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Stopping Aspirin Within 1 Month After Stenting for Ticagrelor Monotherapy in Acute Coronary Syndrome: The T-PASS Randomized Noninferiority Trial

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BACKGROUND: Stopping aspirin within 1 month after implantation of a drug-eluting stent for ticagrelor monotherapy has not been exclusively evaluated for patients with acute coronary syndrome. The aim of this study was to investigate whether ticagrelor monotherapy after <1 month of dual antiplatelet therapy (DAPT) is noninferior to 12 months of ticagrelor-based DAPT for adverse cardiovascular and bleeding events in patients with acute coronary syndrome.

METHODS: In this randomized, open-label, noninferiority trial, 2850 patients with acute coronary syndrome who underwent drug-eluting stent implantation at 24 centers in South Korea were randomly assigned (1:1) to receive either ticagrelor monotherapy (90 mg twice daily) after <1 month of DAPT (n=1426) or 12 months of ticagrelor-based DAPT (n=1424) between April 24, 2019, and May 31, 2022. The primary end point was the net clinical benefit as a composite of all-cause death, myocardial infarction, definite or probable stent thrombosis, stroke, and major bleeding at 1 year after the index procedure in the intention-to-treat population. Key secondary end points were the individual components of the primary end point.

RESULTS: Among 2850 patients who were randomized (mean age, 61 years; 40% ST-segment–elevation myocardial infarction), 2823 (99.0%) completed the trial. Aspirin was discontinued at a median of 16 days (interquartile range, 12–25 days) in the group receiving ticagrelor monotherapy after <1 month of DAPT. The primary end point occurred in 40 patients (2.8%) in the group receiving ticagrelor monotherapy after <1-month DAPT, and in 73 patients (5.2%) in the ticagrelor-based 12-month DAPT group (hazard ratio, 0.54 [95% CI, 0.37–0.80]; $P<0.001$ for noninferiority; $P=0.002$ for superiority). This finding was consistent in the per-protocol population as a sensitivity analysis. The occurrence of major bleeding was significantly lower in the ticagrelor monotherapy after <1-month DAPT group compared with the 12-month DAPT group (1.2% versus 3.4%; hazard ratio, 0.35 [95% CI, 0.20–0.61]; $P<0.001$).

CONCLUSIONS: This study provides evidence that stopping aspirin within 1 month for ticagrelor monotherapy is both noninferior and superior to 12-month DAPT for the 1-year composite outcome of death, myocardial infarction, stent thrombosis, stroke, and major bleeding, primarily because of a significant reduction in major bleeding, among patients with acute coronary syndrome receiving drug-eluting stent implantation. Low event rates, which may suggest enrollment of relatively non–high-risk patients, should be considered in interpreting the trial.

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Clinical Perspective

What Is New?

- In this randomized clinical trial that included 2850 patients who underwent drug-eluting stent implantation for acute coronary syndrome, a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding at 1 year occurred in 40 patients (2.8%) in the group receiving ticagrelor monotherapy after <1 month of dual antiplatelet therapy and in 73 patients (5.2%) in the 12-month dual antiplatelet therapy group, which supports both noninferiority and superiority.
- The significant reduction in major bleeding in the ticagrelor monotherapy after <1 month of dual antiplatelet therapy group was the primary component of the composite outcome driving these findings (1.2% versus 3.4%).

What Are the Clinical Implications?

- Among patients with acute coronary syndrome, stopping aspirin within 1 month after implantation of drug-eluting stents for ticagrelor monotherapy is a reasonable alternative to 12-month dual antiplatelet therapy for adverse cardiovascular and bleeding events.

Nonstandard Abbreviations and Acronyms

ACS	acute coronary syndrome
BARC	Bleeding Academic Research Consortium
DAPT	dual antiplatelet therapy
DES	drug-eluting stent
HR	hazard ratio
T-PASS	Ticagrelor Monotherapy in Patients Treated With New-Generation Drug-Eluting Stents for Acute Coronary Syndrome

Antiplatelet therapy is the principal treatment, along with timely revascularization when indicated, for the management of acute coronary syndrome (ACS).[1,2] Current guidelines recommend at least 12 months of dual antiplatelet therapy (DAPT), in the form of a combination of aspirin and a P2Y12 inhibitor, after implantation of a drug-eluting stent (DES) in patients with ACS, unless bleeding risks prevail.[3–5] However, maintaining long-term DAPT may be associated with excessive risk of bleeding.[5] Several randomized trials have evaluated de-escalation strategies for early stopping of aspirin to decrease bleeding events,[5–12] and recent meta-analyses from randomized trials have shown that eliminating aspirin after 1 to 3 months of treatment reduced the occurrence of bleeding events without increasing the number of ischemic events.[13–15] However, stopping aspirin within 1 month after implantation of a DES for ticagrelor monotherapy has not been exclusively evaluated for patients with ACS.

Therefore, the T-PASS trial (Ticagrelor Monotherapy in Patients Treated With New-Generation Drug-Eluting Stents for Acute Coronary Syndrome) assessed the hypothesis of noninferiority of ticagrelor monotherapy after <1 month of DAPT compared with 12 months of ticagrelor-based DAPT in terms of a composite outcome of death, myocardial infarction, stent thrombosis, stroke, and major bleeding in patients with ACS treated with DES implantation. If significant, superiority was subsequently evaluated. A noninferiority trial design was based on the expectation that noninferiority of stopping aspirin even sooner than 1 month followed by ticagrelor monotherapy would be an attractive alternative compared with DAPT if net clinical benefits such as a composite of ischemic and bleeding events are comparable because of a lesser major bleeding.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Oversight

An investigator-initiated, multicenter, open-label, randomized clinical trial was conducted at 24 centers in South Korea. The trial protocol was approved by the institutional review board of each participating center, including Yonsei University Health System (4-2018-0782). This trial was preregistered with clinicaltrials.gov (REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03797651). The study was performed in accordance with the principles of the Declaration of Helsinki. Study coordination, data management, and site

management services were performed at the Cardiovascular Research Center (Seoul, Korea). Designated trial monitors reviewed the accuracy and completeness of the investigational data at appropriate intervals to ensure compliance with the study protocol. The data and safety monitoring board reviewed the blinded safety data provided by a statistician for a discussion of whether early stopping was warranted in the event of safety concerns and evaluated the appropriateness of study progress. All authors had full access to the data and vouch for the accuracy and completeness of the reported data and for the fidelity of the study to the protocol.

Study Population

Patients were candidates for participation if they had an ACS and had undergone DES implantation with a biodegradable polymer sirolimus-eluting stent (Orsiro, Biotronik, Switzerland). ACS included myocardial infarction (with or without electrocardiographic evidence of ST-segment elevation) and unstable angina, defined as typical symptoms such as recurrent chest pain at rest or with minimal exertion and manifestation of severe angina initiated or aggravated within 4 weeks before the index procedure. Key exclusion criteria were an increased risk of bleeding such as anemia and thrombocytopenia, and a need for oral anticoagulation therapy. Detailed criteria for inclusion and exclusion are provided in Table S1. All participants provided written informed consent.

