR who had received implantation of a durable-polymer everolimus-eluting stent, and patients without HBR who had received implantation of a durable-polymer zotarolimus-eluting stent. The stents used in the current study are representative contemporary stents that have shown similar performance to other DESs.[29] Nonetheless, many aspects of the device, including the polymer, antiproliferative drug, and stent platforms, have various effects on stabilisation after PCI. Therefore, we might not be able to extrapolate our results to patients who receive different stent types or drug-coated balloons. Sixth, 8·9% of patients in the HBR stratum and 5·4% in the non-HBR stratum did not adhere to the allocated regimen. However, this rate was similar to that observed in previous trials in patients with HBR, and the results of the per-protocol analysis were similar to those of the intention-to-treat analysis. Seventh, among the HBR stratum, 17·2% of patients were prescribed oral anticoagulants. Although current guidelines recommend a short duration of triple antithrombotic agents during the periprocedural period,[30] DAPT duration was not adjusted in these patients because our trial was planned and initiated before such recommendations. Furthermore, current recommendations lack the support of robust evidence for the specific duration of triple antithrombotic therapy. Lastly, the findings might not be generalisable to all ethnic groups because our trial enrolled exclusively east Asian patients, who are known to have higher bleeding risk. Therefore, the clinical impact of shorter versus longer DAPT might differ in other populations.[31] However, the results of the HBR stratum, showing a higher thrombotic risk and similar bleeding risk in 1-month DAPT compared with 3-month DAPT, could be reproduced or even more amplified in certain populations that have a relatively higher thrombotic and lower bleeding risk.

In conclusion, HOST-BR showed that, in east Asian individuals with HBR, 1-month DAPT did not meet non-inferiority to 3-month DAPT for net clinical events. In east Asian individuals without HBR, a 3-month DAPT regimen reduced bleeding risk without increasing thrombotic risk and might be preferable to a 12-month regimen.

Contributors

JK, KWP, YJC, SRL, Y-HL, and H-SK conceived and designed the study. JK, SP, and H-SK accessed and verified the data. JK, KWP, DH, and SP participated in data analysis and data interpretation. JK and KWP wrote the first draft and reviewed and revised the manuscript. All authors participated in patient enrolment and clinical follow-up, and contributed to critical revision of the draft for important intellectual content. All authors approved the final version of the manuscript and vouch for the accuracy or integrity of all data reported herein. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

JK reports grants or contracts from Medtronic Korea, Edwards Lifesciences Korea, and Boston Scientific Korea. KWP reports consulting fees from Shockwave Medical, Novartis, and Amgen; and payment or honoraria for lectures from Daiichi Sankyo, Novartis, Amgen, HK inno.N, Daewoong Pharmaceutical, and Sanofi-Aventis. YJC reports grants or contracts from Medtronic Korea and Edwards Lifesciences Korea; and payment or honoraria for lectures from Covidien Korea, Organon Korea, Servier Korea, Youhan, Daewoong Pharmaceutical, Hanmi Pharmaceutical, and Chong Kun Dang Pharmaceutical. H-SK reports grants or contracts from Boston Scientific; and consulting

fees from Biotronik and B Braun. All other authors declare no competing interests.

Data sharing

The HOST-BR trial is planning to continue analysis, including post-hoc subgroup analyses. Until then, no individual participant data will be available. Any relevant inquiries should be emailed to H-SK (hyosoo@snu.ac.kr) or JK (medikang@snu.ac.kr).

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References

1 Vrints C, Andreotti F, Koskinas KC, et al. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024; **45:** 3415–537.

2 Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2022; **145:** e18–114.

3 Costa F, Van Klaveren D, Feres F, et al. Dual antiplatelet therapy duration based on ischemic and bleeding risks after coronary stenting. *J Am Coll Cardiol* 2019; **73:** 741–54.

4 Urban P, Mehran R, Colleran R, et al. Defining high bleeding risk in patients undergoing percutaneous coronary intervention: a consensus document from the Academic Research Consortium for High Bleeding Risk. *Eur Heart J* 2019; **40:** 2632–53.

5 Carvalho PEP, Gewehr DM, Nascimento BR, et al. Short-term dual antiplatelet therapy after drug-eluting stenting in patients with acute coronary syndromes: a systematic review and network meta-analysis. *JAMA Cardiol* 2024; **9:** 1094–105.

6 Giacoppo D, Matsuda Y, Fovino LN, et al. Short dual antiplatelet therapy followed by P2Y12 inhibitor monotherapy *vs* prolonged dual antiplatelet therapy after percutaneous coronary intervention with second-generation drug-eluting stents: a systematic review and meta-analysis of randomized clinical trials. *Eur Heart J* 2021; **42:** 308–19.

7 Windecker S, Latib A, Kedhi E, et al. Polymer-based or polymer-free stents in patients at high bleeding risk. *N Engl J Med* 2020; **382:** 1208–18.

8 Varenne O, Cook S, Sideris G, et al. Drug-eluting stents in elderly patients with coronary artery disease (SENIOR): a randomised single-blind trial. *Lancet* 2018; **391:** 41–50.

9 Valgimigli M, Frigoli E, Heg D, et al. Dual antiplatelet therapy after PCI in patients at high bleeding risk. *N Engl J Med* 2021; **385:** 1643–55.

