



Aspirin-Free Prasugrel Monotherapy After Percutaneous Coronary Intervention in Patients With Non-ST Elevation Acute Coronary Syndrome

Kotaro Miyashita, MD; Takashi Muramatsu, MD, PhD; Pruthvi C. Revaiah, MD; Gaku Nakazawa, MD, PhD; Yuki Ishibashi, MD, PhD; Ken Kozuma, MD, PhD; Taku Asano, MD, PhD; Yuki Katagiri, MD, PhD; Takayuki Okamura, MD, PhD; Yoshihiro Morino, MD, PhD; Norihiro Kogame, MD, PhD; Masafumi Ono, MD, PhD; Yosuke Miyazaki, MD, PhD; Shimpei Nakatani, MD, PhD; Masato Nakamura, MD, PhD; Akihiro Tobe, MD; Asahi Oshima, MD; Tsung Ying-Tsai, MD; Scot Garg, MD, PhD; Kengo Tanabe, MD, PhD; Yukio Ozaki, MD, PhD; Patrick W. Serruys, MD, PhD; Yoshinobu Onuma, MD, PhD

Background: In the presence of a potent P2Y₁₂ inhibitor such as prasugrel, the additional clinical antithrombotic benefit of aspirin is unclear. The feasibility of prasugrel monotherapy without aspirin after percutaneous coronary intervention (PCI) has been demonstrated in chronic coronary syndrome, but is yet to be assessed in patients with non-ST elevation acute coronary syndrome (NSTEMI-ACS) and low anatomical complexity.

Methods and Results: ASET-Japan is a single-arm study investigating the safety of prasugrel 12-month monotherapy with a locally approved dose (loading 20 mg; maintenance 3.75 mg), started immediately after successful PCI using platinum-chromium everolimus-eluting SYNERGY stents. The primary ischemic endpoint is a composite of cardiac death, spontaneous target vessel myocardial infarction, or definite stent thrombosis; the primary bleeding endpoint is Bleeding Academic Research Consortium (BARC) Type 3 and 5 bleeding. ASET-Japan recruited 101 NSTEMI-ACS patients from 11 Japanese sites. The mean (\pm SD) age was 69.1 \pm 12.3 years and 36.6% had a PRECISE-DAPT score >25 . The mean anatomical SYNTAX score was 7.9 \pm 4.7. At 1 year, the primary ischemic endpoint occurred in 1 patient (1.0%; cardiac death). Two BARC Type 3a bleeding events occurred (2.0%): 1 due to a gastric ulcer and 1 to a descending colon malignancy.

Conclusions: Low-dose (3.75 mg/day) prasugrel monotherapy started immediately after SYNERGY stent deployment was feasible and safe in selected NSTEMI-ACS patients.

Key Words: Acute coronary syndrome (ACS); Antiplatelet monotherapy; Drug-eluting stent (DES); Percutaneous coronary intervention (PCI); Prasugrel

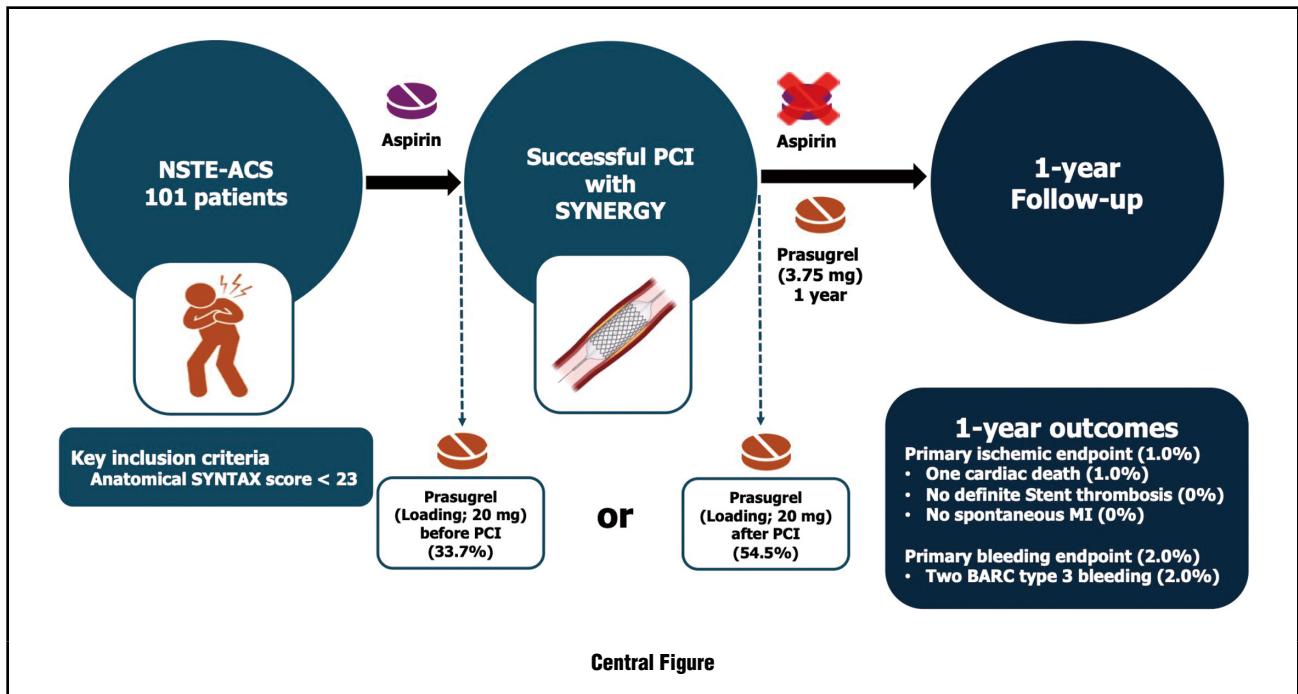
Dual antiplatelet therapy (DAPT) with aspirin and a P2Y₁₂ inhibitor is the standard of care following percutaneous coronary intervention (PCI) with a drug-eluting stent (DES), with a longer duration typically recommended for those patients presenting with acute

coronary syndrome (ACS) compared with chronic coronary syndrome (CCS). The 2019 Japanese ACS guidelines¹ and the latest guidelines from the European Society of Cardiology (ESC)² both give 12-month DAPT a Class I, Level of Evidence A recommendation in patients with ACS

Received May 8, 2025; revised manuscript received June 8, 2025; accepted June 28, 2025; J-STAGE Advance Publication released online September 4, 2025 Time for primary review: 24 days

School of Medicine, University of Galway, Galway (K.M., P.C.R., A.T., A.O., T.Y.-T., P.W.S., Y. Onuma), Ireland; Department of Cardiology, Fujita Health University Hospital, Aichi (T.M.); Department of Cardiology, Kindai University, Osaka (G.N.); Department of Cardiology, St. Marianna University School of Medicine, Kanagawa (Y.I.); Department of Cardiology, Teikyo University Hospital, Tokyo (K.K.); Department of Cardiology, St. Luke International Hospital, Tokyo (T.A., M.O.); Department of Cardiology, Sapporo Higashi Tokushukai Hospital, Sapporo (Y.K.); Division of Cardiology, Department of Medicine and Clinical Science, Yamaguchi University Graduate School of Medicine, Yamaguchi (T.O., Y. Miyazaki); Division of Cardiology, Iwate Medical University, Iwate (Y. Morino); Department of Cardiology, Tokyo Rosai Hospital, Tokyo (N.K.); Department of Cardiology, JCHO Hoshigaoka Medical Center, Osaka (S.N.); Division of Cardiovascular Medicine, Toho University Ohashi Medical Center, Tokyo (M.N.), Japan; Department of Cardiology, Royal Blackburn Hospital, Blackburn (S.G.); School of Medicine, University of Central Lancashire, Preston (S.G.), UK; Division of Cardiology, Mitsui Memorial Hospital, Tokyo (K.T.); and Department of Cardiology, Fujita Health University Okazaki Medical Center, Aichi (Y. Ozaki), Japan

(Footnote continued the next page.)



treated with PCI.

