Circulation Reports
Circ Rep 2022; **4:** 194–204
doi:10.1253/circrep.CR-22-0032

ORIGINAL ARTICLE
Cardiovascular Intervention

Changes in Antithrombotic Therapy Over Time and Durability of a Prasugrel WOEST-Like Regimen for Percutaneous Coronary Intervention Patients With Atrial Fibrillation

— Post Hoc Analysis of the PENDULUM Mono and PENDULUM Registries —

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Background: Previously published randomized atrial fibrillation (AF) percutaneous coronary intervention (PCI) trials have demonstrated the safety and efficacy of a WOEST-like regimen (oral anticoagulant [OAC] plus $P2Y_{12}$ inhibitor) in patients with AF PCI within 1 year. However, the efficacy of this regimen in real-world practice has not been fully confirmed, especially the efficacy of the WOEST-like regimen using the approved dose of prasugrel in Japan.

Methods and Results: This post hoc analysis included 186 and 220 patients from the PENDULUM mono and PENDULUM registries, respectively. Endpoints were the cumulative incidences of clinically relevant bleeding (CRB) and major adverse cardiac and cerebrovascular events (MACCE) at 12 months after PCI. Differences in the enrollment period led to an increase in OAC prescriptions (from 64.7% to 81.2%) and a reduction in the median duration of triple antithrombotic therapy (from 203.0 to 32.0 days) in the PENDULUM vs. PENDULUM mono registries, respectively. After adjustment by the inverse probability of treatment method, in patients with OAC, PENDULUM mono AF significantly reduced CRB without increasing MACCE compared with PENDULUM AF.

Conclusions: A WOEST-like regimen with prasugrel may reduce CRB, without increasing MACCE, in Japanese patients with AF and high bleeding risk undergoing PCI.

Key Words: Atrial fibrillation; Bleeding; Japan; Percutaneous coronary intervention; Prasugrel

The WOEST (What is the Optimal antiplatElet & Anticoagulant Therapy in Patients With Oral Anticoagulation and Coronary StenTing),[1] PIONEER AF-PCI (Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects with Atrial Fibrillation who Undergo Percutaneous Coronary Intervention),[2] RE-DUAL PCI (Randomized Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patients with Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention),[3] AUGUSTUS (a two-by-two factorial, randomized, controlled clinical trial),[4] and ENTRUST-AF PCI (Edoxaban Treatment Versus

Received March 29, 2022; accepted March 29, 2022; J-STAGE Advance Publication released online April 21, 2022 Time for primary review: 1 day

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Vitamin K Antagonist in Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention)[5] studies compared the safety and efficacy of dual antithrombotic therapy (WOEST-like regimen: concomitant use of an oral anticoagulant [OAC] and a $P2Y_{12}$ inhibitor) and triple antithrombotic therapy (TAT; concomitant use of an OAC, $P2Y_{12}$ inhibitor, and aspirin) in patients undergoing percutaneous coronary intervention (PCI) complicated by atrial fibrillation (AF).[6] These studies have established the efficacy and safety of the WOEST-like regimen and have led to its adoption in recent guidelines.[7] However, this evidence was obtained outside of Japan and, more importantly, does not include patients treated with the Japanese-specific dose of prasugrel (3.75 mg). Patients were enrolled in the PENDULUM[8] and PENDULUM mono[9] registries from 2015 to 2018, at a time when a large amount of evidence on antithrombotic therapy for AF PCI patients had been accumulated through randomized controlled trials (RCTs). Although the Japanese Society of Cardiology guidelines had not been revised at that time, such evidence may not only reflect physicians' prescriptions, but may also influence prescribing patterns. Therefore, analysis of AF PCI patients in the PENDULUM and PENDULUM mono registries may provide deep insights into the antithrombotic management of AF PCI in real-world practice. To clarify the impact of these prescription changes on outcomes, we analyzed the relationship between these changes and clinical outcomes. In particular, this study focused on the WOEST-like regimen with prasugrel.

Methods

Study Design

This was a post hoc analysis of 2 multicenter non-interventional prospective registration studies (PENDULUM mono[8] and PENDULUM[9]). Specifically, we conducted a post hoc subgroup analysis of patients from a previously published historical comparison of the PENDULUM mono and PENDULUM registries who presented with AF.[10]

The study protocols for the PENDULUM and PENDULUM mono studies were approved by the Ethics Committee of Toho University Ohashi Medical Center on 14 December 2015 (Reference code: 15–71) and 31 May 2017 (Reference code: H17006), respectively. Both studies were performed in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent. PENDULUM mono also complied with the Guidelines on Standards for the Conduct of Clinical Trials of Medicinal Products of the International Conference on Harmonization of Medicinal Products Regulations of the United States, Japan, and the European Union.[11] Both studies were registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry under the identifier numbers UMIN000028023 (PENDULUM mono) and UMIN000020332 (PENDULUM).

Study Population

Patients eligible for this analysis were AF patients from PENDULUM mono enrolled between June 2017 and December 2018 (197 of 1,222) and those from PENDULUM enrolled between December 2015 and July 2017 (538 of 6,422). The full inclusion and exclusion criteria for patients in the PENDULUM mono and PENDULUM registries have been described previously.[8,9] This was an intention-to-treat analysis, and patients were analyzed if they were prescribed prasugrel as the $P2Y_{12}$ inhibitor on the day of PCI (n=197 and 249 in PENDULUM mono and PENDULUM, respectively).