10 Urban P, Meredith IT, Abizaid A, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med* 2015; **373:** 2038–47.

11 Ariotti S, Adamo M, Costa F, et al. Is bare-metal stent implantation still justifiable in high bleeding risk patients undergoing percutaneous coronary intervention?: a pre-specified analysis from the ZEUS Trial. *JACC Cardiovasc Interv* 2016; **9:** 426–36.

12 Kang J, Yun J, Park KW, et al. Long-term outcomes of high bleeding risk patients undergoing percutaneous coronary intervention: a Korean nationwide registry. *Eur Heart J* 2024; **45:** 3721–31.

13 Mehran R, Baber U, Sharma SK, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. *N Engl J Med* 2019; **381:** 2032–42.

14 Capodanno D, Morice MC, Angiolillo DJ, et al. Trial design principles for patients at high bleeding risk undergoing PCI: *JACC* scientific expert panel. *J Am Coll Cardiol* 2020; **76:** 1468–83.

15 Hahn JY, Song YB, Oh JH, et al. Effect of P2Y12 inhibitor monotherapy *vs* dual antiplatelet therapy on cardiovascular events in patients undergoing percutaneous coronary intervention: the SMART-CHOICE randomized clinical trial. *JAMA* 2019; **321:** 2428–37.

16 Han JK, Hwang D, Yang S, et al. Comparison of 3- to 6-month versus 12-month dual antiplatelet therapy after coronary intervention using the contemporary drug-eluting stents with ultrathin struts: the HOST-IDEA randomized clinical trial. *Circulation* 2023; **147:** 1358–68.

17 Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011; **123:** 2736–47.

18 Baber U, Mehran R, Giustino G, et al. Coronary thrombosis and major bleeding after PCI with drug-eluting stents: risk scores from PARIS. *J Am Coll Cardiol* 2016; **67:** 2224–34.

19 Watanabe H, Domei T, Morimoto T, et al. Details on the effect of very short dual antiplatelet therapy after drug-eluting stent implantation in patients with high bleeding risk: insight from the STOPDAPT-2 trial. *Cardiovasc Interv Ther* 2021; **36:** 91–103.

20 Smits PC, Tonino PAL, Hofma SH, et al. Comparison of ultrathin- versus thin-strut stents in patients with high bleeding risk PCI: results from the COMPARE 60/80 HBR trial: an open-label, randomized, controlled trial. *Circ Cardiovasc Interv* 2024; **17:** e014042.

21 Valgimigli M, Cao D, Angiolillo DJ, et al. Duration of dual antiplatelet therapy for patients at high bleeding risk undergoing PCI. *J Am Coll Cardiol* 2021; **78:** 2060–72.

22 Padfield GJ, Newby DE, Mills NL. Understanding the role of endothelial progenitor cells in percutaneous coronary intervention. *J Am Coll Cardiol* 2010; **55:** 1553–65.

23 Inoue T, Croce K, Morooka T, Sakuma M, Node K, Simon DI. Vascular inflammation and repair: implications for re-endothelialization, restenosis, and stent thrombosis. *JACC Cardiovasc Interv* 2011; **4:** 1057–66.

24 Kuno T, Watanabe A, Shoji S, et al. Short-term DAPT and DAPT de-escalation strategies for patients with acute coronary syndromes: a systematic review and network meta-analysis. *Circ Cardiovasc Interv* 2023; **16:** e013242.

25 Park DW, Kwon O, Jang JS, et al. Clinically significant bleeding with ticagrelor versus clopidogrel in Korean patients with acute coronary syndromes intended for invasive management: a randomized clinical trial. *Circulation* 2019; **140:** 1865–77.

26 Kim CJ, Park MW, Kim MC, et al. Unguided de-escalation from ticagrelor to clopidogrel in stabilised patients with acute myocardial infarction undergoing percutaneous coronary intervention (TALOS-AMI): an investigator-initiated, open-label, multicentre, non-inferiority, randomised trial. *Lancet* 2021; **398:** 1305–16.

27 Goto S, Huang CH, Park SJ, Emanuelsson H, Kimura T. Ticagrelor *vs* clopidogrel in Japanese, Korean and Taiwanese patients with acute coronary syndrome—randomized, double-blind, phase III PHILO study. *Circ J* 2015; **79:** 2452–60.

28 Valgimigli M, Hong SJ, Gragnano F, et al. De-escalation to ticagrelor monotherapy versus 12 months of dual antiplatelet therapy in patients with and without acute coronary syndromes: a systematic review and individual patient-level meta-analysis of randomised trials. *Lancet* 2024; **404:** 937–48.

29 El-Hayek G, Bangalore S, Casso Dominguez A, et al. Meta-analysis of randomized clinical trials comparing biodegradable polymer drug-eluting stent to second-generation durable polymer drug-eluting stents. *JACC Cardiovasc Interv* 2017; **10:** 462–73.

30 Angiolillo DJ, Bhatt DL, Cannon CP, et al. Antithrombotic therapy in patients with atrial fibrillation treated with oral anticoagulation undergoing percutaneous coronary intervention: a North American perspective: 2021 update. *Circulation* 2021; **143:** 583–96.

31 Kang J, Park KW, Palmerini T, et al. Racial differences in ischaemia/bleeding risk trade-off during anti-platelet therapy: individual patient level landmark meta-analysis from seven RCTs. *Thromb Haemost* 2019; **119:** 149–62.