However, this 12-month DAPT regimen has been challenged because it was established without robust prospective evidence and potentially leads to overtreatment and associated bleeding. Notably, this standard 12-month duration for DAPT was introduced on the back of findings from the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial in which the average duration of DAPT was 9, not 12, months.³ Furthermore, contemporary studies investigating the clinical benefit of shorter durations of DAPT in ACS suggest the lack of additional benefit with 12-month DAPT regimens in ACS patients at high bleeding risk (HBR).⁴⁻⁶ Recent meta-analyses demonstrated that treating patients with ACS with monotherapy using a potent P2Y₁₂ inhibitor halves the incidence of bleeding without increasing ischemic events compared with standard DAPT.⁷⁻¹³ Studies investigating de-escalating DAPT or shortening its duration have consistently demonstrated a reduction in bleeding complications without increasing the risk of cardiovascular or ischemic events compared with a 12-month regimen.

The locally approved standard dose of P2Y₁₂ inhibitor is lower in Japanese and Taiwanese patients compared with the rest of the world.¹⁴ Pharmacokinetic studies in healthy populations have shown that East Asian patients, including Japanese, Korean, and Chinese patients, have blood concentrations of active prasugrel metabolites $\geq 40\%$ higher

than patients in Europe and the US, resulting in a significant suppression of platelet aggregation.¹⁵ The “East Asian paradox” is the term given to the phenomenon whereby East Asian populations have a higher risk of bleeding and a lower risk of ischemia compared with European populations. The Prasugrel Compared With Clopidogrel for Japanese Patients With ACS Undergoing PCI (PRASFIT-ACS) trial¹⁶ compared low-dose prasugrel and clopidogrel in patients with ACS. The prasugrel group, which received an initial loading dose of 20 mg prasugrel in combination with aspirin, followed by a low maintenance dose of 3.75 mg/day prasugrel from the next day, had a lower rate of cardiovascular events than the clopidogrel group without an increase in major bleeding events.¹⁶ The results of that study and the pharmacokinetic study¹⁵ were the basis for the decision to use a 20-mg loading dose of prasugrel and a 3.75-mg maintenance dose in Japanese patients with CCS and ACS. Previously, the safety of prasugrel monotherapy after PCI was demonstrated in 206 Japanese patients with CCS (The Acetyl Salicylic Elimination Trial Japan [ASET-Japan] Phase 1).¹⁷ Since the safety of an aspirin-free strategy in ACS had never been demonstrated, the present study (ASET-Japan Phase 2) was designed to include low-risk ACS patients to carefully investigate the safety of this approach in a stepwise extension of the population from CCS.

The feasibility of low-dose prasugrel monotherapy

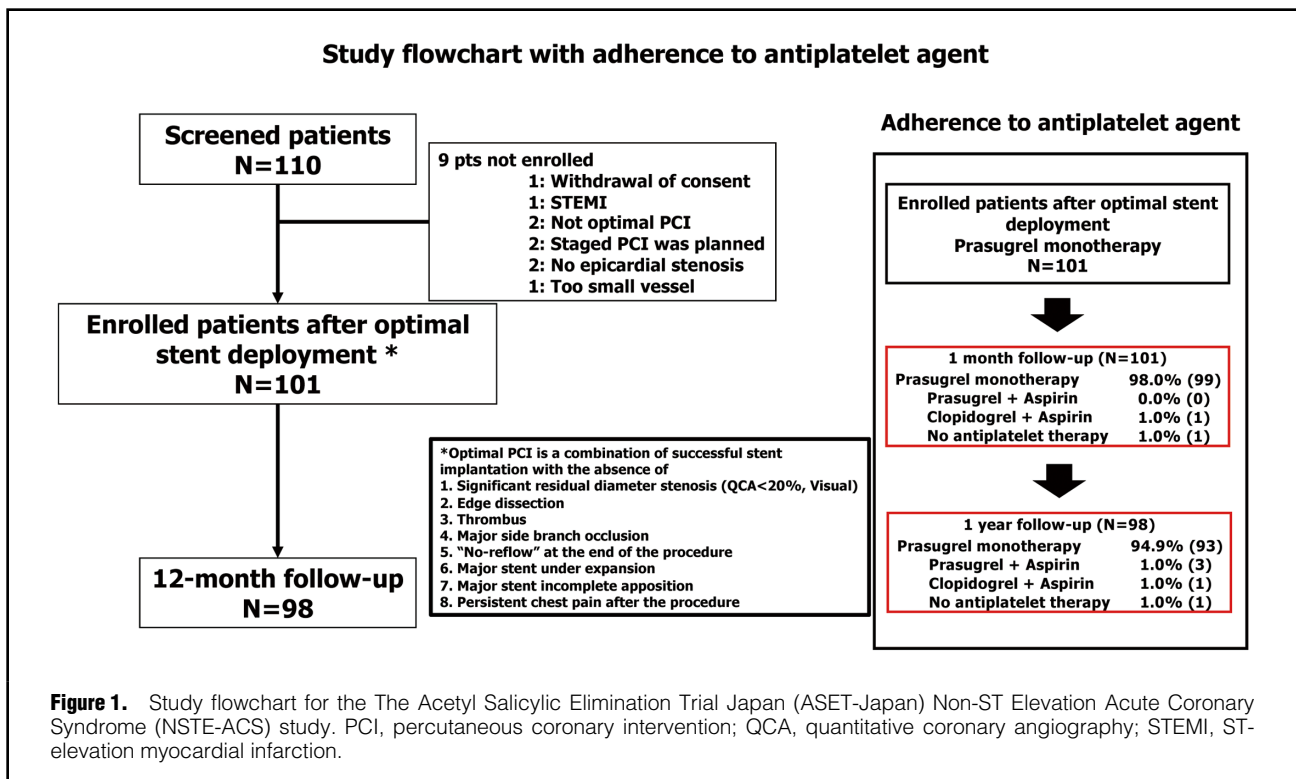
The first three authors contributed equally to this study (K.M., T.M., P.C.R.).

Mailing address: Yoshinobu Onuma, MD, PhD, FESC, FACC, Professor in Interventional Cardiology, University of Galway, Medical Director of the Cardiovascular Research Centre for Advanced Imaging and Core Laboratory (CORRIB) (Cardiovascular Imaging and Atherosclerosis), University Road, Galway, H91 TK33, Ireland. email: yoshinobuonuma@gmail.com and Patrick W. Serruys, MD, PhD, FESC, FACC, Established Professor of Interventional Medicine and Innovation at the University of Galway, and Senior Consultant of the Cardiovascular Research Centre for Advanced Imaging and Core Laboratory (CORRIB), Investigator of the Science Foundation of Ireland, University Road, Galway, H91 TK33, Ireland. email: patrick.w.j.c.serruys@gmail.com

All rights are reserved to the Japanese Circulation Society. For permissions, please email: cj@j-circ.or.jp

ISSN-1346-9843





after PCI has been demonstrated in Japanese patients with CCS and low anatomical complexity.¹⁷ As an extension of the ASET-Japan CCS study, this ASET-Japan non-ST elevation ACS (NSTEMI-ACS) study evaluated the feasibility and safety of low-dose prasugrel monotherapy (3.75 mg/day) without aspirin after optimal PCI using biodegradable polymer platinum-chromium everolimus-eluting stents (EES) in selected Japanese patients with NSTEMI-ACS.