Randomization and Study Procedures

After the index procedure, patients were randomized at a 1:1 ratio to receive either ticagrelor monotherapy after <1 month of DAPT (aspirin plus ticagrelor) or 12 months of ticagrelor-based DAPT. A web-response permuted block randomization (mixed blocks of 4 or 6) was used at each participating site to allocate the treatment to patients, who were stratified by the presence of diabetes and a clinical presentation of ST-segment–elevation myocardial infarction. The allocation sequence was computer-generated by an external programmer who was not involved in the trial, and physicians or a research coordinator accessed the web-response system.

A loading dose of 300 mg of aspirin and 180 mg of ticagrelor was given if the participants were not taking them at the time of randomization. For both groups, 100 mg of aspirin and 90 mg of ticagrelor twice daily were given orally as a DAPT. For the ticagrelor monotherapy group after <1 month of DAPT, aspirin was discontinued at the first visit after discharge (within 1 month after the index procedure), and 90 mg of ticagrelor twice daily alone was maintained as a single antiplatelet therapy. In the 12-month DAPT group, aspirin was maintained along with ticagrelor for up to 12 months. Concomitant use of other antiplatelet agents or anticoagulants was not allowed. Guideline-directed medical therapy was strongly recommended for optimal management of patient comorbidities (eg, control of hypertension or diabetes, achievement of target low-density lipoprotein cholesterol with high-intensity statin, cessation of cigarette smoking, and management of heart failure).

Follow-up visits were scheduled at 1 to 4 weeks and 3, 6, and 12 months after the index procedure. Information about the participants' general health status, medication use, and the occurrence of clinical end points or adverse events was collected at scheduled follow-up visits, all of which were scheduled on site.

Study End Points

The primary end point was the 1-year net clinical benefit as a composite of all-cause death, myocardial infarction, stent thrombosis, stroke, and major bleeding. The secondary end points were: (1) all-cause death, (2) cardiovascular death, (3) myocardial infarction, (4) stent thrombosis, (5) stroke, (6) major bleeding, (7) minor or major bleeding, and (8) major adverse cardiac events composed of cardiovascular death, myocardial infarction, stent thrombosis, and ischemia-driven target-vessel revascularization. Major bleeding was defined as Bleeding Academic Research Consortium (BARC) type 3 to 5 bleeding, and minor or major bleeding was defined as type 2 to 5 bleeding. Cardiovascular death was defined as death caused by myocardial infarction, sudden cardiac death including unwitnessed death, heart failure, stroke, cardiovascular procedure-related complications, cardiovascular hemorrhage, and any death for which a cardiac cause could not be excluded as adjudicated by a clinical end point adjudication committee.[16,17] Stent thrombosis was defined as definite or probable stent thrombosis according to the Academic Research Consortium.[16] Stroke was defined as an acute cerebrovascular event resulting in a neurological deficit within 24 hours or the presence of acute infarction as demonstrated by imaging studies.[17,18] The type of bleeding by BARC was defined as previously reported.[19] Ischemia-driven target-vessel revascularization was defined as a repeat percutaneous coronary intervention or bypass surgery of the target vessel with a percent diameter stenosis ≥50% and any of the following indications: a positive history of recurrent angina pectoris, presumably related to the target vessel; objective signs of ischemia at rest or during exercise test, presumably related to the target vessel; abnormal results of any invasive functional diagnostic test; and a diameter stenosis ≥70% even in the absence of the abovementioned ischemic signs or symptoms.[17] Routine follow-up angiography in the absence of symptoms was not recommended.

Suspected adverse events, including bleeding and ischemic outcomes, were reported promptly on an electronic case report form, with source documents centrally collected. The study coordination center and the local institutional review board conducted monitoring to identify potential adverse events that had not been reported. After collection of adverse events centrally, any document that could lead to unblinding of treatment assignment was obliterated before submission to the clinical event committee. All adverse events were categorized according to predefined criteria by an independent clinical event adjudication committee, the members of which were unaware of the assignment group or the primary results of the trial.

Statistical Analysis

The sample size was calculated for a noninferiority comparison of the experimental group (ticagrelor monotherapy after <1 month of DAPT) versus the reference group (ticagrelor-based 12-month DAPT treatment) with respect to the occurrence of the primary end point (a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding). According to a previous study conducted in South Korea, Japan, and Taiwan, the occurrence rate of a composite outcome of all-cause mortality, myocardial infarction, and stroke was 9.2%, and major bleeding occurred in 10.3% of the ticagrelor-based DAPT group.[20] In the PLATO trial (Platelet Inhibition and Patient

Outcomes), the rate of death, myocardial infarction, or stroke was 10.2%, and the rate of thrombolysis in myocardial infarction major bleeding was 7.9%.[21] Because 25% of the patients in the PLATO trial encountered both ischemic and bleeding events,[22] the anticipated event rate of a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding in this trial was 14% in both treatment groups. A relative noninferiority margin of 30% using a hazard ratio (HR) scale was chosen in a discussion among the investigators by clinically acceptable relevance according to the margins in previous major trials comparing antiplatelet regimens after DES implantation and the feasibility of patient enrollment.[23–26] A total of 2850 patients was required, with a 5% one-sided α error rate, 80% power, and a loss-to-follow-up rate of 10% by the sample size determination for the log-rank test of noninferiority.[27]

A major analysis was conducted in the intention-to-treat population with all randomized patients according to randomization group. Those with missing outcome data were censored at the time of loss to follow-up or withdrawal of consent. Kaplan-Meier estimates were used to determine the cumulative incidences of the primary and secondary end points. HRs and CIs were generated using Cox proportional hazards models. As for the primary end point, a hierarchical testing for the 2 hypotheses was prespecified. The HR for the ticagrelor monotherapy group after <1 month of DAPT versus the 12-month DAPT group was assessed for noninferiority using an HR margin of 1.3. If the upper limit of the 1-sided 95% CI of the HR was less than the prespecified noninferiority margin, the ticagrelor monotherapy group after <1 month of DAPT was considered noninferior to the 12-month DAPT group. If noninferiority was demonstrated, superiority was tested sequentially. The validity of the proportional hazards assumption was assessed by a log-minus-log-survival function and found to hold; it also was confirmed that the treatment variable and interaction with time was not significant.

The prespecified additional analyses using the per-protocol population were repeated to confirm the robustness of the primary result as a sensitivity analysis. Patients who did not discontinue aspirin at <1 month, or those who continued with P2Y12 inhibitors other than ticagrelor as DAPT or monotherapy (unless they discontinued the allocated therapy because of adverse events), were excluded in the group receiving ticagrelor monotherapy after <1 month of DAPT. In the ticagrelor-based 12-month DAPT group, patients who did not maintain 12 months of ticagrelor-based DAPT were excluded. Post hoc analyses were performed for the patients in the as-treated population considering the actual treatments received. Post hoc analyses of worst-case scenario were also examined as a sensitivity analysis assuming that patients lost to follow-up or who withdrew consent in the ticagrelor monotherapy group after <1 month of DAPT had the primary end point event, whereas those in the ticagrelor-based 12-month DAPT group did not have the event.