Outcomes

The endpoints were the cumulative incidences of clinically relevant bleeding (CRB; Bleeding Academic Research Consortium [BARC] Types 2, 3, and 5), major bleeding (BARC Types 3 and 5), and major adverse cardiac and cerebrovascular events (MACCE) 12 months after PCI. MACCE was defined as all-cause death, non-fatal myocardial infarction, non-fatal stroke, and stent thrombosis occurring 12 months after the index PCI.[12] Bleeding risk at the time of PCI was evaluated using the mean number of high bleeding risk (HBR) criteria.[13]

Statistical Analysis

A propensity score method was used to reduce the effect of treatment selection bias and potential confounders, and thus objectively compare data from the PENDULUM mono and PENDULUM registries. Age, body weight, estimated glomerular filtration rate, hemoglobin, direct OAC (DOAC) use at discharge, diabetes mellitus, acute coronary syndrome, platelet count, peripheral artery disease, gastrointestinal bleeding, non-steroidal anti-inflammatory drug/steroid use at discharge, ischemic stroke/transient ischemic attack/intracerebral hemorrhage, and complex PCI were the variables used in multivariate logistic regression to calculate the propensity scores. These variables were chosen based on the Japanese Circulation Society 2020 guideline and a previous report.[7,14] Background bias of patients enrolled in both studies was adjusted using the inverse probability treatment weighting (IPTW) method. Standardized mean differences were calculated for baseline characteristics to verify the confounders' balance between the 2 groups.

The dual antiplatelet therapy (DAPT) discontinuation rate was calculated based on patients who discontinued either aspirin or $P2Y_{12}$. If these patients restarted DAPT later, they were excluded from the analysis of DAPT discontinuation. The DAPT and TAT discontinuation rates were estimated using the Kaplan-Meier method.

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T.U., A. Hirayama, and Y.M. are members of *Circulation Reports*' Editorial Team.

The results of this study were presented in the Late Breaking Clinical Trials sessions at the 85th Annual Scientific Meeting of the Japanese Circulation Society web-based online meeting held March 26–28, 2021.

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ISSN-2434-0790

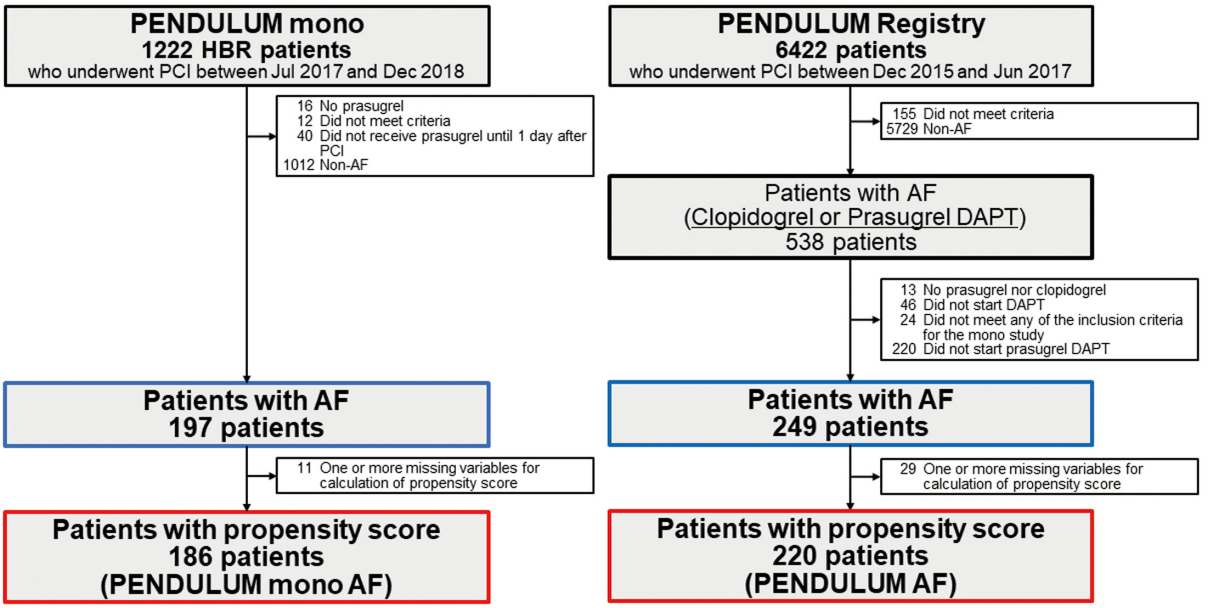

Figure 1. Patient disposition. Note, some patients met >1 exclusion criterion. AF, atrial fibrillation; DAPT, dual antiplatelet therapy; HBR, high bleeding risk; PCI, percutaneous coronary intervention.

The Kaplan-Meier method was used to calculate the cumulative incidences of CRB, major bleeding, and MACCE and the corresponding 95% confidence intervals (CIs) at 12 months before and after adjusting for background factors using the IPTW method. The Cox regression model was used to calculate hazard ratios (HRs) and 95% CIs. The risk of MACCE and BARC 2, 3, or 5 bleeding events according to antithrombotic treatment regimen was estimated using Cox regression models. Statistical significance was set at two-sided $P<0.05$. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patient Characteristics

Patient disposition is shown in **Figure 1**. Of the 1,222 patients in PENDULUM mono, 197 patients with AF were included in this study. Of these, 186 patients with propensity scores were evaluated (PENDULUM mono AF). Among the 6,422 patients enrolled in PENDULUM, 249 patients with AF were included in this study. Of these, 220 patients with propensity scores were evaluated (PENDULUM AF).

The characteristics of AF patients before propensity score weighting are presented in **Table 1**. Patient background characteristics after adjustment and standardized mean differences after adjustment are presented in **Supplementary Table 1**. The most common comorbidity was hypertension. In the PENDULUM mono AF and PENDULUM AF groups, 18.8% and 14.9% of patients, respectively, had a history of ischemic stroke and 4.6% and 2.8%, respectively, had a history of intracranial hemorrhage. Clinical manifestations included acute coronary syndrome in 26.4% and 31.7% of patients in the PENDULUM mono AF and PENDULUM AF groups, respectively. Mean±SD $CHADS_2$ scores before adjusting for background factors using the IPTW method were 2.7±1.2 and 2.4±1.2 in the PENDULUM mono AF and PENDULUM AF groups, respectively (**Supplementary Table 2**).