Methods

Study Design

The design of the ASET-Japan pilot study has been described elsewhere;¹⁸ briefly, it is a multicenter, single-arm, open label, proof-of-concept trial conducted at 11 Japanese centers with a stopping rule based on the occurrence of definite stent thrombosis (ST). This study was approved by the Certified Review Board at Fujita Health University (Reference no. CRB4180003), with additional approval obtained from local ethics committees at participating centers if necessary. All enrolled patients provided written informed consent, and the study complied with the Declaration of Helsinki. The study protocol was registered with the Japanese Registry of Clinical Trials (jRCTs042200053) and ClinicalTrials.gov (NCT05117866). The trial initially planned to recruit 200 NSTEMI-ACS patients; however, due to a prolonged enrolment period caused by the COVID-19 pandemic and subsequent financial constraints, a protocol amendment was made and study enrolment was terminated after 101 patients had been recruited.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria have been reported elsewhere (Supplementary Table 1).¹⁸ Briefly, patients requir-

ing PCI for ACS who had an anatomical SYNTAX score <23 were screened and considered for enrolment. The SYNTAX score was calculated on angiography performed at the time of presentation of NSTEMI-ACS. All planned procedures had to be performed using the SYNERGY EES (Boston Scientific, Marlborough, MA, USA). For patients having staged procedures, the last planned procedure was considered the index procedure. Any patient without optimal acute implantation results, as defined by protocol criteria, was considered a screening failure and excluded from enrollment; detailed reasons for these screening failures are presented in Figure 1.

PCI Procedures

The index PCI was performed with the intention of achieving an optimal result in ≥ 1 lesions with angiographic diameter stenosis $\geq 50\%$, as identified by the local interventional cardiologist. Periprocedural anticoagulation was used at the operator's discretion according to local guidelines. All target lesions were treated exclusively with a SYNERGY EES. The definition of an optimal acute coronary stenting result is a combination of successful stent implantation at the target lesion with the absence of significant residual diameter stenosis (<20%), edge dissection, thrombus, major side branch occlusion, no reflow at the end of the procedure, major stent underexpansion or major stent incomplete apposition, and the absence of persistent chest pain after the procedure.

All patients were loaded according to local practice with standard DAPT (aspirin 81–330 mg and clopidogrel 300 mg, prasugrel 20 mg, or ticagrelor 180 mg unless the patient is on long-term [≥ 5 days prior to the index PCI] therapy with prasugrel) before their PCI procedure.

Inclusion in the trial required the achievement of optimal

Table 1. Baseline Patient Characteristics (n=101)

| | |
|---|--------------------|
| Age (years) | 69.1±12.3 |
| Sex | |
| Male | 75 (75.2) |
| Female | 24 (24.8) |
| Body mass index (kg/m ²) | 24.9±3.4 |
| Current smoking | 25 (24.8) |
| Diabetes | 28 (27.7) |
| Insulin-dependent | 3 (3.0) |
| Hypertension | 72 (71.3) |
| Dyslipidemia | 64 (63.4) |
| Family history of CAD ^A | 10 (9.9) |
| Established PVD | 6 (5.9) |
| COPD | 7 (6.9) |
| History of HF | 2 (2.0) |
| History of major bleeding ^B | 1 (1.0) |
| Renal insufficiency ^C | 14 (13.9) |
| Previous PCI | 15 (14.9) |
| Previous MI | 10 (9.9) |
| Previous CABG | 3 (3.0) |
| LVEF (%) | 58±9 |
| Anatomical SYNTAX score | 8±5 |
| Clinical presentation | |
| Unstable angina | 20 (19.4) |
| NSTEMI | 81 (80.6) |
| Cardiac arrest | 0 (0) |
| Cardiogenic shock | 0 (0) |
| Current HF | 0 (0) |
| GRACE risk score | 108±25 |
| Low risk (≤108) | 50 (49.5) |
| Intermediate risk (109–140) | 40 (39.6) |
| High risk (>140) | 11 (10.9) |
| Cardiac troponin normalized by ULN^D | |
| Before PCI | |
| Troponin I (n=58) | 3.64 [0.91–38.73] |
| Troponin T (n=40) | 2.50 [1.21–9.09] |
| After PCI | |
| Troponin I (n=43) | 13.85 [4.36–48.77] |
| Troponin T (n=28) | 5.91 [1.93–27.30] |

Data are mean±SD, median [interquartile range], or n (%).

^AHistory of coronary artery disease (CAD) in a first-degree relative.

^BHistory of bleeding events requiring hospitalization within the previous 1 year. ^CRenal insufficiency was defined as an estimated glomerular filtration rate <60 mL/min/1.73 m². ^DCardiac troponin levels were standardized by dividing the absolute value by the upper limit of normal (ULN) specific to each participating site. A ratio of 1.0 corresponds to the institutional ULN; values >1.0 indicate elevation above the normal range. CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

stent implantation according to local standards of care using angiography, quantitative coronary angiography (QCA) and/or intracoronary imaging (intravascular ultrasound [IVUS] or optical coherence tomography [OCT]), and was defined as successful stent implantation in the target lesion with a visual residual diameter stenosis <20% and no edge

dissection, thrombus, major side branch occlusion, no reflow, major stent underexpansion, or major incomplete stent apposition.¹⁹ The use of intracoronary imaging before and/or after stent implantation for optimization was left to the discretion of the operator.

Protocol for Antiplatelet Therapy

After achievement of optimal SYNERGY stent implantation, patients were enrolled in the study and were loaded with 20 mg prasugrel immediately after enrollment while still in the catheter laboratory to avoid any further delay in loading with the study drug (if the patient had already been loaded prior to the procedure or was on long-term prasugrel, there was no need for additional loading) and maintained on 3.75 mg prasugrel once daily for 12 months. For patients who had been loaded with 20 mg prasugrel just before the PCI, the next maintenance dose of prasugrel (3.75 mg) was administered the day after the index procedure.

Collection of Clinical Follow-up Data

Clinical follow-up was performed with outpatient visits at 1 and 12 months and telephone contact at 3, 6, and 13 months. An assessment of angina status, cardiovascular drug use, and any serious adverse events was recorded during clinical follow-up visits. Optimal medical therapy, with strict control of low-density lipoprotein cholesterol, was strongly recommended, along with optimization of all medications according to current guidelines. Information regarding the use of other medications (e.g., β -blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers) was also collected.¹⁸

Study Endpoints

The primary ischemic endpoint was a composite of cardiac death, target vessel myocardial infarction (MI) >48 h after the index PCI, or definite ST occurring ≤12 months after the index procedure.²⁰ The primary bleeding endpoint was Bleeding Academic Research Consortium (BARC) Type 3 or 5 bleeding occurring ≤12 months after the index PCI.²¹ Spontaneous MI was defined according to the fourth universal definition,²² and periprocedural MI (<48 h after PCI) was defined according to the 2013 Society for Cardiovascular Angiography and Interventions definition.²³ Death and ST were defined according to the Academic Research Consortium-2 definition.²⁴ Secondary endpoints included all-cause death, stroke (subclassified as ischemic, hemorrhagic, or unknown), all MIs, repeat revascularization, definite, probable, or possible ST, BARC Types 1–5 bleeding, and each individual component of the primary endpoint. All clinical endpoints were adjudicated by an independent clinical events committee (**Supplementary Appendix**). An independent Data and Safety Monitoring Board oversaw the safety of all patients during enrolment and follow-up, and was assigned the critical role of applying the stopping rule, which stated that study recruitment would have to be terminated if during active trial enrolment there were ≥3 cases of definite ST ≤3 months of the index PCI. Importantly, operators were obliged to report ST events ≤24 h, and this was monitored daily.