Because the same treatment was supplied to both groups during the first 30 days (at the first visit), 30-day landmark analyses were planned after excluding the patients who experienced adverse events within this period. Prespecified subgroup analyses were performed for clinically relevant factors: age, sex, hypertension, diabetes, chronic kidney disease, clinical presentation, multivessel disease, and total stent length. The heterogeneity of effects in subgroups was assessed using interaction terms in a Cox proportional hazards model. Because of the potential for type I error caused by multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory. The findings of subgroup analyses should also be interpreted as exploratory because of the lack of adjustment for multiple testing of subgroups.

Categorical variables are reported as numbers and percentages and compared using a χ^2 test or Fisher exact test. Continuous variables are reported as mean±SD or median and interquartile range (as appropriate) and compared using a *t* test or Mann-Whitney test. All analyses were conducted using SAS Version 9.2 (SAS Institute). All tests were 2-sided except for the noninferiority test. A *P* value <0.05 was considered statistically significant.

RESULTS

Between April 24, 2019, and May 31, 2022, a total of 2850 patients at 24 sites in South Korea were enrolled; 1426 patients were randomly assigned to receive ticagrelor monotherapy after <1 month of DAPT, and 1424 patients were assigned to receive 12 months of ticagrelor-based DAPT (Figure 1). Randomization was primarily conducted within 1 day after percutaneous coronary intervention (96% on the day of index procedure and 2% on day 1 after index procedure; Table S2). In the group receiving ticagrelor monotherapy after <1 month of DAPT, 1221 patients (86%) completed the allocated therapy, and 1260 patients (88%) completed the allocated therapy in the ticagrelor-based 12-month DAPT group (Figure 1). Aspirin was discontinued at a median of 16 days (interquartile range, 12–25 days), and 1304 patients (91%) discontinued aspirin within 30 days in the group receiving ticagrelor monotherapy after <1 month of DAPT (Table S3; Figure S1). Details about antiplatelet therapy and reasons for failure to complete the allocated antiplatelet therapy are provided in Table S3 and Table S4. Other medications are presented in Table S5. Except for less frequent use of proton-pump inhibitors in the group receiving ticagrelor monotherapy after <1 month of DAPT compared with the ticagrelor-based 12-month DAPT group between 90 and 180 days (37% versus 41%; *P*=0.03) and between 180 and 360 days (36% versus 43%; *P*<0.001), no other medications differed between the groups during the study period (Table S5). At the time of database lock (June 2023), 28 patients had died, and clinical follow-up was completed for all but 27 patients (2823 of 2850; 99.1%); 10 patients (0.4%) withdrew consent, and 17 (0.6%) were lost to follow-up (Figure 1).

Clinical, lesion, and procedural characteristics were well-balanced between the treatment groups (Table 1). The mean age was 61 years, 83% of patients were men, 29% had diabetes, and 8% had chronic kidney disease. Most patients (2106 [74%]) were admitted by the emergency department. The distribution for ACS among enrolled participants was 1150 (40%) for ST-segment–elevation myocardial infarction, 992 (35%) for

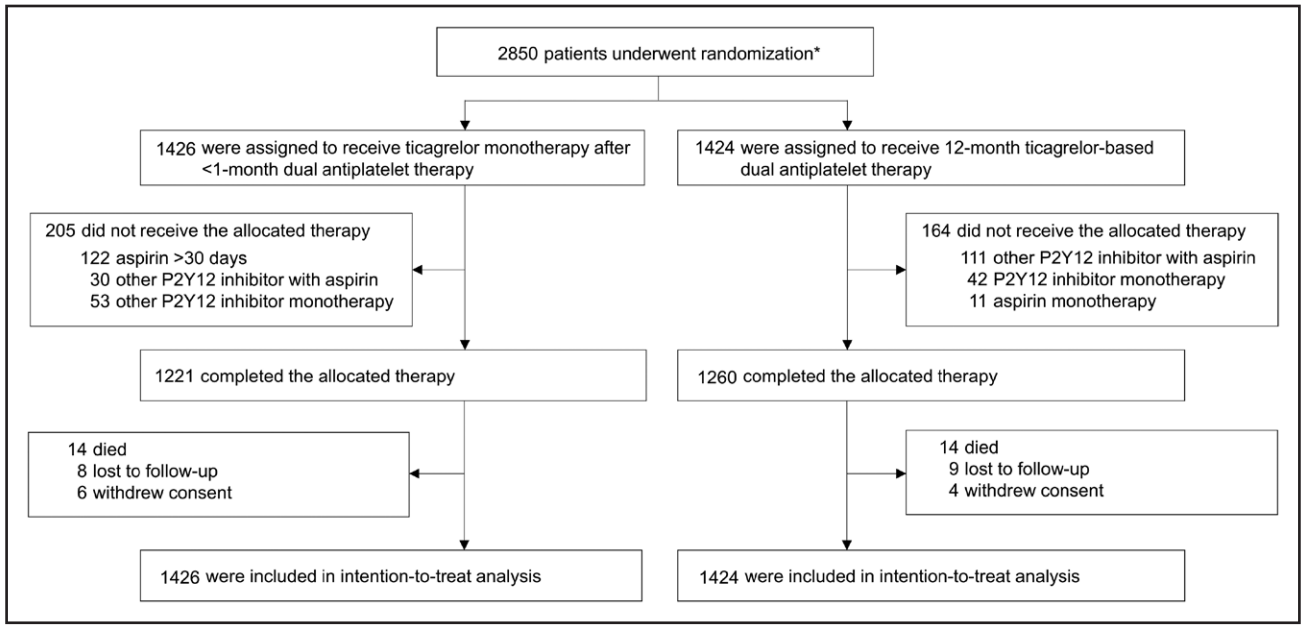

Figure 1. Participant flow in the T-PASS randomized clinical trial.
*Study sites were not required to provide a screening log. Data on reasons for ineligibility are not available. T-PASS indicates Ticagrelor Monotherapy in Patients Treated With New-Generation Drug-Eluting Stents for Acute Coronary Syndrome.

non–ST-segment–elevation myocardial infarction, and 708 (25%) for unstable angina. A transradial approach was used in 1913 patients (67%). A mean of 1.2±0.5 lesions were treated with 37±23 mm in total stent length and 1.4±0.7 number of stents. Detailed information about angiographic and procedural characteristics of all treated lesions at index procedure is supplied in Table S6; no significant differences were noted between the groups.

The primary end point of net clinical benefit (a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding) occurred in 40 patients (2.8%) in the group receiving ticagrelor monotherapy after <1 month of DAPT and in 73 patients (5.2%) in the ticagrelor-based 12-month DAPT group (HR, 0.54 [95% CI, 0.37–0.80]; *P*<0.001 for noninferiority; *P*=0.002 for superiority; Figure 2A; Table 2). Although 30-day landmark analyses between 31 and 360 days proving the noninferiority were not performed because of nonproportional hazards in this period, the primary end point occurred in 28 patients (2.0%) in the group receiving ticagrelor monotherapy after <1 month of DAPT and in 58 patients (4.1%) in the ticagrelor-based 12-month DAPT group (Figure 2B; Table S7). Among each component of the primary end point as a key secondary end point, the incidence of major bleeding (BARC type 3–5 bleeding) was 1.2% in the group that received ticagrelor monotherapy after <1 month of DAPT and 3.4% in the group that received ticagrelor plus aspirin for 12 months (HR, 0.35 [95% CI, 0.20–0.61]; *P*<0.001; Figure 2C; Table 2). Between 31 and 360 days after the index procedure, major bleeding occurred in 9 patients (0.6%) in the group receiving ticagrelor monotherapy after <1 month of DAPT and 39 patients (2.8%) in the ticagrelor-based 12-month DAPT group (*P*<0.001; Table S7). Gastrointestinal bleeding was the most common site of bleeding (Table S8). Other components of the primary end point, including all-cause death, myocardial infarction, stent thrombosis, and stroke, did not significantly differ between the 2 groups (Table 2).