Changes in Antithrombotic Prescription

The percentage of patients without OACs at discharge decreased from 35.3% in the PENDULUM AF group to 18.8% in the PENDULUM mono AF group. This was accompanied by an increase in the prescription of DOACs in the PENDULUM AF group vs. the PENDULUM mono AF group (from 47.8% to 67.5%). In the case of antiplatelet administration, the mean duration of DAPT was 61.7 days in the PENDULUM mono AF group and 199.0 days in the PENDULUM AF group, whereas the median duration of DAPT therapy was 32 days in the PENDULUM mono AF group and 203 days in the PENDULUM AF group. The percentage of patients continuing DAPT reached 75% on Day 27 in the PENDULUM mono AF group and on Day 73 in the PENDULUM AF group. The percentage of patients continuing DAPT reached 50% on Day 35 in the PENDULUM mono AF group and on Day 211 in the PENDULUM AF group (**Supplementary Figure**).

Outcomes

The cumulative incidence of CRB (BARC Types 2, 3, and 5) at 12 months after PCI was 8.1% in the PENDULUM mono AF group and 9.2% in the PENDULUM AF group (HR 0.81; 95% CI 0.41–1.58; P=0.528; **Figure 2A**). The cumulative incidence of major bleeding (BARC Types 3 and 5) at 12 months after PCI was 6.4% in the PENDULUM mono AF group and 7.5% in the PENDULUM AF group (HR 0.77; 95% CI 0.37–1.64; P=0.502; **Figure 2B**). The

cumulative incidence of MACCE at 12 months after PCI did not tend to increase in the PENDULUM mono AF group and did not differ from that in the PENDULUM AF group (HR 0.88; 95% CI 0.41–1.90; P=0.752; **Figure 2C**).

Comparison Between PENDULUM Mono AF and PENDULUM AF Patients With and Without OAC Use

The incidences of CRB and MACCE in the PENDULUM mono AF and PENDULUM AF groups with and without anticoagulant use before IPTW adjustment are presented in **Table 2**. In both the PENDULUM mono AF and PENDULUM AF groups, the incidence of MACCE was two to threefold higher in patients who were treated with antiplatelet agents only. The incidence of CRB was high in the PENDULUM AF group with OAC, but higher in the PENDULUM mono AF group without OAC.

Differences in the Timing of Initiation of the WOEST-Like Regimen

The cumulative incidences of CRB, major bleeding, and MACCE after IPTW adjustment are shown in **Figure 3**. Bleeding events were numerically higher in the PENDULUM AF group, including both patients with and without OACs.

The cumulative incidences of CRB, major bleeding,

Table 1. Characteristics of Patients With AF Before Adjusting for Background Factors Using the Inverse Probability Treatment Weighting Method

Characteristic	PENDULUM mono AF (n=197)	PENDULUM AF (n=249)	Standardized mean difference
Age (years)	75.9±8.0	74.0±8.4	0.236
Male sex	148 (75.1)	192 (77.1)	−0.046
Body weight (kg)	60.6±11.6	62.7±13.0	−0.172
Hypertension	173 (87.8)	211 (84.7)	0.090
Hyperlipidemia	140 (71.1)	174 (69.9)	0.026
Diabetes mellitus	74 (37.6)	99 (39.8)	−0.045
Current smoker	19 (9.6)	49 (19.7)	−0.287
Heart failure	60 (30.5)	75 (30.1)	0.007
Peripheral arterial disease	16 (8.1)	14 (5.6)	0.099
Atrial fibrillation	197 (100.0)	249 (100.0)	–
Malignancy	16 (8.1)	26 (10.4)	−0.080
History			
Myocardial infarction	42 (21.3)	64 (25.7)	−0.103
PCI	74 (37.6)	96 (38.6)	−0.020
CABG	8 (4.1)	10 (4.0)	0.002
Ischemic stroke	37 (18.8)	37 (14.9)	0.105
ICH	9 (4.6)	7 (2.8)	0.093
Gastrointestinal bleeding	15 (7.6)	15 (6.0)	0.063
Clinical presentation			
Non-ACS	145 (73.6)	170 (68.3)	0.118
ACS	52 (26.4)	79 (31.7)	−0.118
Unstable angina	27 (13.7)	29 (11.6)	0.062
NSTEMI	14 (7.1)	15 (6.0)	0.044
STEMI	11 (5.6)	35 (14.1)	−0.288
Baseline laboratory values			
Hemoglobin (g/dL)	12.9±1.8	12.9±2.0	0.013
eGFR (mL/min/1.73 m^2)	50.8±20.9	54.4±22.4	−0.169
WBC (×10^9/L)	6.2±1.9	6.9±2.4	−0.319
Platelet count (×10^4/μL)	19.6±6.9	20.9±6.5	−0.201
Medication at discharge			
Prasugrel	196 (99.5)	226 (90.8)	0.414
3.75 mg	184 (93.4)	225 (90.4)	0.111
2.5 mg	12 (6.1)	1 (0.4)	0.325
Clopidogrel	0 (0.0)	21 (8.4)	−0.429
Aspirin	155 (78.7)	242 (97.2)	−0.593
Anticoagulant	160 (81.2)	161 (64.7)	0.379
DOAC	133 (67.5)	119 (47.8)	0.407
Warfarin	27 (13.7)	42 (16.9)	−0.088
PPI	174 (88.3)	219 (88.0)	0.012
NSAIDs (except aspirin)	12 (6.1)	17 (6.8)	−0.030
Steroids	8 (4.1)	14 (5.6)	−0.073

(**Table 1** continued the next page.)