Retrospective Analysis by an Imaging Core Laboratory

QCA, Murray law-based quantitative flow ratio (μ QFR), and quantitative IVUS/OCT analyses were performed retrospectively by a central academic core laboratory

| Table 2. Lesion and Procedural Characteristics (n=101 Patients, n=117 Lesions) | |
|---|-----------|
| Access | |
| Femoral | 10 (9.9) |
| Radial | 91 (90.1) |
| Brachial | 0 (0.0) |
| Guidewire catheter size | |
| 5 Fr | 1 (1.0) |
| 6 Fr | 56 (55.4) |
| 7 Fr | 44 (43.6) |
| 8 Fr | 0 (0.0) |
| No. lesions treated per patient | |
| 1 | 88 (87.1) |
| 2 | 20 (19.8) |
| ≥3 | 3 (3.0) |
| No. stents used per patient | |
| 1 | 90 (89.1) |
| 2 | 11 (10.9) |
| ≥3 | 0 (0.0) |
| Total stent length per patient (mm) | 32.9±9.5 |
| Treated lesions (n=117) | |
| Left main coronary artery | 3 (2.6) |
| Left anterior descending coronary artery | 62 (53.0) |
| Left circumflex coronary artery | 20 (17.1) |
| Right coronary artery | 32 (27.4) |
| AHA lesion type | |
| A | 33 (28.2) |
| B1 | 37 (31.6) |
| B2 | 28 (23.9) |
| C | 19 (16.2) |
| Imaging for stent optimization | |
| Angiography alone | 0 (0.0) |
| IVUS | 76 (75.2) |
| OCT/OFDI | 25 (24.8) |

(Table 2 continued the next column.)

| | |
|---|---------------|
| Preprocedural lesion preparation | |
| Direct stenting | 29 (24.8) |
| Predilatation with non-compliant or compliant balloon | 67 (57.3) |
| Predilatation with cutting balloon | 6 (5.1) |
| Predilatation with scoring balloon | 9 (7.7) |
| Rotational atherectomy | 0 (0.0) |
| Directional coronary atherectomy | 0 (0.0) |
| Other | 6 (5.1) |
| Post-dilatation | 70 (59.8) |
| TIMI flow grade | |
| Preprocedural | |
| 0 | 10 (8.5) |
| 1 | 15 (12.8) |
| 2 | 34 (29.1) |
| 3 | 58 (49.6) |
| Postprocedural | |
| 0 | 0 (0.0) |
| 1 | 0 (0.0) |
| 2 | 0 (0.0) |
| 3 | 117 (100.0) |
| Per-stent characteristics (n=112 stents) | |
| SYNERGY stent used | 112 (100.0) |
| Stent length (mm) | 27.0±9.5 |
| Stent nominal diameter (mm) | 3.4±2.5 |
| Procedure time (min) | 69±27 |
| Duration of hospitalization (days) | 5.0 [2.0–9.0] |
| Timing of prasugrel loading dose (20 mg) | |
| After successful PCI procedure | 55 (54.5) |
| Before PCI | 34 (33.7) |
| Loading dose not given ^A | 12 (11.9) |
| Loading dose of aspirin on date of PCI | 49 (48.5) |
| On maintenance dose of aspirin on date of PCI | 52 (51.5) |

Data are given as the mean±SD, median [interquartile range], or n (%). ^APatients on a maintenance dose of prasugrel (3.75 mg) on the date of the PCI, so a loading dose was not given. AHA, American Heart Association; IVUS, intravascular ultrasound; OCT, optical coherence tomography; OFDI, optical frequency domain imaging; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

(CORRIB CORELAB, University of Galway, Galway, Ireland) using dedicated offline software (CAAS v8.2.4 [Pie Medical Imaging, Maastricht, Netherlands], AngioPlus Core [Pulse Medical Imaging Technology, Shanghai, China], and QIvus v3.1 [MEDIS, Leiden, Netherlands], respectively).

Statistical Analysis

Continuous variables are expressed as the mean±SD or as the median with interquartile range, as appropriate. Categorical variables are expressed as frequencies and percentages. Binomial exact calculation was used to calculate 95% confidence intervals (CIs). All analyses were performed using SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA).

Because this study was designed as a feasibility study, no formal sample size calculation was performed; however, as mentioned above, the stopping rule was implemented to ensure the safety of enrolled patients. Based on previous studies with similar designs, a sample of 200 CCS patients and 200 NSTEMI-ACS patients were to be enrolled. However,

in NSTEMI-ACS patients, if more than three (>3) patients experience definite ST following index procedure (day 0) till 12 months follow-up, or if more than two (>2) sudden death cases occur till 30 days follow-up, the trial would be stopped.

Results

Study Population

The study flowchart is shown in **Figure 1**. During the recruitment period, 795 patients with NSTEMI-ACS were treated by PCI, 101 (12.7%) of whom were enrolled in the study. As described above, enrolment was stopped at 101 patients due to the prolonged study duration and associated budgetary restrictions. After enrolment, 2 patients withdrew consent. The number of patients recruited and the total number of PCIs performed for NSTEMI-ACS during the enrolment period at each site are presented in **Supplementary Table 2**.

Table 3. Pre- and Post-Procedural QCA, Intravascular Imaging, and Quantitative Flow Ratio Analyses

| QCA | |
|---|-------------|
| Before procedure (n=96 lesions) | |
| Reference diameter (mm) | 2.79±0.61 |
| Minimum lumen diameter (mm) | 0.96±0.46 |
| DS (%) | 66.03±13.15 |
| Lesion length (mm) | 23.62±11.68 |
| After procedure (n=100 lesions) | |
| In-stent analysis | |
| Minimum lumen diameter (mm) | 2.61±0.49 |
| Reference diameter (mm) | 3.04±0.05 |
| DS (%) | 10.71±7.78 |
| Residual DS >20%, % (n) | 9 (9.0) |
| Segment length (mm) | 30.59±15.90 |
| In-segment analysis (including 5 mm proximal and distal to stent) | |
| Minimum lumen diameter (mm) | 2.30±0.51 |
| Reference diameter (mm) | 2.82±0.61 |
| DS (%) | 18.36±9.92 |
| Segment length (mm) | 39.07±15.44 |
| μ QFR (n=107 treated vessels) | |
| Before procedure | 0.79±0.21 |
| After procedure | 0.94±0.06 |
| Post-procedural μ QFR \geq 0.91 | 85 (79.4) |
| Post-procedural IVUS (n=74 lesions) | |
| Stent length (mm) | 27.93±9.43 |
| Mean stent area (mm ²) | 7.74±2.57 |
| Minimum stent area (mm ²) | 5.93±2.20 |
| Minimum stent area >5.5 mm ² | 36 (48.6) |
| Minimum lumen area (mm ²) | 5.89±2.22 |
| Minimum lumen diameter (mm) | 2.70±0.49 |
| Proximal reference area (mm ²) | 9.25±3.28 |
| Distal reference area (mm ²) | 6.79±3.08 |
| Stent expansion index (%) | 77.5±18.9 |
| Stent expansion index <80% | 45 (61) |
| UFR (n=74 lesions) | |
| Postprocedural UFR | 0.92±0.06 |
| Postprocedural UFR \geq 0.91 | 51 (66.2) |
| Post-procedural OCT (n=26 lesions) | |
| Stent length (mm) | 24.14±6.20 |
| Mean stent area (mm ²) | 8.62±1.91 |
| Minimum stent area (mm ²) | 6.64±1.77 |
| Minimum stent area >4.5 mm ² | 19 (76.0) |
| Minimum lumen area (mm ²) | 6.46±1.73 |
| Minimum lumen diameter (mm) | 2.84±0.40 |
| Proximal reference area (mm ²) | 9.25±3.46 |
| Distal reference area (mm ²) | 8.81±4.49 |
| Stent expansion index (%) | 77.1±18.5 |
| Stent expansion index <80% | 12 (46.0) |
| OFR (n=16 lesions) | |
| Postprocedural OFR | 0.95±0.03 |
| Postprocedural OFR \geq 0.91 | 13 (81.3) |