There was no significant difference in the occurrence of major adverse cardiac events (a composite of cardiovascular death, myocardial infarction, stent thrombosis, and ischemia-driven target-vessel revascularization: 21 [1.5%] in the group receiving ticagrelor monotherapy after <1 month of DAPT versus 31 [2.2%] in the ticagrelor-based 12-month DAPT group; HR, 0.68 [95% CI, 0.39–1.18]; *P*=0.165). As a component of major adverse cardiac events, clinical end points of ischemia-driven revascularization are presented in Table S9. Comparisons between the group receiving ticagrelor monotherapy after <1 month of DAPT versus the group receiving 12 months of ticagrelor-based DAPT showed no significant differences in the incidence of ischemia-driven target-vessel revascularization (11 [0.8%] versus 18 [1.3%]; HR, 0.61 [95% CI, 0.29–1.29]; *P*=0.197; Table 2; Table S9). A composite of death, myocardial infarction, stent thrombosis, or stroke, and a composite of death, myocardial infarction, or stroke were not different between the 2 groups (Figure 2D; Table 2).

Baseline characteristics for the per-protocol and as-treated populations are presented in Table S10 and Table S11. For the primary end point, the results were consistent in the per-protocol population (Table S12; Figure S2) and in the as-treated population (Table S13; Figure S2). The post hoc analyses of worst-case scenario for the primary end point were also consistent when the patients lost to follow-up or who withdrew consent in the

Table 1. Clinical, Lesion, and Procedural Characteristics

Characteristics	Ticagrelor monotherapy after <1 month of DAPT (N=1426)	Ticagrelor-based 12-month DAPT (N=1424)
Age, mean (SD), y	61 (10)	61 (10)
Men	1193 (84)	1181 (83)
Women	233 (16)	243 (17)
Body mass index, mean (SD), kg/m^2	25.1 (3.6)	25.0 (3.5)
Previous myocardial infarction	27 (2)	25 (2)
Previous percutaneous coronary intervention	92 (7)	92 (7)
Previous coronary bypass graft surgery	4 (<1)	2 (<1)
Previous stroke	43 (3)	49 (3)
Hypertension	669 (47)	679 (48)
Diabetes	422 (30)	408 (29)
Diabetes with insulin treatment	40 (3)	32 (2)
Chronic kidney disease*	118 (8)	104 (7)
End-stage kidney disease on dialysis	11 (<1)	13 (<1)
Dyslipidemia	1048 (74)	1058 (74)
Current smoker	557 (39)	537 (38)
Admission by emergency department	1056 (74)	1050 (74)
Clinical presentation		
ST-segment–elevation myocardial infarction	572 (40)	578 (41)
Non–ST-segment–elevation myocardial infarction	507 (36)	485 (34)
Unstable angina	347 (24)	361 (25)
Transradial approach	959 (67)	954 (67)
Intra-aortic balloon pump	21 (2)	24 (2)
Percutaneous cardiopulmonary support	6 (<1)	6 (<1)
Multivessel coronary artery disease	749 (53)	738 (52)
Left main disease	23 (2)	31 (2)
Use of glycoprotein IIb/IIIa inhibitors	93 (7)	99 (7)
Bifurcation lesion	219 (15)	215 (15)
Previous stented lesion	23 (2)	16 (1)
Use of intravascular imaging	242 (17)	259 (18)
Use of thrombectomy	79 (6)	76 (5)
Multilesion intervention	299 (21)	279 (20)
Multivessel intervention	233 (16)	231 (16)
Treated lesions per patient, mean (SD)	1.3 (0.5)	1.2 (0.5)
Total number of stents per patient, mean (SD)	1.4 (0.8)	1.4 (0.7)
Total stent length per patient, mean (SD), mm	38 (23)	37 (22)

Data are n (%) unless otherwise noted.
DAPT indicates dual antiplatelet therapy.
*Chronic kidney disease was defined as an estimated glomerular filtration rate of <60 mL/min per 1.73 m^2 of body surface area.

ticagrelor monotherapy group after <1 month of DAPT were assumed to have the primary end point events (HR, 0.70 [95% CI, 0.48–0.98]; $P<0.001$ for noninferiority; $P=0.044$ for superiority). Secondary end points for the per-protocol population and the as-treated population are also presented in Table S12 and Table S13.

Subgroup analyses for the primary end point are presented in Figure 3. The absence of significant interactions suggests that the effect of ticagrelor monotherapy after <1 month of DAPT versus 12 months of ticagrelor-based DAPT was consistent across all subgroups.

DISCUSSION

This study suggests that among patients with ACS who underwent DES implantation, stopping aspirin within 1 month for ticagrelor monotherapy was deemed noninferior and provided evidence for superiority to 12 months of ticagrelor-based DAPT for a 1-year composite outcome of death, myocardial infarction, stent thrombosis, stroke, and major bleeding. The significant reduction in major bleeding in the ticagrelor monotherapy group after <1 month of DAPT was the primary component of the composite outcome driving these findings.

For patients with ACS, to lower the risk of thrombosis related to stents and to reduce adverse events from nonstented segments, DAPT needs to be administered for at least 12 months.[3,4] Several antiplatelet strategies were also assessed to reduce bleeding risks accompanied by a long-term use of aspirin plus potent P2Y12 inhibitors.[5] Recent meta-analyses of randomized trials showed that P2Y12 inhibitor monotherapy after 1- to 3-month DAPT is associated with a similar risk of ischemic events and lower rates of major bleeding events.[13–15] Therefore, the present findings from the T-PASS trial are in line with recent studies comparing P2Y12 inhibitor monotherapy with DAPT,[13–15] and also support recent European and US guidelines.[28,29] European guidelines for the management of ACS recommend considering single antiplatelet therapy (preferably with a P2Y12 inhibitor) in patients who are event-free after 3 to 6 months of DAPT and who are not at high ischemic risk.[28] The US guidelines recommend that 1 to 3 months of DAPT with a subsequent transition to P2Y12 inhibitor monotherapy is reasonable for selected patients undergoing percutaneous coronary intervention.[29]

