ORIGINAL ARTICLE

Early Discontinuation of Aspirin after PCI in Low-Risk Acute Myocardial Infarction

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ABSTRACT

BACKGROUND

An appropriate duration of dual antiplatelet therapy after percutaneous coronary intervention for acute myocardial infarction that has been treated with guideline-recommended complete revascularization and a contemporary drug-eluting stent remains unclear.

METHODS

We conducted a multicenter, open-label, randomized trial at 40 European sites. Adults with acute myocardial infarction who had undergone successful complete revascularization within 7 days after the infarction and had subsequently completed 1 month of dual antiplatelet therapy with no ischemic or major bleeding events were randomly assigned to transition to a P2Y12 inhibitor as monotherapy or to continue dual antiplatelet therapy for an additional 11 months. The primary outcome was a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding (defined by the Bleeding Academic Research Consortium [BARC] as a bleeding event of type 3 or 5) at 11 months after randomization (tested for noninferiority with a margin of 1.25 percentage points). The main secondary outcome was BARC type 2, 3, or 5 bleeding (clinically relevant bleeding) at 11 months after randomization (tested for superiority).

RESULTS

Among the 2246 enrolled patients, 1942 underwent randomization: 961 to receive P2Y12-inhibitor monotherapy and 981 to continue dual antiplatelet therapy. A primary-outcome event occurred in 20 patients (2.1%) in the P2Y12-inhibitor monotherapy group and in 21 patients (2.2%) in the dual antiplatelet therapy group (difference, −0.09 percentage points; 95% confidence interval [CI], −1.39 to 1.20; P=0.02 for noninferiority). BARC type 2, 3, or 5 bleeding occurred in 2.6% of the patients in the P2Y12-inhibitor monotherapy group and in 5.6% of those in the dual antiplatelet therapy group (hazard ratio, 0.46; 95% CI, 0.29 to 0.75; P=0.002 for superiority). Stent thrombosis was infrequent, and the incidence was similar in the two groups. The incidence of serious adverse events appeared to be similar in the two groups.

CONCLUSIONS

Among low-risk patients with acute myocardial infarction who had undergone early complete revascularization and had completed 1 month of dual antiplatelet therapy without complications, P2Y12-inhibitor monotherapy was noninferior to continued dual antiplatelet therapy with respect to the occurrence of adverse cardiovascular and cerebrovascular events and resulted in a lower incidence of bleeding events. (Funded by MicroPort [France]; TARGET-FIRST ClinicalTrials.gov number, NCT04753749.)

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The advent of drug-eluting stents revolutionized the management of ischemic heart disease by substantially reducing the risk of restenosis. However, first-generation stents were associated with late thrombotic complications, which led to recommendations for prolonged dual antiplatelet therapy, particularly in patients with increased platelet activation and thrombotic risk associated with acute coronary syndrome.[1,2] Despite its effectiveness, dual antiplatelet therapy increases the risk of bleeding across the spectrum of patients with ischemic heart disease, including those who are not at high risk for bleeding. Observational studies, such as ADAPT-DES (Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents), have linked dual antiplatelet therapy to complications and death after percutaneous coronary intervention (PCI) in all-comer populations.[3,4] The introduction of newer-generation drug-eluting stents, with lower doses of drugs and improved biocompatibility, has markedly reduced the risk of late stent thrombosis; there has been a renewed interest in refining antiplatelet strategies, including earlier de-escalation to monotherapy on the basis of individual risk profiles.[5,6] Although abbreviated dual antiplatelet therapy has been studied in patients with a high bleeding risk,[7] in unselected patient populations,[8,9] and in East Asian patients with an acute coronary syndrome,[8,10-12] only a few trials have evaluated early discontinuation of aspirin specifically in patients with acute myocardial infarction.