Data are mean±SD or n (%). DS, diameter stenosis; IVUS, intravascular ultrasound; OCT, optical coherence tomography; QCA, quantitative coronary angiography; μ QFR, Murray law-based quantitative flow ratio; OFR, optical coherence tomography-derived quantitative flow ratio; UFR, ultrasound-derived quantitative flow ratio.

Baseline Characteristics

Baseline patient characteristics are presented in **Table 1**. The mean age was 69.1±12.3 years and 75.1% of patients were male. The prevalence of diabetes was 27.7%, with 3.0% being insulin-dependent; 14.9% of patients had undergone prior PCI. The mean site-reported anatomical SYNTAX score was 7.9±4.7. The clinical indication for PCI was NSTEMI-ACS and unstable angina in 80.6% and 19.4% of patients, respectively. Overall, 36.6% of the cohort met the PRECISE DAPT criteria of HBR (\geq 25).²⁵

Lesion and Procedural Characteristics

Lesion and procedural characteristics are presented in **Table 2**. Radial access was used predominantly (90.1%); 89.1% of patients received 1 SYNERGY stent, and \geq 59.8% of lesions were American Heart Association Type A or B1. There were 2 periprocedural MIs according to biomarker elevations meeting the Society for Cardiovascular Angiography and Interventions definition, although neither patient had any symptoms or required any additional treatment after the PCI.

Although optimal stent deployment was a prerequisite of enrolment, 10.1% of stented lesions were retrospectively found to have a residual diameter stenosis \geq 20% by QCA (**Table 3**). Post-procedure Thrombolysis In Myocardial Infarction Grade 3 flow was achieved in all patients. Intravascular imaging was performed in 112 (99.1%) lesions; of these, 12 lesions could not be analyzed due to suboptimal image quality and a lack of visualization of the entire stent. A minimum stent area >5.5 mm² by IVUS or >4.5 mm² by OCT was achieved in 48.6% and 76.0% of lesions, respectively. IVUS and OCT revealed a stent expansion index <80% in 61.0% and 46.0% of lesions, respectively (**Table 3**). The mean post-procedure μ QFR was 0.92±0.06, with a μ QFR \geq 0.91 achieved in 81.7% of treated vessels (**Figure 2**).

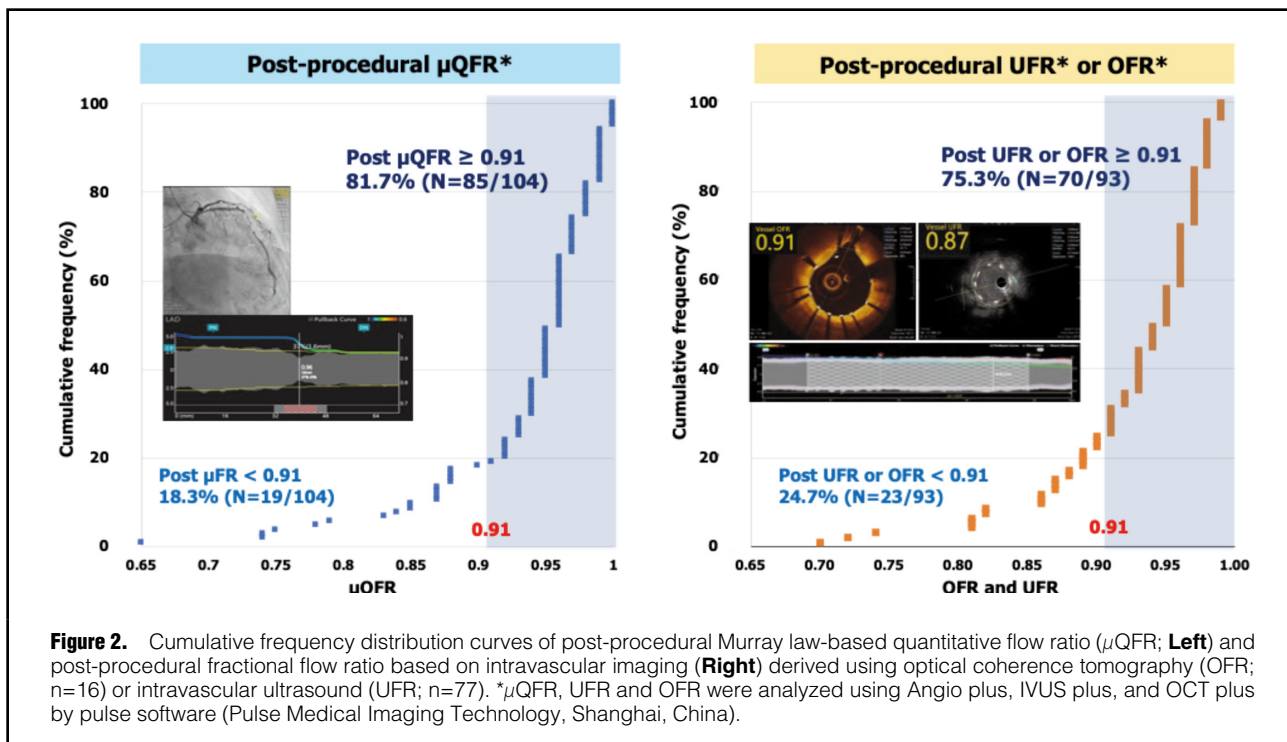
Clinical Outcomes at 1 Year

At 1 year, clinical follow-up was completed in 98% of patients (n=98). The primary ischemic composite endpoint occurred in 1 (1.0%) patient who died due to a cardiac cause (**Table 4**). This patient died suddenly at home 11 months after trial enrolment and although they were transported to hospital, resuscitation was unsuccessful. A detailed investigation into the cause of death, such as an autopsy, was not conducted, and therefore the exact cause of death remains unknown. However, the event adjudication committee classified it as a cardiac death.

The primary bleeding composite endpoint occurred in 2 (2.0%) patients. Both patients had BARC Type 3a bleeding. One patient had bleeding due to descending colon cancer, and the other had bleeding due to multiple gastric ulcers, which were later diagnosed as cancer.