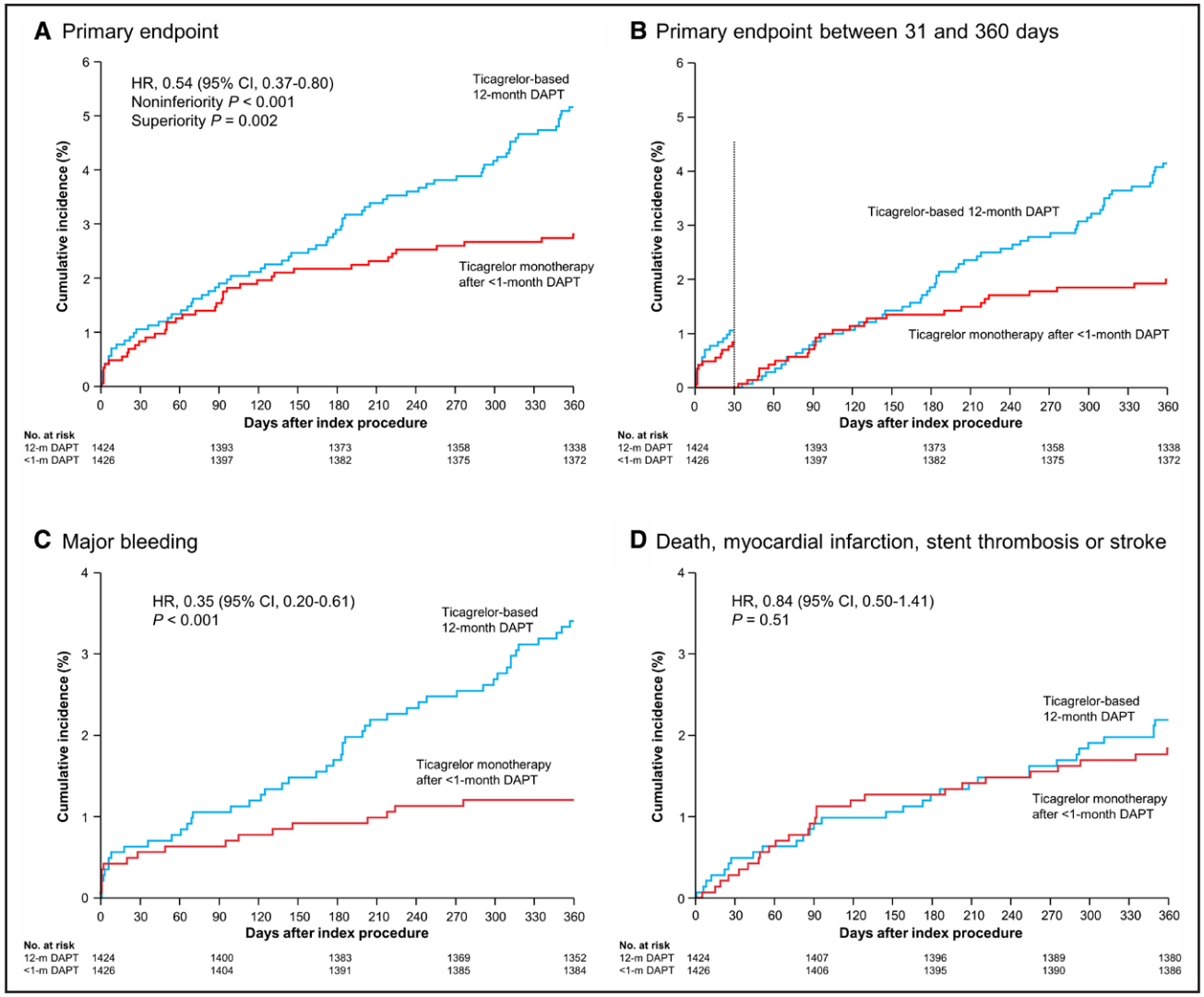

Figure 2. Time-to-event curves for the clinical outcomes.
The primary end point was defined as a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding. Because of nonproportional hazards between 31 and 360 days, time-to-event curves are only presented without statistical tests. DAPT indicates dual antiplatelet therapy; and HR, hazard ratio.

In addition, the T-PASS trial provides evidence about the appropriate timing to switch to single antiplatelet therapy from DAPT and the choice of the single antiplatelet therapy when DAPT is completed, particularly for patients with ACS, when P2Y12 inhibitor monotherapy after short-term DAPT is considered. As for the timing to switch to single antiplatelet therapy from DAPT, concerns have been raised about shortening the duration of DAPT, particularly for patients with ACS, because the risk of thrombotic complications is particularly high, given the thrombotic milieu provoked by plaque rupture and angioplasty-induced endothelial cell injury in the vulnerable period, particularly for ischemic events.[2] It has therefore been suggested that the ischemic vulnerable period is relatively longer for patients with ACS than for those presenting with stable coronary artery disease.[2] According to the SMART-DATE trial (Smart Angioplasty Research Team: Safety of Six-Month Duration of Dual Antiplatelet Therapy After Percutaenous Coronary Intervention in Patients With Acute Coronary Syndrome), 6 months of DAPT was associated with an increased risk of myocardial infarction compared with 12 months of DAPT, although aspirin monotherapy was used in the SMART-DATE trial.[30] With the use of a P2Y12 inhibitor, it was possible to shorten DAPT to 3 months in the SMART-CHOICE (Smart Angioplasty Research Team: Comparison Between P2Y12 Antagonist Monotherapy vs Dual Antiplatelet Therapy in Patients Undergoing Implantation of Coronary Drug-Eluting Stents), TICO (Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus-eluting Stent for Acute Coronary Syndrome), and TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention) trials.[8,11,12] In the present trial, aspirin was discontinued at a median of 16 days, which suggests that <1 month of DAPT is feasible if ticagrelor monotherapy is

Table 2. Clinical Outcomes 1 Year After Index Procedure

Clinical outcomes	Ticagrelor monotherapy after <1 month of DAPT (N=1426)*	Ticagrelor-based 12-month DAPT (N=1424)*	Hazard ratio (95% CI)	*P* value
Primary end point				
Net clinical benefit (a composite of death, myocardial infarction, stent thrombosis, stroke, and major bleeding)	40 (2.8)	73 (5.2)	0.54 (0.37–0.80)	0.002†
Secondary end points				
All-cause death	14 (1.0)	14 (1.0)	1.00 (0.48–2.10)	>0.99
Cardiovascular death	6 (0.4)	9 (0.6)	0.67 (0.24–1.88)	0.44
Myocardial infarction	7 (0.5)	8 (0.6)	0.88 (0.32–2.41)	0.80
Stent thrombosis	2 (0.1)	2 (0.1)	1.00 (0.14–7.09)	>0.99
Stroke	8 (0.6)	11 (0.8)	0.73 (0.29–1.81)	0.49
Ischemic	6	8		
Hemorrhagic	2	3		
Death, myocardial infarction, or stroke (post hoc)	26 (1.8)	31 (2.2)	0.84 (0.50–1.41)	0.51
Death, myocardial infarction, stent thrombosis, or stroke (post hoc)	26 (1.8)	31 (2.2)	0.84 (0.50–1.41)	0.51
Major bleeding (BARC type 3–5)	17 (1.2)	48 (3.4)	0.35 (0.20–0.61)	<0.001
Type 3a	11	25		
Type 3b	4	19		
Type 3c	0	4		
Type 5	2	0		
All bleeding (BARC type 2–5)	28 (2.0)	64 (4.5)	0.43 (0.28–0.68)	<0.001
Type 2	11	16		
Major adverse cardiac event (a composite of cardiovascular death, myocardial infarction, stent thrombosis, and ischemia-driven target-vessel revascularization)	21 (1.5)	31 (2.2)	0.68 (0.39–1.18)	0.17
Ischemia-driven target-vessel revascularization	11 (0.8)	18 (1.3)	0.61 (0.29–1.29)	0.20

BARC indicates Bleeding Academic Research Consortium; and DAPT, dual antiplatelet therapy.