It would be important to evaluate the effects of early discontinuation of aspirin in patients with acute myocardial infarction who had undergone early complete revascularization with a contemporary stent — particularly in cases in which the risk of bleeding may outweigh the residual ischemic risk, which could make antiplatelet de-escalation a beneficial option. Therefore, we conducted a multicenter, randomized trial in which early discontinuation of aspirin at 1 month was compared with standard dual antiplatelet therapy in low-risk patients with acute myocardial infarction who had been treated with PCI and a contemporary drug-eluting stent.

Methods

Trial Design and Oversight

TARGET-FIRST was a prospective, multicenter, open-label, randomized, controlled trial that was conducted at 40 sites across Europe. The trial design has been described previously.[13] The trial protocol (available with the full text of this article at NEJM.org) was designed by the steering committee, approved by applicable regulatory authorities and ethics committees, and conducted in accordance with the principles of the Declaration of Helsinki. The sponsor (MicroPort [France]) oversaw the conduct and monitoring of the trial, which were performed by a contract research organization (the Cardiovascular European Research Center [France]). The steering committee and the sponsor vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. The data analysis involved contributions from a contract research organization (Valos [Genoa, Italy]). The first author wrote the first draft of the manuscript, and the sponsor and all the authors agreed to submit the manuscript for publication. An independent data safety monitoring board periodically reviewed the safety data against the predefined stopping criteria. An independent clinical events committee adjudicated all the outcome events. A detailed list of the participating sites and committees is provided in the Supplementary Appendix (available at NEJM.org).

Trial Population

Patients were eligible for enrollment if they were at least 18 years of age, were hospitalized for ST-segment elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI), and had undergone complete revascularization with an abluminal biodegradable-polymer rapamycin-eluting stent (Firehawk Liberty, MicroPort) without complications. Complete revascularization was defined as treatment of all clinically significant lesions (as determined on angiography) during the index or staged (within 7 days after myocardial infarction) PCI procedure. The final decision regarding the lesion treatment strategy was at the investigator's discretion. Patients were excluded if they had a high risk of bleeding (i.e., if they had secondary fibrinolysis, were receiving oral anticoagulant therapy, had an estimated glomerular filtration rate of <30 ml per minute per 1.73 m^2 of body-surface area or were undergoing dialysis, had active bleeding, had a pre-PCI hemoglobin level of <13 g per deciliter [men] or <12 g per deciliter [women], had liver cirrhosis, had a history of bleeding diathesis, or had thrombocytopenia). Patients were also excluded if they had a high risk

of an ischemic event (i.e., if they had undergone complex PCI, had a chronic total occlusion, had left main coronary artery disease, had received stents that totaled >80 mm in length, or had severe calcification). Full inclusion and exclusion criteria are provided in Table S1 in the Supplementary Appendix.

RANDOMIZATION

After at least 30 days of dual antiplatelet therapy (aspirin plus a P2Y12 inhibitor), patients were evaluated. If they were free from ischemic or major bleeding events, they were randomly assigned in a 1:1 ratio to transition to P2Y12-inhibitor monotherapy (intervention) or to continue receiving dual antiplatelet therapy (control) for an additional 11 months. Randomization was performed with the use of a computer-generated sequence with random block sizes of two or four and stratified according to trial site, diabetes status, and type of myocardial infarction (STEMI or NSTEMI).

TREATMENTS AND FOLLOW-UP

The choice of P2Y12 inhibitor (prasugrel, ticagrelor, or clopidogrel) was determined by the investigator and aligned with the guidelines of the European Society of Cardiology and local practice. Investigators were encouraged to use a potent P2Y12 inhibitor (prasugrel or ticagrelor) and to use the same P2Y12 inhibitor throughout the trial unless there was a clinical reason to switch. Follow-up assessments were conducted by means of a telephone call or office visit at 6 months after PCI and by a mandatory on-site visit at 12 months after PCI. Information regarding patient-reported adherence to the assigned therapy, concomitant medications, and adverse events were documented at each visit. Nonadherence to the assigned therapy was defined according to the criteria listed in Table S2.