Adherence to Antiplatelet Therapy up to 12 Months

Medication use at discharge and at the 12-month follow-up according to the presence or absence of clinical events is summarized in **Supplementary Table 3**. Adherence to antiplatelet agents is shown in **Figure 1** (detailed adherence at each follow-up period is provided in **Supplementary Table 4**). At the 12-month follow-up, 93 (94.9%) patients were on prasugrel monotherapy, whereas 3 (3.2%) were on DAPT (aspirin and prasugrel; n=3), 1 (1.0%) was on aspirin monotherapy, and 1 (1.0%) was on clopidogrel monotherapy. These changes to antiplatelet medication were made at the discretion of the investigators and were Type



3, Subtype I, and Subtype U non-adherence, as per the Non-adherence Academic Research Consortium (NARC) criteria.²⁶ One patient permanently discontinued all anti-platelet therapy because they were diagnosed with gastric cancer and multiple metastases after a BARC Type 3a bleeding event. This patient was treated conservatively and died 6 months after the index PCI. Due to the gastric cancer, the patient had difficulties with oral intake, leading to the oncologist permanently discontinuing prasugrel (NARC Type 3, Subtype M, Subtype R). In addition, 3 patients temporarily discontinued prasugrel: 1 patient switched from prasugrel to aspirin for 20 days due to surgery for descending colon cancer and resumed prasugrel postoperatively (NARC Type 2, Subtype M, Subtype R); another patient had a 1-day interruption for treatment on a vocal cord polyp (NARC Type 2, Subtype M); and the last patient had a 5-day interruption for a polypectomy (NARC Type 2, Subtype M) (**Supplementary Table 5**).

Discussion

In this select cohort of Japanese patients with NSTEMI-ACS and low anatomical disease complexity, low-dose prasugrel monotherapy was feasible and safe. At 1 year, the primary ischemic event rate was 1.0% and the primary bleeding event rate was 2.0% (two BARC Type 3a bleeding events).

The clinical feasibility and benefit of P2Y₁₂ inhibitor monotherapy after PCI has been investigated in many previous, and on-going, single-arm and randomized trials (**Table 5**). Salient observations from these studies are as follows.

- the dose of prasugrel was lower in the 3 Japanese studies (3.75 mg in ASET-Japan,¹⁷ STOPDAPT-3,^{27,28} and PREMIUM) than in the 4 non-Japanese studies (10 mg in ASETBrazil,²⁹ OPTICA,³⁰ LEGACY,³¹ and

NEOMINDSET³²)

- a specific type of stent was used in 4 studies,^{17,27–29} whereas in 3 studies stent selection was left to the operator's discretion
- aspirin use during PCI ranged from 21% (STOPDAPT-3) to 100% depending on the timing of enrolment and/or randomization (before or after PCI).

As expected, studies with post-PCI enrolment had high rates of aspirin use at the time of the procedure because it had already been prescribed as per local practice (e.g., in the ambulance). The absence of aspirin during the index PCI may increase procedure-related thrombotic events, especially when the dose of prasugrel monotherapy is as low as 3.75 mg (STOPDAPT-3^{27,28} and PREMIUM). The results of ongoing trials comparing P2Y₁₂ inhibitor monotherapy to DAPT, such as the NEOMINDSET (NCT04360720),³² PREMIUM (NCT05709626), and LEGACY (NCT05125276)³¹ trials, are awaited and will provide further clarity on the need for aspirin at the time of PCI, and its impact on ischemic and bleeding events.

One of the objectives at the time of the design of ASET-Japan was to provide preliminary event rates for a future large-scale study. Notwithstanding this, and despite the lack of preceding data, a randomized comparison between prasugrel monotherapy and STOPDAPT-3 has already been reported.²⁷ The STOPDAPT-3 trial enrolled 6,002 patients with ACS or HBR, randomizing them to prasugrel (3.75 mg/day) monotherapy or DAPT with aspirin (81–100 mg/day) and prasugrel (3.75 mg/day) following a 20-mg prasugrel loading dose in both groups. At 1 month after PCI, the aspirin-free strategy with low-dose prasugrel was comparable to the DAPT strategy for major bleeding (4.47% and 4.71%, respectively; hazard ratio 0.95; 95% CI 0.75–1.20; P_{superiority}=0.66) and non-inferior for cardiovascular events (4.12% and 3.69%, respectively; hazard

| Table 4. Clinical Outcomes | | |
|--|------------------|--------------------------|
| | No. patients (%) | 95% CI of event rate (%) |
| Primary ischemic endpoint: Composite of cardiac death, target-vessel spontaneous MI, or definite ST | 1 (1.0) | 0.02–5.3 |
| Cardiac death | 1 (1.0) | 0.02–5.3 |
| Target vessel spontaneous MI (48h after index PCI) | 0 (0) | 0.00–3.59 |
| Definite ST | 0 (0) | 0.00–3.59 |
| Primary bleeding endpoint: BARC type 3 or 5 bleeding | 2 (2.0) | 0.24–6.97 |
| Secondary endpoints | | |
| All-cause death | 2 (2.0) | 0.24–6.97 |
| Cardiac death | 1 (1.0) | 0.02–5.3 |
| Stroke | | |
| Ischemic | 1 (1.0) | 0.02–5.3 |
| Hemorrhagic | 0 (0) | 0.00–3.59 |
| Unknown | 0 (0) | 0.00–3.59 |
| MI | | |
| Target vessel-related | 0 (0) | 0.00–3.59 |
| Non-target vessel-related | 0 (0) | 0.00–3.59 |
| Bleeding: BARC Types 1–5 | | |
| Type 1 | 0 (0) | 0.00–3.59 |
| Type 2 | 1 (1.0) | 0.02–5.3 |
| Type 3a | 2 (2.0) | 0.24–6.97 |
| Type 3b | 0 (0) | 0.00–3.59 |
| Type 3c | 0 (0) | 0.00–3.59 |
| Type 4 | 0 (0) | 0.00–3.59 |
| Type 5a | 0 (0) | 0.00–3.59 |
| Type 5b | 0 (0) | 0.00–3.59 |
| All revascularizations | | |
| Target vessel revascularization | 0 (0) | 0.00–3.59 |
| Non-target vessel revascularization | 1 (1.0) | 0.02–5.3 |
| ST | | |
| Definite | 0 (0) | 0.00–3.59 |
| Probable | 0 (0) | 0.00–3.59 |

BARC, Bleeding Academic Research Consortium; CI, confidence interval; MI, myocardial infarction; PCI, percutaneous coronary intervention; ST, stent thrombosis.

ratio 1.12; 95% CI 0.87–1.45; $P_{\text{non-inferiority}}=0.01$).²⁷

Compared with the STOPDAPT-3 trial, event rates in the ASET-Japan NSTEMI-ACS study were lower, with rates of the composite endpoint (cardiovascular death, MI, and definite ST) of 0% vs 4.12%, respectively, and BARC Type 3 or 5 bleeding of 2.0% vs 4.55%, respectively. A plausible reason for these differences is the different populations enrolled in each study. In the ASET-Japan NSTEMI-ACS study, 36.0% of patients were classified as at HBR based on the PRECISE-DAPT score (Supplementary Figure).³³ Furthermore, in the ASET-Japan NSTEMI-ACS study, the proportion of patients with left main stem/left anterior descending artery lesions and multivessel disease was 55.6% and 10.9%, respectively; the mean SYNTAX score was as low as 7.9. In contrast, in STOPDAPT-3, 54.5% of patients were at HBR and 40% had multivessel disease;³⁴ therefore, compared with the ASET-Japan NSTEMI-ACS study population, patients in STOPDAPT-3 had relatively

simple lesions and less bleeding risk, emphasizing that the feasibility observed in this study only applies to selected NSTEMI-ACS populations. There was 1 BARC Type 3 bleeding event in a patient with colon cancer. In the setting of emergency procedures for patients such as those with ACS, preoperative patient assessment could be insufficient and may miss the presence of malignancy.