Characteristic	PENDULUM mono AF (n=197)	PENDULUM AF (n=249)	Standardized mean difference
Angiographic features			
No. diseased vessels			
1	101 (51.3)	104 (41.8)	0.191
2	60 (30.5)	83 (33.3)	−0.062
3	34 (17.3)	57 (22.9)	−0.141
Left main trunk	8 (4.1)	17 (6.8)	−0.122
Procedural data			
Puncture site			
Femoral	38 (19.3)	76 (30.5)	−0.262
Brachial	11 (5.6)	12 (4.8)	0.034
Radial	147 (74.6)	164 (65.9)	0.192
Imaging-guided			
IVUS or OCT/OFDI	186 (94.4)	234 (94.0)	0.019
Complex PCI			
All	35 (17.8)	55 (22.1)	−0.108
≥3 stents	13 (6.6)	19 (7.6)	−0.040
≥3 treatment lesions	13 (6.6)	20 (8.0)	−0.055
Bifurcation with 2 stents	2 (1.0)	3 (1.2)	−0.018
Total stent length >60 mm	23 (11.7)	27 (10.8)	0.026
Chronic total occlusion	11 (5.6)	20 (8.0)	−0.097
HBR criteria			
HBR	193 (98.0)	224 (90.0)	0.341
OAC use	160 (81.2)	161 (64.7)	0.379
Severe CKD (eGFR <30 mL/min/1.73 m^2)	26 (13.2)	28 (11.2)	0.060
Severe anemia (Hb <11 g/dL)	32 (16.2)	48 (19.3)	−0.079
Platelet count <100×10^9/L	5 (2.5)	7 (2.8)	−0.017
Liver cirrhosis	0 (0.0)	1 (0.4)	−0.090
Malignancy	16 (8.1)	26 (10.4)	−0.080
Prior ICH	9 (4.6)	7 (2.8)	0.093
Age ≥75 years	126 (64.0)	119 (47.8)	0.330
Moderate CKD (eGFR 30–<60 mL/min/1.73 m^2)	101 (51.3)	112 (45.0)	0.126
Moderate anemia (Hb 11–13 g/dL in men, 11–12 g/dL in women)	49 (24.9)	57 (22.9)	0.046
NSAIDs or steroid use	17 (8.6)	26 (10.4)	−0.062
Prior ischemic stroke without ICH	33 (16.8)	34 (13.7)	0.086
Prior gastrointestinal bleeding	15 (7.6)	15 (6.0)	0.063

Unless indicated otherwise data are given as n (%) or as the mean±SD. ACS, acute coronary syndrome; AF, atrial fibrillation; CABG, coronary artery bypass graft; CKD, chronic kidney disease; DOAC, direct oral anticoagulant; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HBR, high bleeding risk; ICH, intracranial hemorrhage; IVUS, intravascular ultrasound; NSAIDs, non-steroidal anti-inflammatory drugs; NSTEMI, non-ST segment elevation myocardial infarction; OAC, oral anticoagulant; OCT, optical coherence tomography; OFDI, optical frequency domain imaging; PCI, percutaneous coronary intervention; PPI, proton-pump inhibitor; STEMI, ST-elevation myocardial infarction; WBC, white blood cell count.

and MAACE in patients treated with OACs from the PENDULUM mono AF and PENDULUM AF groups after IPTW adjustment are shown in **Figure 4**. In the PENDULUM mono AF group, the cumulative incidence of CRB was significantly lower than in the PENDULUM AF group without any increase in MACCE.

Cox Regression Analysis of Different Antithrombotic Regimens

Figure 5 shows the difference in outcomes by different antithrombotic regimens for AF patients who underwent PCI with the WOEST-like regimen as a reference. Although there was a difference between the WOEST-like and TAT regimes in terms of CRB, there were no statistically significant differences between the WOEST-like regimen and other formulations, although there was a tendency for the WOEST-like formulation to show benefits.

Discussion

The present multicenter study is the first to evaluate the use of the prasugrel maintenance dose marketed in Japan (3.75 mg) for Japanese patients with AF and HBR who underwent PCI. The frequency of AF PCI was 8.3%, consistent with the reported frequency in large PCI registries (CREDO-Kyoto).[14] In contrast, AF PCI was 16.1% in