OUTCOMES

The primary outcome was net adverse clinical and cerebrovascular events, defined as a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding (defined by the Bleeding Academic Research Consortium [BARC] as a bleeding event of type 3 or 5)[14] at 11 months after randomization. The main secondary outcome was BARC type 2, 3, or 5 bleeding (clinically relevant bleeding, which ranges from overt bleeding for which medical attention is warranted [type 2] to fatal bleeding [type 5]) at 11 months after randomization. Key additional prespecified secondary outcomes were the individual components of the primary and main secondary outcomes; a device-oriented outcome, defined as a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven revascularization of the target lesion; a patient-oriented outcome, defined as a composite of death from any cause, myocardial infarction, definite or probable stent thrombosis (according to Academic Research Consortium criteria[14]), stroke, ischemia-driven repeat revascularization, or BARC type 2, 3, or 5 bleeding; major adverse cardiovascular events, defined as a composite of death from cardiovascular causes, myocardial infarction, or ischemia-driven revascularization of the target vessel; and individual components of these additional secondary outcomes. Serious adverse events were also recorded. A description of the outcomes is provided in Table S3.

STATISTICAL ANALYSIS

The sample size was calculated under the assumption that a primary-outcome event would occur in 3.5% of the patients in the dual antiplatelet therapy group and in 2.5% of those in the P2Y12-inhibitor monotherapy group; a sample of 1908 randomly assigned patients would provide the trial with 80% power at a one-sided alpha level of 2.5%. The planned enrollment of 2246 patients accounted for expected attrition. The anticipated incidence of a primary-outcome event was informed by previous randomized trials in which abbreviated dual antiplatelet therapy was investigated in patients with low-risk acute coronary syndrome,[8,10,15] as well as by internal data derived from feasibility assessments at participating sites.

The primary analysis evaluated whether P2Y12-inhibitor monotherapy was noninferior to dual antiplatelet therapy with respect to net adverse clinical and cerebrovascular events at 11 months after randomization. Noninferiority was defined as an absolute difference between the groups in the incidence of events not exceeding 1.25 percentage points; noninferiority would be concluded if the upper boundary of the two-sided 95% confidence interval was less than 1.25 percentage points.

If noninferiority for the primary outcome was shown, then superiority for BARC type 2, 3, or 5 bleeding (the main secondary outcome) would be tested by means of a hierarchical approach with