*Data are presented for the intention-to-treat population. The percentages are Kaplan-Meier estimates at day 360.

†The upper limit of the 1-sided 95% CI for the primary end point was 0.75, meeting criteria for a noninferiority margin of 1.3 ($P<0.001$ for noninferiority).

P values for the superiority test were derived from the log-rank test.

maintained, even in patients with ACS. However, of note, the survival curves of the primary end point (net clinical benefit) did not diverge much until 150 days, indicating the trade-off between major bleeding and ischemic events (death, myocardial infarction, stent thrombosis, or stroke) in this period, although the curves of the major bleeding separated at 30 days, much earlier than those of the primary end point.

On the choice of P2Y12 inhibitors as a single antiplatelet therapy after short-term DAPT, this trial maintained ticagrelor monotherapy, not clopidogrel monotherapy, in the experimental group, unlike the STOPDAPT-2 ACS trial (Short and Optimal Duration of Dual Antiplatelet Therapy After Everolimus-Eluting Cobalt Chromium Stent-2 for the Patients With ACS).[10] Ticagrelor, a direct-acting antagonist of P2Y12 receptors, provides more potent platelet inhibition than does clopidogrel, which was traditionally and commonly used in DAPT.[21,31] In addition, the effectiveness of clopidogrel may be limited by high interindividual variability,[31,32] and 1 to 2 months of DAPT followed by clopidogrel monotherapy failed to demonstrate noninferiority to 12 months of DAPT for the primary end point (a composite of cardiovascular death, myocardial infarction, stroke, definite stent thrombosis, and major or minor bleeding) according to the STOPDAPT-2 ACS trial (3.2% versus 2.8%; HR, 1.14 [95% CI, 0.80–1.62]; $P=0.06$ for noninferiority).[10] It is also notable that recent findings from the STOPDAPT-3 trial compared prasugrel monotherapy at a dose of 3.75 mg/d and DAPT in a total of 5966 patients undergoing percutaneous coronary intervention for ACS or at high bleeding risk.[33] Aspirin was not used in the experimental group even immediately after percutaneous coronary intervention. The primary bleeding end point, major bleeding events (BARC 3 or 5) for prasugrel monotherapy versus DAPT, was not superior (4.47% versus 4.71%; HR, 0.95 [95% CI, 0.75–1.20]; $P=0.66$). Although the coprimary cardiovascular end point (a composite of cardiovascular death, myocardial infarction, definite stent thrombosis, or stroke) at 1 month met a noninferiority (4.12% versus

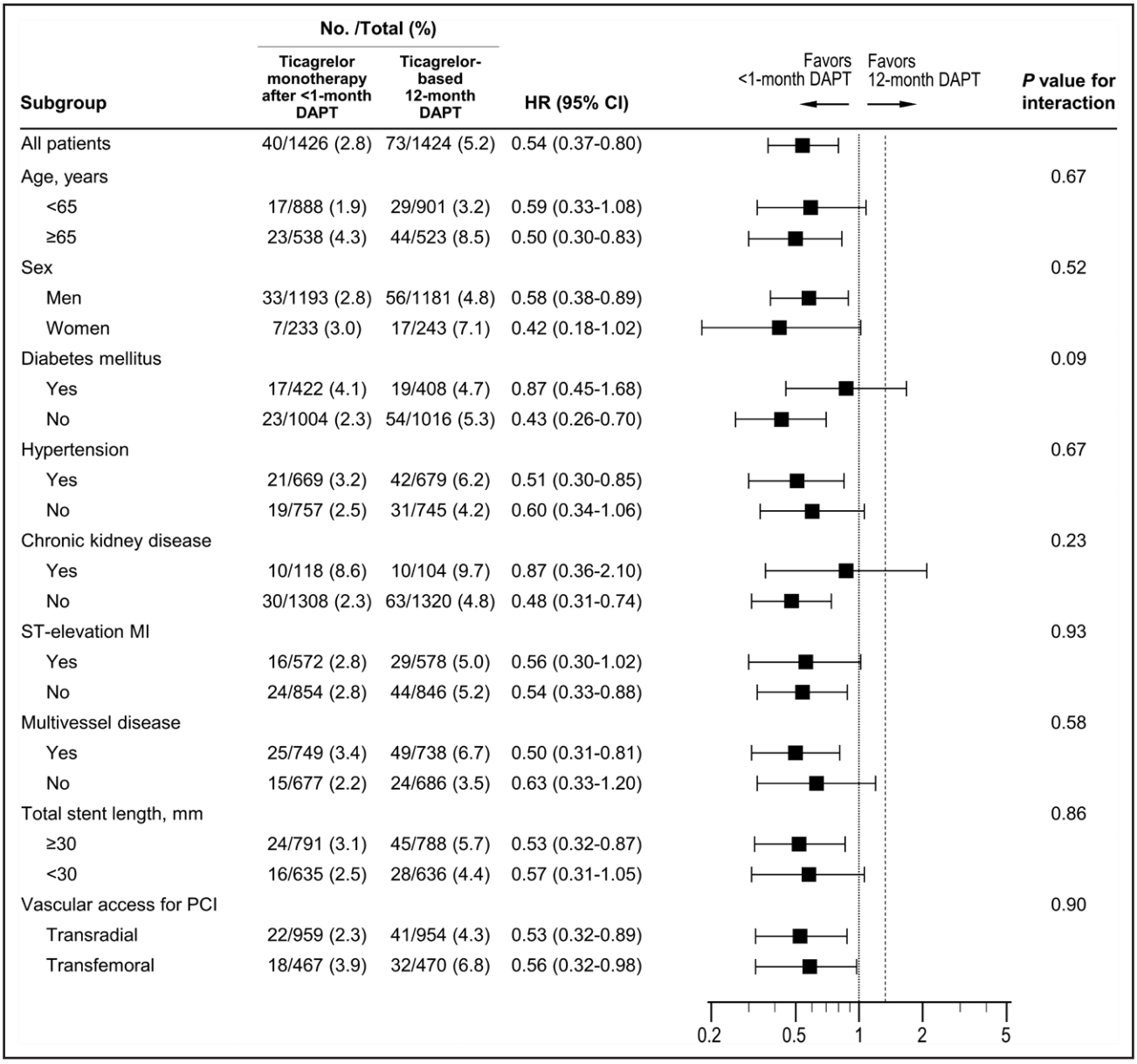

Figure 3. Subgroup analyses for the primary end point.
Numbers and percentages shown are number of patients with events/number of patients at risk and incidences at 1 year. All subgroup analyses were prespecified except vascular access for PCI. *P* values for interaction were calculated using interaction terms in a Cox proportional hazard model. The vertical dashed line indicates the prespecified a noninferiority HR margin of 1.3. DAPT indicates dual antiplatelet therapy; HR, hazard ratio; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