Of note, the enrollment for the present study stopped prematurely, primarily due to the impact of the global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus during the recruitment period. This delay subsequently resulted in financial constraints to completing the trial and eventually resulted in the premature termination of enrollment at a reduced sample size of 101 patients, instead of the initially planned 200 patients. The relatively small sample size may limit the sensitivity to detect a safety signal in low-frequency events such as early, late, or very late ST. Moreover, this reduction in sample size may affect the robustness and generalizability of our findings, specifically there may not be sufficient statistical power to detect rare complications (e.g., definite ST) that typically have incidence rates below 1%.³⁵ Although the results of the present study support the feasibility and preliminary safety of prasugrel monotherapy, caution is warranted in interpreting these outcomes, and larger, adequately powered trials are needed to confirm our exploratory observations.

Study Limitations

The present study has several limitations. First, in addition to the small sample size, as discussed above, this trial was a pilot study limited to Japanese patients with NSTEMI-ACS. As a result, the findings cannot be directly applied to other ethnic groups, such as Western populations usually treated with a 10-mg prasugrel maintenance dose. Second, the study was limited to patients with an anatomical SYNTAX score ≤ 23 . Although it was not mandated in the protocol, intravascular imaging was performed in all patients, reflecting the local practice in Japan, as is demonstrated in other Japanese studies, including STOPDAPT-3 (intravascular imaging use: 93%).³¹ The high usage of intravascular imaging is likely related to the optimal stent implantation, as well as the low ischemic event rate in this study. The inclusion was not specific for bleeding risk, resulting in the majority of patients (64% per PRECISE DAPT) being non-HBR.

Conclusions

In selected Japanese NSTEMI-ACS patients at low ischemic and bleeding risk, the use of low-dose prasugrel monotherapy and no aspirin after successful/optimal SYNERGY stent deployment was feasible and safe at the 1-year follow-up.

Acknowledgments

The authors sincerely thank the study participants.

Sources of Funding

ASET-Japan study is an investigator-initiated study supported by a grant provided by Boston Scientific, which was not involved in the study process, including site selection and management, data collection, and analysis. The study sponsor was Meditrix Research. The sponsor was not involved in study design, study operation, or writing of the manuscript.

Table 5. Overview of Antiplatelet Therapy Strategies in PCI Studies

| Study | Population | Timing of enrolment | Timing of randomization | Stent type | P2Y ₁₂ inhibitor monotherapy and loading/maintenance dose ^A | Aspirin at the time of procedure? |
|--|-----------------------------------|---------------------|-------------------------|-----------------------|--|---|
| Randomized trials | | | | | | |
| STOPDAPT-3 ^{27,28} (NCT04609111) | STEMI and NSTEMI-ACS/HBR patients | Before PCI | Before PCI | XIENCE | Prasugrel 20 mg/3.75 mg | The protocol does not allow aspirin after randomization, but 21% of patients were on chronic aspirin on the date of the procedure |
| PREMIUM (NCT05709626) | STEMI | Before PCI | Before PCI | SYNERGY | Prasugrel 20 mg/3.75 mg | Not specified in ClinicalTrials.gov |
| NEOMINDSET ³² (NCT04360720) | STEMI and NSTEMI-ACS | After PCI | After PCI | Latest-generation DES | Prasugrel 60 mg/10 mg or ticagrelor 180 mg/90 mg | Use any combination of antiplatelet agents permitted as per local practice |
| LEGACY ³¹ (NCT05125276) | NSTEMI-ACS | After PCI | After PCI | Not specified | The choice of a specific P2Y ₁₂ inhibitor was at the discretion of the treating physician | Complete omission of aspirin immediately after PCI |
| Single-arm studies | | | | | | |
| OPTICA ³⁰ (NCT04766437) | NSTEMI-ACS | Before PCI | Not applicable | New-generation DES | Prasugrel 60 mg/10 mg or ticagrelor 180 mg/90 mg | 93.3% of patients received loading or chronic aspirin |
| ASET-Japan NSTEMI-ACS (NCT05117866) | NSTEMI-ACS and CCS | After PCI | Not applicable | SYNERGY | Prasugrel 20 mg/3.75 mg | In NSTEMI-ACS population, 100% (101/101) of patients received aspirin on the day of or 1 day prior to PCI |
| ASET-Brazil ²⁹ (NCT03469856) | CCS | After PCI | Not applicable | SYNERGY | Prasugrel 60 mg/10 mg | 96.5% of patients received aspirin on the day of or 1 day prior to PCI |

^AIn the P2Y₁₂ inhibitor monotherapy arm for randomized studies. CCS, chronic coronary syndrome; HBR, high bleeding risk; NSTEMI-ACS, non-ST elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction.

Disclosures

K.K., Y. Morino, and Y. Ozaki are members of *Circulation Journal's* Editorial Team. T.M. has received honoraria from Boston Scientific and Daiichi Sankyo. G.N. has received honoraria from Abbott Medical, Boston Scientific, Terumo Corp., HeartFlow Japan, Daiichi Sankyo, OrbusNeich, Amgen, Shockwave Medical Japan, and Medtronic Japan. K.K. has received honoraria for lectures from Daiichi Sankyo and Boston Scientific. Y. Morino has received an unrestricted research grant and honoraria from Boston Scientific Japan and Daiichi Sankyo. M.N. has received honoraria from Daiichi Sankyo and Boston Scientific Japan and an endowed course supported by Boston Scientific Japan. A.T. received a grant to study overseas from Fukuda Foundation for Medical Technology. S.G. has received consultant fees from BIOSENSORS. K.T. has received honoraria for lectures from Boston Scientific and Daiichi Sankyo. P.W.S. is a consultant for Sahajanand Medical Technologies, Meril Life Sciences, Philips, and Xeltis, outside the submitted work. The other authors have no conflicts of interest to declare relevant to the contents of this paper.

IRB Information

This study was approved by the Certified Review Board at Fujita Health University (Reference no. CRB4180003).

Data Availability

The deidentified participant data will not be shared.