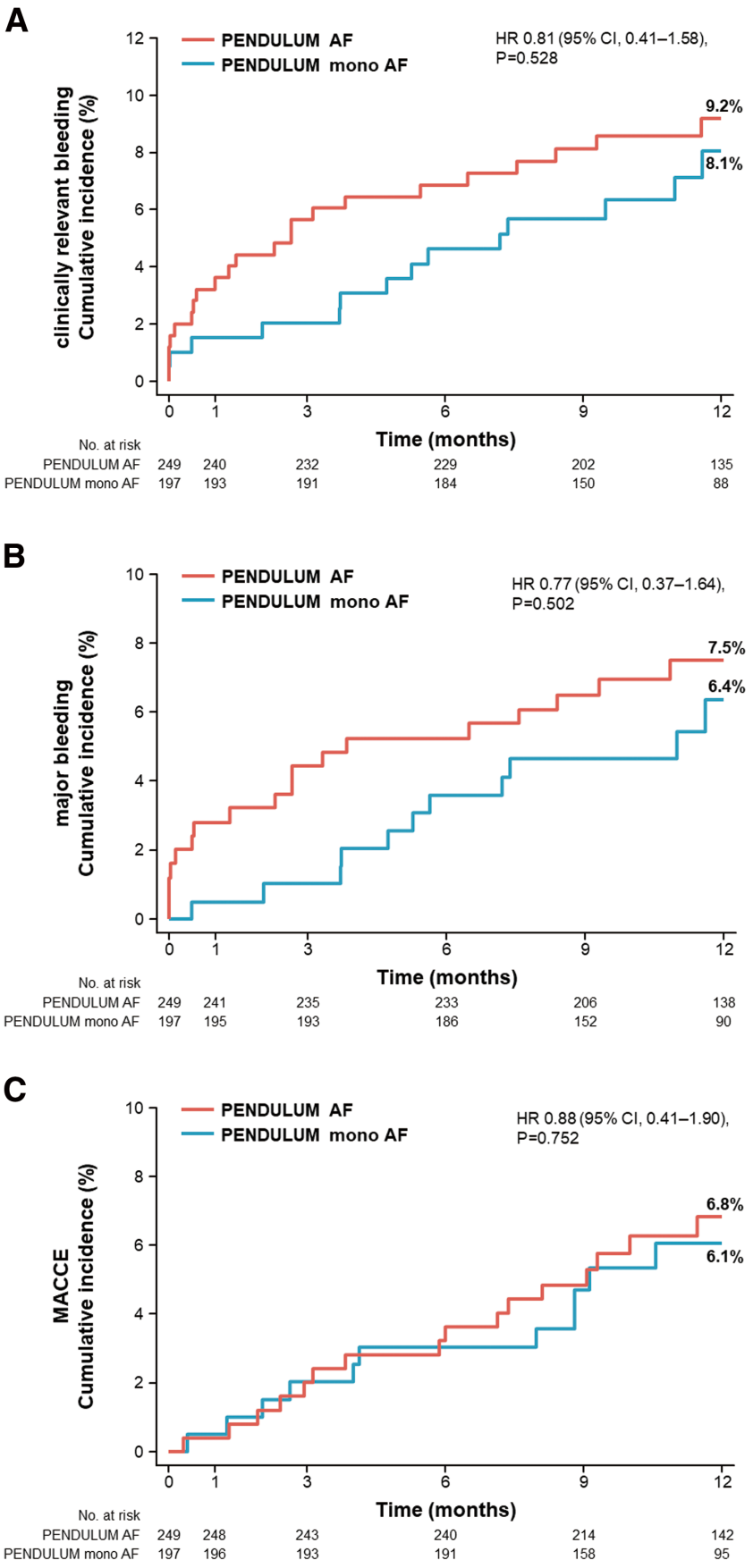

Figure 2. Cumulative incidence before inverse probability treatment weighting adjustment of (**A**) clinically relevant bleeding (Bleeding Academic Research Consortium [BARC] Types 2, 3, and 5), (**B**) major bleeding (BARC Types 3 and 5), and (**C**) major adverse cardiac and cerebrovascular events (MACCE). AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

Table 2. Comparison of the Incidence of CRB and MACCE in the PENDULUM Mono AF and PENDULUM AF Groups According to OAC Use Before Inverse Probability Treatment Weighting Adjustment

	With OAC			Without OAC		
	PENDULUM mono AF (n=160)	PENDULUM AF (n=161)	HR (95% CI)	PENDULUM mono AF (n=37)	PENDULUM AF (n=88)	HR (95% CI)
CRB	10 (6.9)	18 (11.2)	0.55 (0.25–1.19)	4 (10.8)	4 (4.5)	2.49 (0.62–10.00)
MACCE	7 (4.4)	6 (3.7)	1.19 (0.40–3.54)	4 (10.8)	10 (11.4)	0.98 (0.31–3.13)

Unless indicated otherwise data show the number of patients in each group with the percentage in parentheses. AF, atrial fibrillation; CI, confidence interval; CRB, clinically relevant bleeding; HR, hazard ratio; MACCE, major adverse cardiac and cerebrovascular events; OAC, oral anticoagulant.