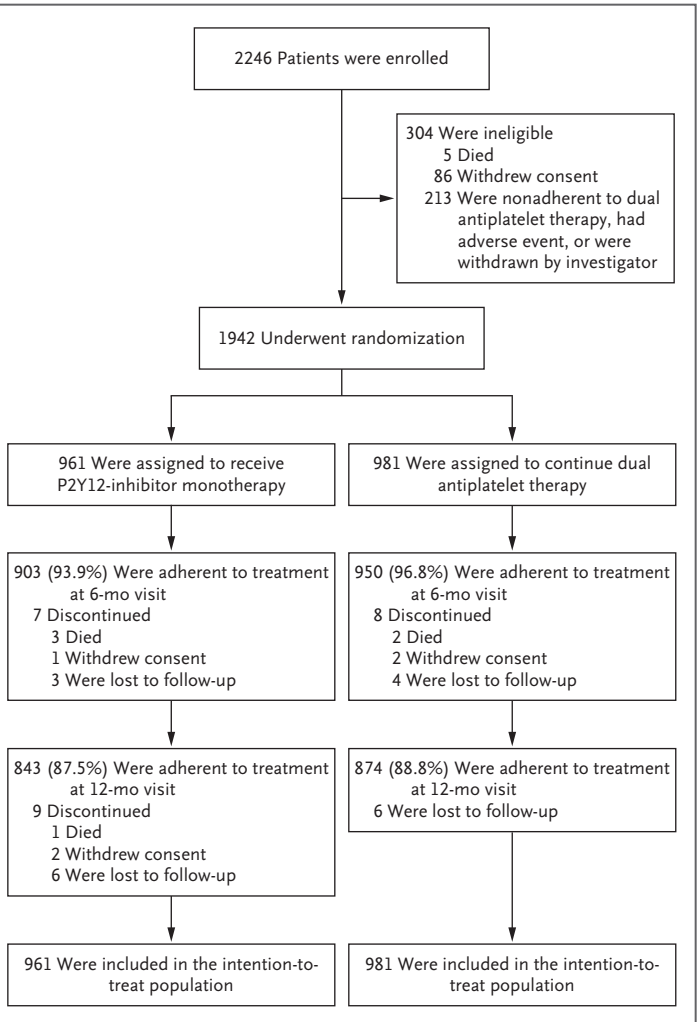


Figure 1. Enrollment, Randomization, and Follow-up.

The percentage of patients who adhered to the assigned treatment was calculated with the use of Kaplan–Meier estimates based on the criteria listed in Table S2.

the use of a Cox proportional-hazards model and reported as hazard ratios and 95% confidence intervals. Adjustment for multiplicity was addressed by application of the prespecified hierarchical testing strategy.

Cumulative incidence functions were estimated with the use of the Kaplan–Meier method or, when applicable, a competing-risks approach that accounted for death as a competing event. Missing data were handled by censoring at the time of last known contact. No interim analyses were planned. Between-group differences with respect to the primary outcome were calculated with the use of the Com-Nougue method with Greenwood's variance.[16]

The intention-to-treat population included all the patients who had undergone randomization; patients were assessed according to their assigned treatment group. The per-protocol population consisted of patients who had undergone randomization and had had no major protocol deviations that could have affected the primary or main secondary outcomes, including adherence to the assigned therapy. The as-treated population included all the patients who had undergone randomization and were assessed according to the treatment they had actually received. The primary analysis was performed in the intention-to-treat population. The per-protocol and as-treated analyses were prespecified in the statistical analysis plan (which is included with the protocol) as sensitivity analyses. Subgroup analyses of the primary and main secondary outcomes were also prespecified and were evaluated with the use of interaction terms in Cox proportional-hazards models. All analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

TRIAL POPULATION

From March 2021 through March 2024, a total of 2246 patients were enrolled at 40 European sites. One month after PCI, 1942 of these patients (86.5%) underwent randomization: 961 to the P2Y12-inhibitor monotherapy group and 981 to the dual antiplatelet therapy group (Fig. 1). The final patient underwent randomization in April 2024, and the database was locked in May 2025. Details regarding patients who did not undergo randomization, major protocol deviations, treatment adherence, and follow-up are provided in Tables S4 through S8. The median time from PCI to randomization was 37 days in each group.

Overall, the mean (±SD) age of the patients who had undergone randomization was 61.0±10.6 years; 78.4% of the patients were men and 21.6% were women (Table 1). A total of 14.5% of the patients had diabetes mellitus, 38.7% had hypertension, and 27.8% had hypercholesterolemia; 50.4% of the patients were hospitalized with STEMI, and 49.6% with NSTEMI. The representativeness of the trial population is presented in Table S9. Procedural characteristics appeared to be similar in the two groups, with a median of

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline (Intention-to-Treat Population).*