References

- Kimura K, Kimura T, Ishihara M, Nakagawa Y, Nakao K, Miyauchi K, et al. JCS 2018 Guideline on diagnosis and treatment of acute coronary syndrome. *Circ J* 2019; **83**: 1085–1196.
- Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023; **44**: 3720–3826.
- Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; **345**: 494–502.
- Baber U, Dangas G, Angiolillo DJ, Cohen DJ, Sharma SK, Nicolas J, et al. Ticagrelor alone vs. ticagrelor plus aspirin following percutaneous coronary intervention in patients with non-ST-segment elevation acute coronary syndromes: TWILIGHT-ACS. *Eur Heart J* 2020; **41**: 3533–3545.
- Vranckx P, Valgimigli M, Juni P, Hamm C, Steg PG, Heg D, et al. 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 multicentre, open-label, randomised superiority trial. *Lancet* 2018; **392**: 940–949.
- Kim BK, Hong SJ, Cho YH, Yun KH, Kim YH, Suh Y, et al. 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.
- Hahn JY, Song YB, Oh JH, Chun WJ, Park YH, Jang WJ, 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**: 2428–2437.
- Hong SJ, Lee SJ, Suh Y, Yun KH, Kang TS, Shin S, et al. Stopping aspirin within 1 month after stenting for ticagrelor monotherapy in acute coronary syndrome: The T-PASS randomized noninferiority trial. *Circulation* 2024; **149**: 562–573.
- Watanabe H, Domei T, Morimoto T, Natsuaki M, Shiomi H, Toyota T, et al. 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.
- Baber U, Dangas G, Angiolillo DJ, Cohen DJ, Sharma SK, Nicolas J, et al. Ticagrelor alone vs. ticagrelor plus aspirin following percutaneous coronary intervention in patients with non-ST-

- segment elevation acute coronary syndromes: TWILIGHT-ACS. *Eur Heart J* 2020; **41**: 3533–3545.
11. Ge Z, Kan J, Gao X, Raza A, Zhang JJ, Mohyidin BS, et al. Ticagrelor alone versus ticagrelor plus aspirin from Month 1 to Month 12 after percutaneous coronary intervention in patients with acute coronary syndromes (ULTIMATE-DAPT): A randomised, placebo-controlled, double-blind clinical trial. *Lancet* 2024; **403**: 1866–1878.
 12. Capranzano P, Moliterno D, Capodanno D. Aspirin-free antiplatelet strategies after percutaneous coronary interventions. *Eur Heart J* 2024; **45**: 572–585.
 13. Galli M, Laudani C, Occhipinti G, Spagnolo M, Gragnano F, D’Amario D, et al. P2Y₁₂ inhibitor monotherapy after short DAPT in acute coronary syndrome: A systematic review and meta-analysis. *Eur Heart J Cardiovasc Pharmacother* 2024; **10**: 588–598.
 14. Ishida M, Shimada R, Takahashi F, Niiyama M, Ishisone T, Matsumoto Y, et al. One-month dual antiplatelet therapy followed by P2Y₁₂ inhibitor monotherapy after biodegradable polymer drug-eluting stent implantation: The REIWA region-wide registry. *Circ J* 2024; **88**: 876–884.
 15. Small DS, Kothare P, Yuen E, Lachno DR, Li YG, Winters KJ, et al. The pharmacokinetics and pharmacodynamics of prasugrel in healthy Chinese, Japanese, and Korean subjects compared with healthy Caucasian subjects. *Eur J Clin Pharmacol* 2010; **66**: 127–135.
 16. Ogawa H, Isshiki T, Kimura T, Yokoi H, Nanto S, Takayama M, et al. Effects of *CYP2C19* allelic variants on inhibition of platelet aggregation and major adverse cardiovascular events in Japanese patients with acute coronary syndrome: The PRASFIT-ACS study. *J Cardiol* 2016; **68**: 29–36.
 17. Muramatsu T, Masuda S, Kotoku N, Kozuma K, Kawashima H, Ishibashi Y, et al. Prasugrel monotherapy after percutaneous coronary intervention with biodegradable-polymer platinum-chromium everolimus eluting stent for Japanese patients with chronic coronary syndrome (ASET-JAPAN). *Circ J* 2023; **87**: 857–865.
 18. Masuda S, Muramatsu T, Ishibashi Y, Kozuma K, Tanabe K, Nakatani S, et al. Reduced-dose prasugrel monotherapy without aspirin after PCI with the SYNERGY stent in East Asian patients presenting with chronic coronary syndromes or non-ST-elevation acute coronary syndromes: Rationale and design of the ASET Japan pilot study. *AsiaIntervention* 2023; **9**: 39–48.
 19. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. Clinical use of intracoronary imaging. Part 1: Guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. *Eur Heart J* 2018; **39**: 3281–3300.
 20. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials: A case for standardized definitions. *Circulation* 2007; **115**: 2344–2351.
 21. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the Bleeding Academic Research Consortium. *Circulation* 2011; **123**: 2736–2747.
 22. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). *Glob Heart* 2018; **13**: 305–338.
 23. Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: An expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol* 2013; **62**: 1563–1570.
 24. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, et al. Standardized end point definitions for coronary intervention trials: The Academic Research Consortium-2 consensus document. *Circulation* 2018; **137**: 2635–2650.
 25. Costa F, van Klaveren D, James S, Heg D, Raber L, Feres F, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: A pooled analysis of individual-patient datasets from clinical trials. *Lancet* 2017; **389**: 1025–1034.
 26. Valgimigli M, Garcia-Garcia HM, Vrijens B, Vranckx P, McFadden EP, Costa F, et al. Standardized classification and framework for reporting, interpreting, and analysing medication non-adherence in cardiovascular clinical trials: A consensus report from the Non-adherence Academic Research Consortium (NARC). *Eur Heart J* 2019; **40**: 2070–2085.
 27. Natsuaki M, Watanabe H, Morimoto T, Yamamoto K, Obayashi Y, Nishikawa R, et al. An aspirin-free versus dual antiplatelet strategy for coronary stenting: STOPDAPT-3 randomized trial. *Circulation* 2024; **149**: 585–600.
 28. Yamamoto K, Natsuaki M, Watanabe H, Morimoto T, Obayashi Y, Nishikawa R, et al. An aspirin-free strategy for patients undergoing staged percutaneous coronary intervention: A subgroup analysis of the STOPDAPT-3 trial. *Circ Rep* 2025; **7**: 451–462.
 29. Kogame N, Guimarães PO, Modolo R, De Martino F, Tinoco J, Ribeiro EE, et al. Aspirin-free prasugrel monotherapy following coronary artery stenting in patients with stable CAD: The ASET pilot study. *JACC Cardiovasc Interv* 2020; **13**: 2251–2262.
 30. van der Sangen NMR, Claessen BEPM, Küçük IT, den Hartog AW, Baan J, Beijl MAM, et al. Single antiplatelet therapy directly after percutaneous coronary intervention in non-ST-segment elevation acute coronary syndrome patients: The OPTICA study. *EuroIntervention* 2023; **19**: 63–72.
 31. van der Sangen NMR, Küçük IT, Sivanesan S, Appelman Y, Ten Berg JM, Verburg A, et al. Less bleeding by omitting aspirin in non-ST-segment elevation acute coronary syndrome patients: Rationale and design of the LEGACY study. *Am Heart J* 2023; **265**: 114–120.
 32. Guimaraes PO, Franken M, Tavares CAM, Silveira FS, Antunes MO, Bergo RR, et al. P2Y₁₂ inhibitor monotherapy versus dual antiplatelet therapy in patients with acute coronary syndromes undergoing coronary stenting: Rationale and design of the NEOMINDSET Trial. *EuroIntervention* 2023; **19**: e323–e329.
 33. Gragnano F, van Klaveren D, Heg D, Räber L, Krucoff MW, Raposeiras-Roubin S, et al. Derivation and validation of the PRECISE-HBR score to predict bleeding after percutaneous coronary intervention. *Circulation* 2025; **151**: 343–355.
 34. Urban P, Mehran R, Collieran R, Angiolillo DJ, Byrne RA, Capodanno D, et al. Defining high bleeding risk in patients undergoing percutaneous coronary intervention. *Circulation* 2019; **140**: 240–261.
 35. Watanabe H, Morimoto T, Natsuaki M, Yamamoto K, Obayashi Y, Ogita M, et al. 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.

Supplementary Files

Please find supplementary file(s);
<https://doi.org/10.1253/circj.CJ-25-0356>