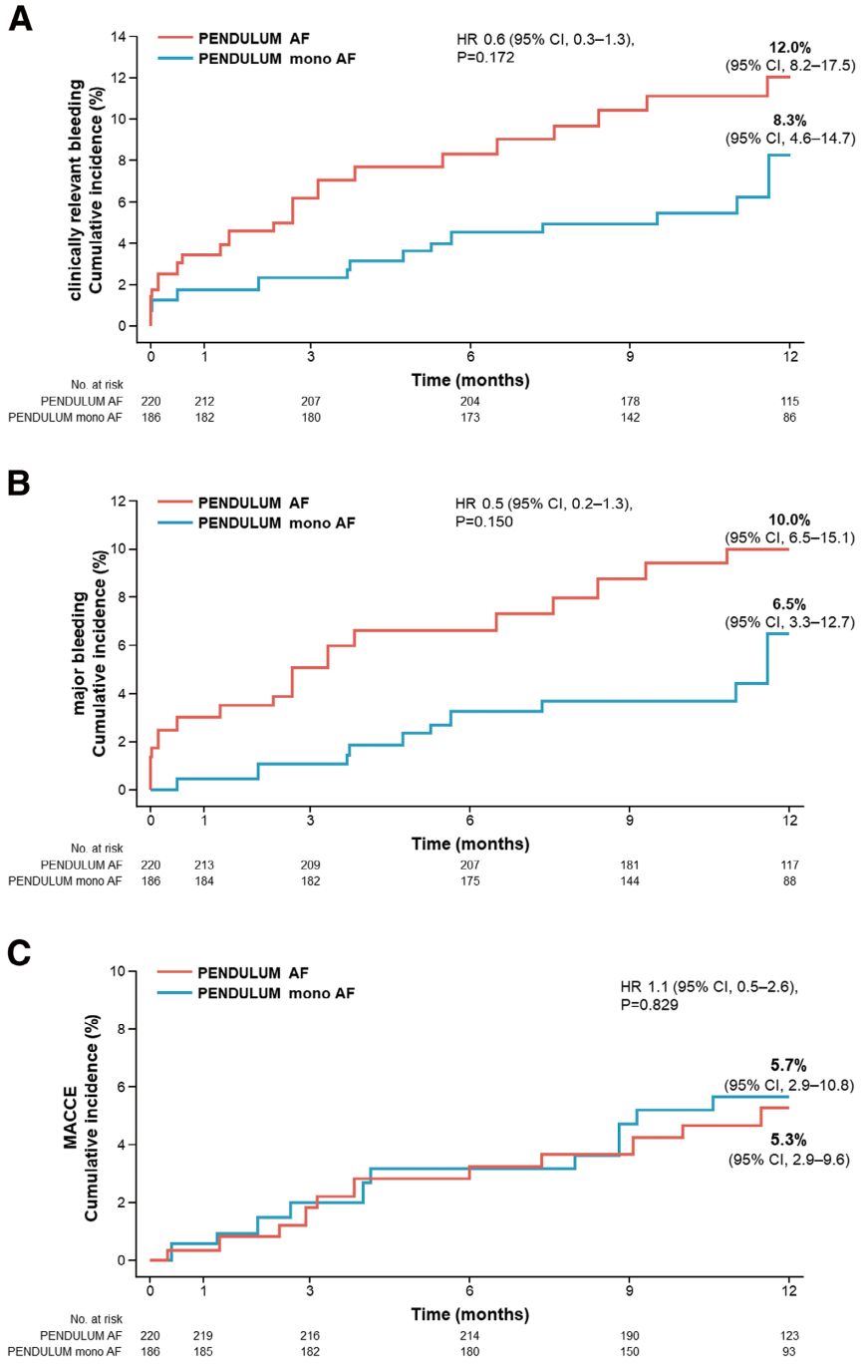

Figure 3. Cumulative incidence after inverse probability treatment weighting adjustment of (**A**) clinically relevant bleeding (Bleeding Academic Research Consortium [BARC] Types 2, 3, and 5), (**B**) major bleeding (BARC Types 3 and 5), and (**C**) major adverse cardiac and cerebrovascular events (MACCE). AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

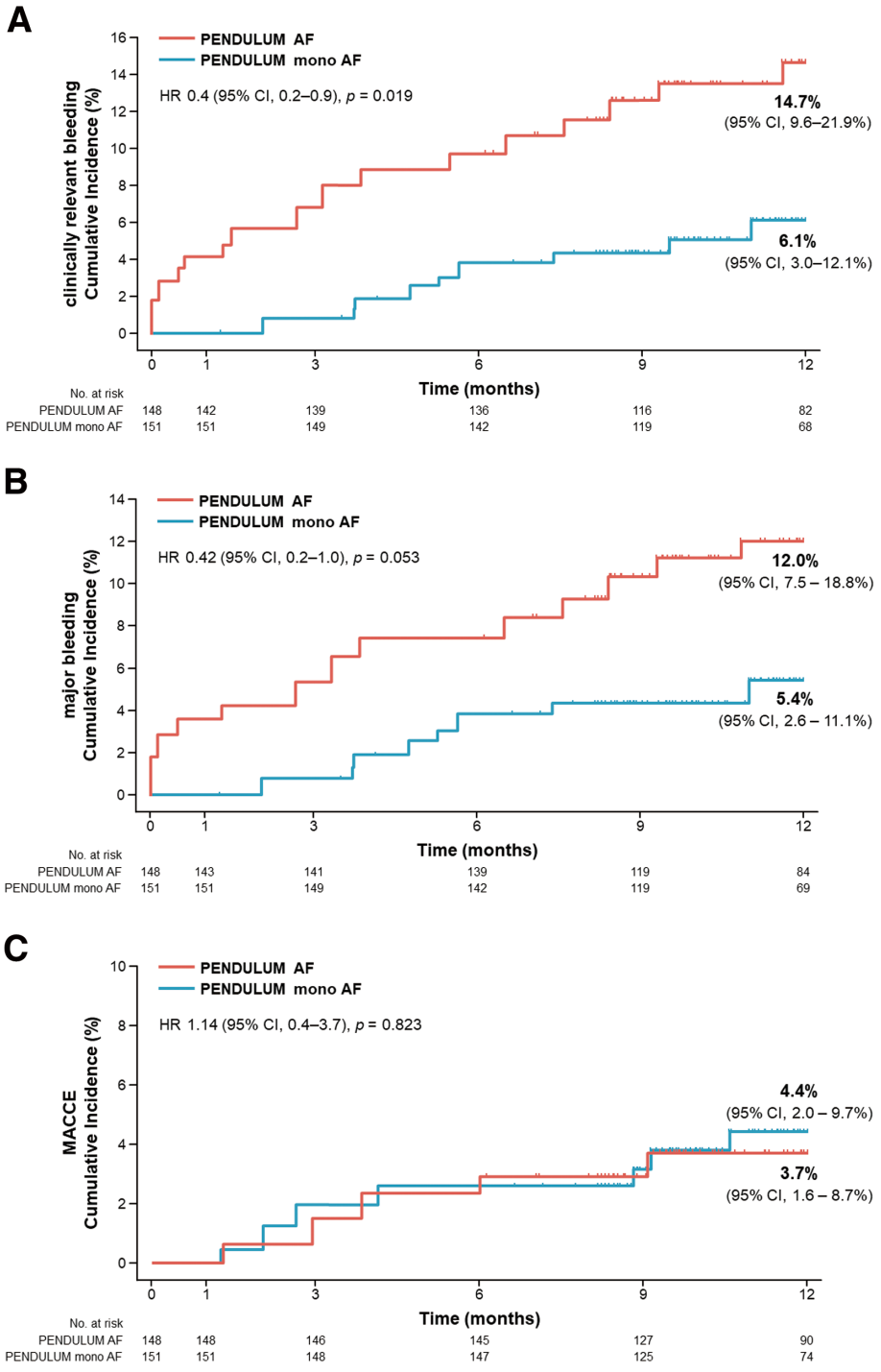

Figure 4. Cumulative incidence after inverse probability treatment weighting adjustment of (**A**) clinically relevant bleeding (Bleeding Academic Research Consortium [BARC] Types 2, 3, and 5), (**B**) major bleeding (BARC Types 3 and 5), and (**C**) major adverse cardiac and cerebrovascular events (MACCE) in patients taking oral anticoagulants. AF, atrial fibrillation; CI, confidence interval; HR, hazard ratio.