Characteristic	P2Y12-Inhibitor Monotherapy (N=961)	Dual Antiplatelet Therapy (N=981)
Age — yr	61.0±10.8	61.0±10.5
Female sex — no. (%)	223 (23.2)	197 (20.1)
Body-mass index†	26.7±4.7	27.4±4.4
Current smoker — no./total no. (%)	402/959 (41.9)	410/981 (41.8)
Diabetes mellitus — no./total no (%)	135/961 (14.0)	146/981 (14.9)
Type 1, treated with insulin	10/959 (1.0)	6/981 (0.6)
Type 2, treated with insulin	26/959 (2.7)	27/981 (2.8)
Hypertension — no. (%)	367 (38.2)	384 (39.1)
Hypercholesterolemia — no. (%)	271 (28.2)	269 (27.4)
Chronic kidney disease — no. (%)	15 (1.6)	21 (2.1)
Family history of coronary disease — no./total no. (%)	260/949 (27.4)	243/970 (25.1)
Peripheral vascular disease — no. (%)	34 (3.5)	25 (2.5)
Previous myocardial infarction or previous PCI — no./total no. (%)	57/959 (5.9)	67/975 (6.9)
Previous cerebrovascular accident — no. (%)	15 (1.6)	20 (2.0)
Left ventricular ejection fraction <40% — no./total no. (%)	25/704 (3.6)	33/702 (4.7)
Indication for PCI — no. (%)		
STEMI	482 (50.2)	497 (50.7)
NSTEMI	479 (49.8)	484 (49.3)
Antiplatelet medication at randomization		
Duration of dual antiplatelet therapy after PCI — days	37.0±4.6	37.0±4.6
P2Y12 inhibitor at 1-month visit — no./total no. (%)		
Ticagrelor	706/961 (73.5)	731/980 (74.6)
Prasugrel	209/961 (21.7)	196/980 (20.0)
Clopidogrel	46/961 (4.8)	53/980 (5.4)

* Plus–minus values are means ±SD. NSTEMI denotes non–ST-segment elevation myocardial infarction, PCI percutaneous coronary intervention, and STEMI ST-segment elevation myocardial infarction.
† The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were available for 949 patients in the P2Y12-inhibitor monotherapy group and for 967 patients in the dual antiplatelet therapy group.

1 implanted stent per patient (interquartile range, 1 to 2) in each group and a mean (±SD) total stent length of 30.3±16.2 mm in the P2Y12-inhibitor monotherapy group and 30.8±16.5 mm in the dual antiplatelet therapy group. Additional procedural characteristics are shown in Table S10. Complete revascularization was achieved in 99.9% of the patients. At the time of randomization, ticagrelor was the most commonly prescribed P2Y12 inhibitor (in 74.0% of the patients), followed by prasugrel (in 20.9%) and clopidogrel (in 5.1%). Cardiovascular therapies at the time of randomization included statins in 97.0% of the patients, beta-blockers in 79.1%, and angiotensin-converting–enzyme inhibitors or angiotensin-receptor blockers in 76.7% (Table S11).

TREATMENT ADHERENCE

Overall, 87.5% of the patients in the P2Y12-inhibitor monotherapy group and 88.8% of those in the dual antiplatelet therapy group were adherent to the assigned antiplatelet regimen at 11 months (Fig. S2 and Table S6). Adherence to treatment was more than 95% for at least 6 months in the P2Y12-inhibitor monotherapy group and for at least 10 months in the dual antiplatelet therapy group. Reasons for nonadherence are provided in Table S12.

PRIMARY AND SECONDARY OUTCOMES

Death from any cause, myocardial infarction, stent thrombosis, stroke, or BARC type 3 or 5 bleeding (the composite primary outcome) occurred in 20 patients (2.1%; 95% confidence interval [CI], 1.4 to 3.2) in the P2Y12-inhibitor monotherapy group and in 21 patients (2.2%; 95% CI, 1.4 to 3.3) in the dual antiplatelet therapy group. The between-group difference was −0.09 percentage points (95% CI, −1.39 to 1.20), which met the criterion for noninferiority (P=0.02) (Fig. 2).

The incidence of death from any cause was 0.4% in the P2Y12-inhibitor monotherapy group and 0.2% in the dual antiplatelet therapy group (hazard ratio, 2.04; 95% CI, 0.37 to 11.14). Myocardial infarction occurred in 0.7% of the patients in the P2Y12-inhibitor monotherapy group and in 1.1% of those in the dual antiplatelet therapy group (hazard ratio, 0.72; 95% CI, 0.27 to 1.88). Definite or probable stent thrombosis occurred in 0.1% of the patients in the P2Y12-inhibitor monotherapy group and in no patients in the dual antiplatelet therapy group. Stroke was reported in 0.3% and 0.2% of the patients in the respective groups (hazard ratio, 1.53; 95% CI, 0.26 to 9.18). BARC type 3 or 5 bleeding occurred in 0.7% of the patients in each group (hazard ratio, 1.02; 95% CI, 0.36 to 2.91) (Table 2). The results of prespecified subgroup analyses are shown in Figure 3 and Table S13, and the results of a post hoc analysis of the primary outcome involving the patients at the highest enrolling sites are shown in Table S14.