3.69%; HR, 1.12 [95% CI, 0.87–1.45]; *P*=0.01 for noninferiority), any unplanned coronary revascularization (1.05% versus 0.57%; HR, 1.83 [95% CI, 1.01–3.30]; *P*<0.05) or subacute definite or probable stent thrombosis (0.58% versus 0.17%; HR, 3.40 [95% CI, 1.26–9.23]; *P*<0.05) was significantly higher in the prasugrel monotherapy group. In contrast with the T-PASS trial, in which ticagrelor monotherapy was used at full dose (90 mg twice daily), prasugrel monotherapy at a lower dose than the default maintenance dose (10 mg daily or 5 mg daily) was used in the STOPDAPT-3 trial (Short and Optimal Duration of Dual Antiplatelet Therapy-3).[33] Another possible explanation that showed harm in interruption of DAPT within the first 30 days in the STOPDAPT-3 trial is that higher-risk patients seemed to have been included than in the current trial. Thirty-day mortality was more than twice as high as 1-year mortality in the current trial.

In addition to the strength of use of a uniform type of P2Y12 inhibitor in this trial, another strength of this trial is that only patients with ACS were enrolled, which suggests a therapeutic option, particularly for patients with ACS. Although the GLOBAL LEADERS trial (A Clinical Study Comparing Two Forms of Anti-platelet Therapy After Stent Implantation), which compared a strategy of

ticagrelor monotherapy initiated at 1 month after percutaneous coronary intervention versus a standard strategy of DAPT for 12 months followed by P2Y12 inhibitor discontinuation, included patients undergoing DES implantation for stable coronary artery disease or ACS,[6] the clinical outcomes between ticagrelor alone and ticagrelor plus aspirin in patients with ACS could be compared by assessing the events occurring 31 to 365 days after randomization in a subset of patients with ACS from the GLOBAL LEADERS trial.[32] Similar to our findings, the discontinuation of aspirin was associated with a reduction in major bleeding events (BARC type 3 or 5 bleeding; 0.8% versus 1.5%; HR, 0.52 [95% CI, 0.33–0.81]; *P*=0.004). These analyses may be different from our trial in that it is a post hoc exploratory landmark analysis in a subgroup of ACS from the parent trial, and investigator reporting was used without central adjudication for secondary outcomes including bleeding events.[32] Taken together, our findings not only support a recommendation of stopping aspirin at 3 to 6 months by European guidelines and at 1 to 3 months by US guidelines but also provide new evidence of feasibility to further shorten the DAPT duration up to <1 month when ticagrelor is used as a monotherapy to decrease bleeding events without an increase in ischemic events, even for patients with ACS who underwent DES.

This study has several limitations. First, this study was an open-label trial that was not placebo-controlled, which may introduce bias in relation to ascertainment or adjudication of outcomes, although clinical outcomes were assessed by members of an independent clinical event committee. Second, this study has no screening log available, and therefore, it may be unclear how selected the patients randomized were. Low event rates may also implicate that relatively non–high-risk patients were included in this trial. The incidence of primary end point at 30 days was lower than that of net adverse clinical events in patients with ACS from the GLOBAL LEADERS trial.[32] The all-cause mortality rate at 1 year in the 12-month ticagrelor-based DAPT group in this trial was 1.0%, whereas it was 4.5% in the corresponding 12-month ticagrelor-based DAPT group in the PLATO trial.[21] Third, this study may have had less power than originally anticipated given the low event rates observed. However, the primary end point for the noninferiority test was met. In addition, because the noninferiority margin was chosen as a risk ratio instead of an absolute difference, there may be less concern about unrealistic optimistic claims of noninferiority as the noninferiority margin widens. Fourth, this study was conducted only in South Korea, therefore, caution is needed when extrapolating the results to populations outside of South Korea. Fifth, this study included patients who had undergone implantation of biodegradable polymer sirolimus-eluting stents, and the results may not extend to patients who receive other stent types.

Conclusions

Among patients who underwent DES implantation for ACS, <1 month of DAPT followed by ticagrelor monotherapy met a noninferiority threshold and provided evidence of superiority to 12 months of ticagrelor-based DAPT for a 1-year composite outcome of death, myocardial infarction, stent thrombosis, stroke, and major bleeding, primarily because of a significant reduction in bleeding events. Low event rates that may suggest enrollment of relatively non–high-risk patients should be considered in interpreting the trial.

ARTICLE INFORMATION

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Supplemental Material

T-PASS Trial Investigators
Table S1–S13
Figure S1–S2

REFERENCES

1. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and treatment of acute coronary syndromes: a review. *JAMA*. 2022;327:662–675. doi: 10.1001/jama.2022.0358
2. Kamran H, Jneid H, Kayani WT, Virani SS, Levine GN, Nambi V, Khalid U. Oral antiplatelet therapy after acute coronary syndrome: a review. *JAMA*. 2021;325:1545–1555. doi: 10.1001/jama.2021.0716
3. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines: an update of

the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/ STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155. doi: 10.1161/CIR.0000000000000404

4. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, Jüni P, Kastrati A, Kolh P, Mauri L, et al; ESC Scientific Document Group. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2018;39:213–260. doi: 10.1093/eurheartj/ehx419
5. Capodanno D, Mehran R, Krucoff MW, Baber U, Bhatt DL, Capranzano P, Collet JP, Cuisset T, De Luca G, De Luca L, et al. Defining strategies of modulation of antiplatelet therapy in patients with coronary artery disease: a consensus document from the Academic Research Consortium. *Circulation*. 2023;147:1933–1944. doi: 10.1161/CIRCULATIONAHA.123.064473
6. Vranckx P, Valgimigli M, Jüni P, Hamm C, Steg PG, Heg D, van Es GA, McFadden EP, Onuma Y, van Meijeren C, et al; GLOBAL LEADERS Investigators. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicenter, open-label, randomized superiority trial. *Lancet*. 2018;392:940–949. doi: 10.1016/S0140-6736(18)31858-0
7. Franzone A, McFadden E, Leonardi S, Piccolo R, Vranckx P, Serruys PW, Benit E, Liebetrau C, Janssens L, Ferrario M, et al; GLASSY Investigators. Ticagrelor alone versus dual antiplatelet therapy from 1 month after drug-eluting coronary stenting. *J Am Coll Cardiol*. 2019;74:2223–2234. doi: 10.1016/j.jacc.2019.08.1038
8. Hahn JY, Song YB, Oh JH, Chun WJ, Park YH, Jang WJ, Im ES, Jeong JO, Cho BR, Oh SK, et al; SMART-CHOICE Investigators. 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;321:2428–2437. doi: 10.1001/jama.2019.8146
9. Watanabe H, Domei T, Morimoto T, Natsuaki M, Shiomi H, Toyota T, Ohya M, Suwa S, Takagi K, Nanasato M, et al; STOPDAPT-2 Investigators. Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI: the STOPDAPT-2 randomized clinical trial. *JAMA*. 2019;321:2414–2427. doi: 10.1001/jama.2019.8145
10. Watanabe H, Morimoto T, Natsuaki M, Yamamoto K, Obayashi Y, Ogita M, Suwa S, Isawa T, Domei T, Yamaji K, et al; STOPDAPT-2 ACS Investigators. Comparison of clopidogrel monotherapy after 1 to 2 months of dual antiplatelet therapy with 12 months of dual antiplatelet therapy in patients with acute coronary syndrome: the STOPDAPT-2 ACS randomized clinical trial. *JAMA Cardiol*. 2022;7:407–417. doi: 10.1001/jamacardio.2021.5244
11. Kim BK, Hong SJ, Cho YH, Yun KH, Kim YH, Suh Y, Cho JY, Her AY, Cho S, Jeon DW, et al; TICO Investigators. Effect of ticagrelor monotherapy vs ticagrelor with aspirin on major bleeding and cardiovascular events in patients with acute coronary syndrome: the TICO randomized clinical trial. *JAMA*. 2020;323:2407–2416. doi: 10.1001/jama.2020.7580
12. Mehran R, Baber U, Sharma SK, Cohen DJ, Angiolillo DJ, Briguori C, Cha JY, Collier T, Dangas G, Dudek D, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. *N Engl J Med*. 2019;381:2032–2042. doi: 10.1056/NEJMoa1908419
13. Valgimigli M, Gragnano F, Branca M, Franzone A, Baber U, Jang Y, Kimura T, Hahn JY, Zhao Q, Windecker S, et al. P2Y12 inhibitor monotherapy or dual antiplatelet therapy after coronary revascularization: individual patient level meta-analysis of randomized controlled trials. *BMJ*. 2021;373:n1332. doi: 10.1136/bmj.n1332
14. O'Donoghue ML, Murphy SA, Sabatine MS. The safety and efficacy of aspirin discontinuation on a background of a P2Y12 inhibitor in patients after percutaneous coronary intervention: a systematic review and meta-analysis. *Circulation*. 2020;142:538–545. doi: 10.1161/CIRCULATIONAHA.120.046251
15. Giacoppo D, Matsuda Y, Fovino LN, D'Amico G, Gargiulo G, Byrne RA, Capodanno D, Valgimigli M, Mehran R, Tarantini G. 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;42:308–319. doi: 10.1093/eurheartj/ehaa739
16. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, et al; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344–2351. doi: 10.1161/CIRCULATIONAHA.106.685313
17. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, et al; Academic Research Consortium. Standardized end point definitions for coronary intervention trials: the Academic Research Consortium-2 consensus document. *Circulation*. 2018;137:2635–2650. doi: 10.1161/CIRCULATIONAHA.117.029289
18. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MS, George MG, Hamdan AD, Higashida RT, et al; American Heart Association Stroke Council, Council on Cardiovascular Surgery and Anesthesia. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44:2064–2089. doi: 10.1161/STR.0b013e318296aeca
19. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation*. 2011;123:2736–2747. doi: 10.1161/CIRCULATIONAHA.110.009449
20. 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;79:2452–2460. doi: 10.1253/circj.CJ-15-0112
21. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, et al; PLATO Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361:1045–1057. doi: 10.1056/NEJMoa0904327
22. Kang HJ, Clare RM, Gao R, Held C, Himmelmann A, James SK, Lim ST, Santoso A, Yu CM, Wallentin L, et al; PLATO Investigators. Ticagrelor versus clopidogrel in Asian patients with acute coronary syndrome: a retrospective analysis from the Platelet Inhibition and Patient Outcomes (PLATO) Trial. *Am Heart J*. 2015;169:899–905.e1. doi: 10.1016/j.ahj.2015.03.015
23. Kim BK, Hong MK, Shin DH, Nam CM, Kim JS, Ko YG, Choi D, Kang TS, Park BE, Kang WC, et al; RESET Investigators. A new strategy for discontinuation of dual antiplatelet therapy: the RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation). *J Am Coll Cardiol*. 2012;60:1340–1348. doi: 10.1016/j.jacc.2012.06.043
24. Gwon HC, Hahn JY, Park KW, Song YB, Chae IH, Lim DS, Han KR, Choi JH, Choi SH, Kang HJ, et al. Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. *Circulation*. 2012;125:505–513. doi: 10.1161/CIRCULATIONAHA.111.059022
25. Feres F, Costa RA, Abizaid A, Leon MB, Marin-Neto JA, Botelho RV, King SB 3rd, Negoita M, Liu M, de Paula JE, et al; OPTIMIZE Trial Investigators. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: the OPTIMIZE randomized trial. *JAMA*. 2013;310:2510–2522. doi: 10.1001/jama.2013.282183
26. Kedhi E, Fabris E, van der Ent M, Buszman P, von Birgelen C, Roolvink V, Zurakowski A, Schotborgh CE, Hoorntje JCA, Eek CH, et al. Six months versus 12 months dual antiplatelet therapy after drug-eluting stent implantation in ST-elevation myocardial infarction (DAPT-STEMI): randomised, multicentre, non-inferiority trial. *BMJ*. 2018;363:k3793. doi: 10.1136/bmj.k3793
27. Jung SH, Chow SC. On sample size calculation for comparing survival curves under general hypothesis testing. *J Biopharm Stat*. 2012;22:485–495. doi: 10.1080/10543406.2010.550701
28. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, Claeys MJ, Dan GA, Dweck MR, Galbraith M, et al. 2023 ESC guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44:3720–3826. doi: 10.1093/eurheartj/ehad191
29. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, Bittl JA, Cohen MG, DiMaio JM, Don CW, 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–e114. doi: 10.1161/CIR.0000000000001038

30. Hahn JY, Song YB, Oh JH, Cho DK, Lee JB, Doh JH, Kim SH, Jeong JO, Bae JH, Kim BO, et al; SMART-DATE Investigators. 6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomized, open-label, non-inferiority trial. *Lancet*. 2018;391:1274–1284. doi: 10.1016/S0140-6736(18)30493-8
31. Hong SJ, Ahn CM, Kim JS, Kim BK, Ko YG, Choi D, Jang Y, Hong MK. Effect of ticagrelor monotherapy on mortality after percutaneous coronary intervention: a systematic review and meta-analysis of randomized trials including 26143 patients. *Eur Heart J Cardiovasc Pharmacother*. 2022;8:48–55. doi: 10.1093/ehjcvp/pvaa119
32. Tomaniak M, Chichareon P, Onuma Y, Deliargyris EN, Takahashi K, Kogame N, Modolo R, Chang CC, Rademaker-Havinga T, Storey RF, et al; GLOBAL LEADERS Trial Investigators. Benefit and risks of aspirin in addition to ticagrelor in acute coronary syndromes: a post hoc analysis of the randomized GLOBAL LEADERS Trial. *JAMA Cardiol*. 2019;4:1092–1101. doi: 10.1001/jamacardio.2019.3355
33. Natsuaki M, Watanabe H, Morimoto T, Yamamoto K, Obayashi Y, Nishikawa R, Ando K, Suwa S, Isawa T, Yamamoto T, et al. Short and optimal duration of dual antiplatelet therapy study after everolimus-eluting cobalt-chromium stent-3 (the STOPDAPT-3 trial). Presented at European Society of Cardiology Congress 2023; August 26, 2023.