PENDULUM mono, which registered patients with HBR. This suggests that AF PCI is a major contributor to HBR in routine practice and is clinically significant. The uniqueness of this study is that patient enrollment occurred at a time when much of the evidence for AF PCI was accumulating. In addition, the prescription of antithrombotic therapy was left to the discretion of physicians. Therefore, antithrombotic therapy is presumed to vary over time, and studies on trends in prescribing may provide different antithrombotic outcomes for AF PCI. In particular, because

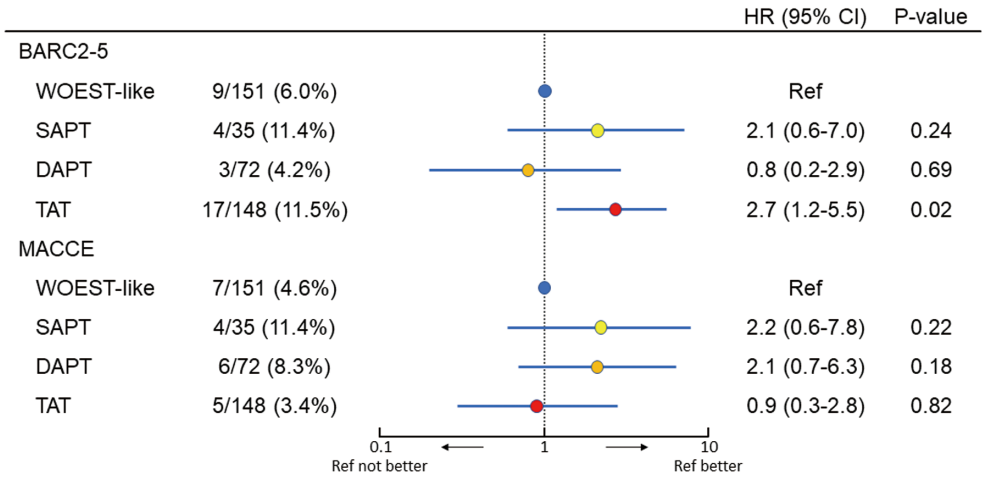

Figure 5. Cox regression model of different antithrombotic strategies using the WOEST-like regimen as a reference.[1–6] BARC2–5, Bleeding Academic Research Consortium Types 2–5; CI, confidence interval; DAPT, dual antiplatelet therapy; HR, hazard ratio; MACCE, major adverse cardiac and cerebrovascular events; SAPT, single antiplatelet therapy; TAT, triple antithrombotic therapy; WOEST-like regimen, concomitant use of an oral anticoagulant and $P2Y_{12}$ inhibitor.

PCI was contemporary PCI (imaging-guided, 94.4%; transradial approach, 72.1%; proton-pump inhibitor, 84.5%),[9] we suggest that the results observed in AF PCI may be largely related to antithrombotic therapy. Indeed, the antithrombotic regimen varied with time. In the PENDULUM registry, conducted prior to the PENDULUM mono AF study, OAC use for AF patients was less frequent and DOACs were prescribed less often, whereas TAT therapy was more prolonged. The incidence of major bleeding was higher than the incidence of MACCE in PENDULUM AF. The relationship between the major bleeding incidence rate and the MACCE incidence rate was opposite to that between major bleeding and MACCE in the entire PENDULUM registry.[12] This difference in the balance between bleeding and MACCE reminds us of the risk of bleeding events in AF PCI and suggests the clinical implication of reducing bleeding events in AF PCI.

Although the cumulative incidences of CRB and major bleeding were lower with PENDULUM mono AF than with PENDULUM AF, the differences were not statistically significant. This finding may be due to the small number of patients studied and the lack of power of the study compared with previously reported RCTs. It may also be explained by the inclusion of a substantial number of patients treated with antiplatelet agents alone in both groups. Importantly, the efficacy of the WOEST-like regimen and the impact of early termination of TAT therapy was clearly demonstrated in the comparison of PENDULUM AF and PENDULUM mono AF with OAC. Patients in the PENDULUM AF group remained on TAT for more than 200 days on average and had more bleeding events than those in the PENDULUM mono AF group (median TAT duration, 36 days), which is consistent with the guideline recommendations before they were revised in 2020.[15] Notably, in this study, the difference in CRB incidence between the PENDULUM mono AF and PENDULUM AF groups increased soon after PCI, which was similar to our previous report.[10]

However, there was no significant difference in the cumulative incidence of MACCE for PENDULUM mono AF compared with PENDULUM AF. This finding is consistent with previous AF PCI RCTs and important because this is the first study to show that a WOEST-like regimen can reduce the risk of bleeding without increasing the risk of MACCE in Japanese patients at the dose of 3.75 mg, which is approved in Japan.

Regarding the balance of bleeding and thrombosis risk, Cox regression analysis in the present study may suggest that a WOEST-like regimen with prasugrel is optimal. The reason for the lack of statistical significance is most likely insufficient power, but this finding is consistent with a previous large cohort study from Denmark[16] and subsequent AF PCI RCTs.[17,18] The results observed in this study are practical and meaningful for daily practice because the study used real-world data from the latest PCI procedures without any notable exclusions.

Study Limitations

The present study was not an RCT, but a matched trial of existing controls. For consistency with PENDULUM mono, the factors used to calculate propensity scores in the present study are unified with PENDULUM mono. OAC use at discharge was adjusted using the IPTW method and the comparison between the 2 groups was balanced; however, the rate of OAC prescription in this study differed between the groups. Therefore, there may be unadjusted confounders, such as ST-elevation myocardial infarction. Because of the observational study design, we could not thoroughly examine the benefits of the WOEST-like regimen with prasugrel. Furthermore, because of the study's observational nature, it was difficult to determine the optimal duration of TAT. Regarding adverse events, the possibility of evaluator bias cannot be excluded. Although the evaluators were the same, the pre-existing controlled trial design allowed the adverse event evaluators to know whether participants were in the PENDULUM mono AF or PENDULUM AF group. Event occurrences in this study were determined by physician judgment (diagnosis), so clinical events may have been underreported. Because this was a post hoc analysis,

it lacks statistical power. In addition, the sample size was not designed with the objective of detecting statistical differences between AF subgroups. This study did not focus on AF, and thus detailed data on the type of AF cannot be provided. Therefore, it would be necessary to conduct an analysis with more AF patients in a future RCT.