BARC type 2, 3, or 5 bleeding (the main secondary outcome), which was tested for superiority, occurred in 25 patients (2.6%; 95% CI, 1.8 to 3.9) in the P2Y12-inhibitor monotherapy group and in 54 patients (5.6%; 95% CI, 4.3 to 7.2) in the dual antiplatelet therapy group. The hazard ratio was 0.46 (95% CI, 0.29 to 0.75; P=0.002 for superiority) (Table 2 and Fig. 2).

OTHER SECONDARY OUTCOMES

Death from cardiovascular causes occurred in 3 patients (0.3%) in the P2Y12-inhibitor monotherapy group and in 2 patients (0.2%) in the dual antiplatelet therapy group. Death from any cause, myocardial infarction, stent thrombosis, stroke, ischemia-driven repeat revascularization, or BARC type 2, 3, or 5 bleeding (the patient-oriented composite outcome) occurred in 43 patients (4.5%) in the P2Y12-inhibitor monotherapy group and in 71 patients (7.2%) in the dual antiplatelet therapy group. Major adverse cardiovascular events — a composite of death from cardiovascular causes, myocardial infarction, or ischemia-driven revascularization of the target vessel — occurred in 1.6% of the patients in each group. Death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven revascularization of the target lesion (the device-oriented composite outcome) occurred in 10 patients (1.1%) in the P2Y12-inhibitor monotherapy group and in 8 patients (0.8%) in the dual antiplatelet therapy group. Ischemia-driven revascularization of the target vessel occurred in 0.7% of the patients in each group (Table 2). The results of analyses of other secondary outcomes are provided in Tables S15 and S16.

SAFETY

A total of 144 serious adverse events were reported in 108 patients (11.2%) in the P2Y12-inhibitor monotherapy group, and 157 serious adverse events were reported in 122 patients (12.4%) in the dual antiplatelet therapy group. A list of all serious adverse events that were reported on or after the randomization visit is shown in Table S17.

DISCUSSION

The TARGET-FIRST trial was a multicenter, randomized trial that evaluated whether early discontinuation of aspirin (at 1 month) and receipt of P2Y12-inhibitor monotherapy was noninferior to dual antiplatelet therapy for a period of 11 months in patients with acute myocardial infarction who had undergone early complete revascularization with a contemporary drug-eluting stent and were at low risk for ischemic and bleeding events. Our trial showed that P2Y12-inhibitor monotherapy was noninferior to continued dual antiplatelet therapy with respect to a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or BARC type 3 or 5 bleeding at 1 year (11 months after randomization) (the primary outcome). In addition, the incidence of bleeding complications (BARC type 2, 3, or 5 bleeding) was significantly lower (by 54%) with P2Y12-inhibitor monotherapy than with dual antiplatelet therapy, and this finding appeared to be consistent across most prespecified subgroups.