Conclusions

The findings of the present study suggest that a WOEST-like regimen with prasugrel may reduce BARC Types 2, 3, and 5 bleeding, without increasing MACCE, in Japanese patients with AF undergoing PCI.

Acknowledgments

The authors thank Michelle Belanger, MD, of Edanz (www.edanz.com) for providing medical writing assistance, which was funded by Daiichi Sankyo Co., Ltd.

Sources of Funding

This study was supported by Daiichi Sankyo Co., Ltd. (Tokyo, Japan). Daiichi Sankyo Co., Ltd. played a role in the design and conduct of the study; collection, management, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclosures

K. Nakao has received remuneration from Daiichi Sankyo Co., Ltd. K. Kadota has received remuneration from Daiichi Sankyo Co., Ltd. and Sanofi K.K. Y. Nakagawa has received remuneration from Bristol Myers Squibb K.K., Kowa Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Bayer Yakuhin Ltd., Sanofi K.K., Boston Scientific Corporation, and Abbott Medical Japan LLC., as well as research funding from Daiichi Sankyo Co., Ltd., Bayer Yakuhin Ltd., Sanofi K.K., Boston Scientific Corporation, and Abbott Medical Japan LLC. J. Shite has received remuneration from Daiichi Sankyo Co., Ltd., Nipro Corporation, Abbott Japan LLC., and Terumo Corporation. H. Yokoi has received remuneration and scholarship funds or donations from Daiichi Sankyo Co., Ltd. K. Kozuma has received remuneration and research funding from Daiichi Sankyo Co., Ltd. K. Tanabe has received remuneration from Daiichi Sankyo Co., Ltd., Sanofi K.K., AstraZeneca K.K., Abbott Medical Japan LLC., Boston Scientific Corporation, and Terumo Corporation. T. Akasaka has received remuneration from Abbot Medical Japan LCC. and Otsuka Pharmaceutical Co., Ltd., research funding from Daiichi Sankyo Co., Ltd., scholarship funds or donations from Abbot Medical Japan LCC., Nipro Corporation, and Terumo Corporation, and has personal relationships with Terumo Corporation. T. Shinke has received remuneration and research funding from Daiichi Sankyo Co., Ltd., Bayer Yakuhin Ltd., Bristol-Myers Squibb K.K., and Nippon Boehringer Ingelheim Co., Ltd. T. Ueno has received consultancy fees from Japan Medical Device Technology Co., Ltd. and Nipro Corporation. A. Hirayama has received remuneration from Daiichi Sankyo Co., Ltd., Bayer Yakuhin Ltd., and Takeda Pharmaceutical Co., Ltd. S. Uemura has received remuneration from Daiichi Sankyo Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Amgen Astellas BioPharma Co., Ltd., Abbot Medical Japan LLC., Sanofi K.K., Terumo Corporation, and Bayer Yakuhin Ltd., research funding from Daiichi Sankyo Co., Ltd., and scholarship funds or donations from Daiichi Sankyo Co., Ltd., Astellas Pharma Inc., Otsuka Pharmaceutical Co., Ltd., Goodman Co., Ltd., Shionogi Inc., Sumitomo Dainippon Pharma Co., Ltd., Boston Scientific Japan K.K., Kaken Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Taisho Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharmaceutical Co., Ltd., Japan Lifeline Co., Ltd., MSD K.K., Nipro Corporation, Actelion Pharmaceuticals Japan Ltd., Pfizer Japan Inc., Abbot Medical Japan LLC., Sanofi K.K., Terumo Corporation, and Bayer Yakuhin Ltd. A. Harada, T. Kuroda, and A. Takita are employees of Daiichi Sankyo Co., Ltd. Y. Murakami has received remuneration from SRD Co., Ltd. S. Saito has received consultancy fees from Japan Lifeline Co., Ltd. and Terumo Corporation, as well as remuneration from Daiichi Sankyo Co., Ltd., Abbott Medical Japan LLC., Boston Scientific Corporation, and Medtronic Japan Co., Ltd. M. Nakamura has received remuneration from Daiichi Sankyo Co., Ltd., Sanofi K.K., Terumo Corporation, and Bristol Myers Squibb K.K., and research funding from Daiichi Sankyo Co., Ltd., Sanofi K.K., and Bayer Yakuhin K.K. R. Iijima has no conflicts of interest to declare.

T. Ueno, A. Hirayama, and Y. Murakami are members of *Circulation Reports*' Editorial Team.

IRB Information

This is a post hoc analysis of data from the PENDULUM mono and PENDULUM registry studies conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent. Protocols for the PENDULUM registry and PENDULUM mono studies were approved by the Ethics Committee of Toho University Ohashi Medical Center on 14 December 2015 (Reference code: 15–71) and 31 May 2017 (Reference code: H17006), respectively. PENDULUM mono also complied with the Guidelines on Standards for the Conduct of Clinical Trials of Medicinal Products of the International Conference on Harmonization of Medicinal Products Regulations of the United States, Japan, and the European Union.

Data Availability

The deidentified participant data and study protocol will be shared on a request basis for up to 36 months after the publication of this article. Researchers who make the request should include a methodologically sound proposal on how the data will be used; the proposal may be reviewed by the responsible personnel at Daiichi Sankyo, and the data requestors will need to sign a data access agreement. Please contact the corresponding author directly to request data sharing.

Author Contributions

All authors provided substantial contributions to the conception or design of the study; or the acquisition, analysis, or interpretation of data; participated in drafting the manuscript or revising it critically for important intellectual content; provided final approval of the version to be published; and are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

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Supplementary Files

Please find supplementary file(s);
http://dx.doi.org/10.1253/circrep.CR-22-0032