Earlier trials that evaluated an abbreviated dura-

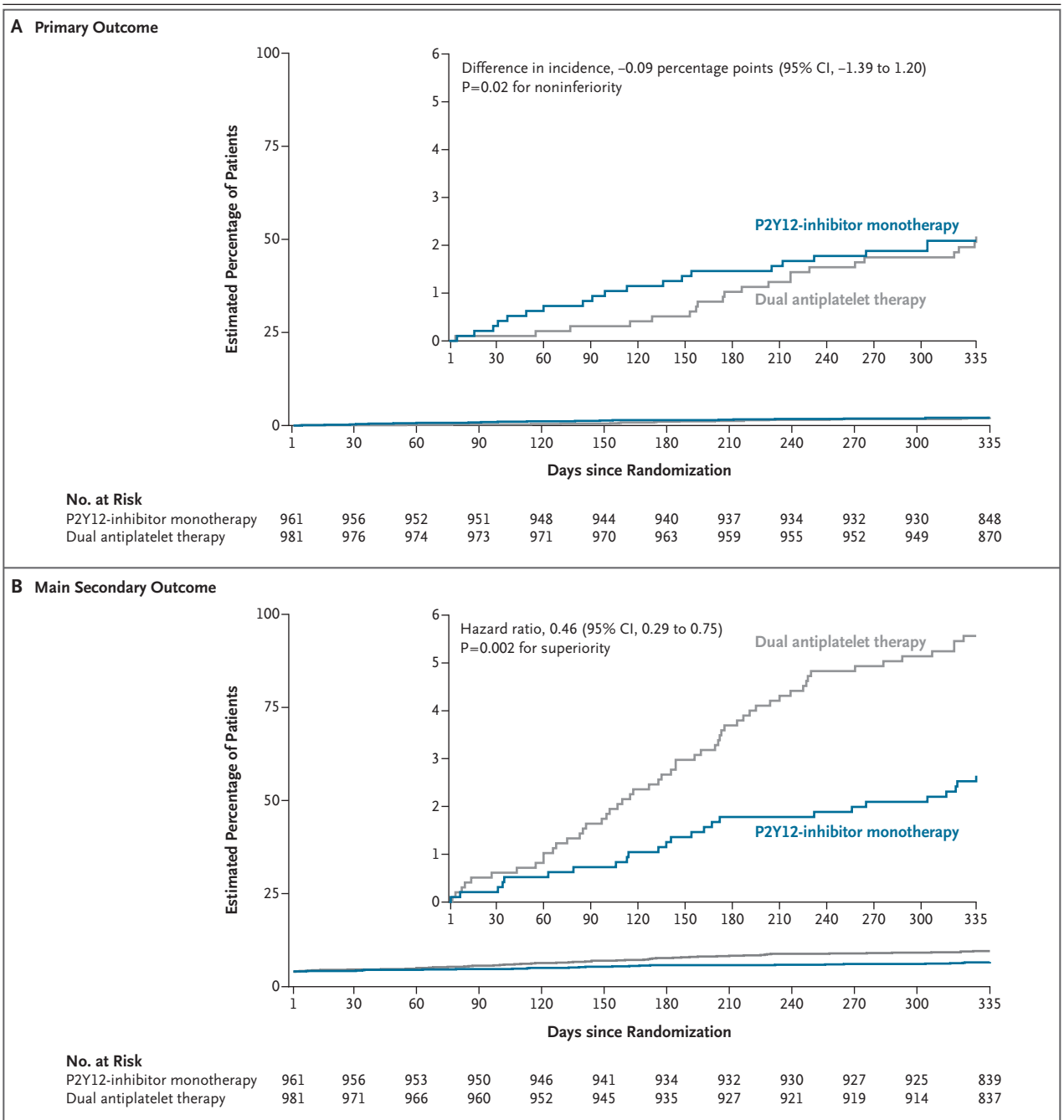


Figure 2. Primary and Main Secondary Outcomes.

Panel A shows the incidence of net adverse clinical and cerebrovascular events, defined as a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding (defined by the Bleeding Academic Research Consortium [BARC] as a bleeding event of type 3 or 5) (the primary outcome). Panel B shows the incidence of BARC type 2, 3, or 5 bleeding (clinically relevant bleeding) (the main secondary outcome). In each panel, the inset shows the same data on an expanded y axis.

tion of dual antiplatelet therapy after PCI involved patients with acute myocardial infarction as a subgroup; focused on higher-risk,[9] unselected,[8] or predominantly East Asian patient populations[10-12,17]; or examined discontinuation of aspirin after a longer duration of dual antiplatelet therapy than that assessed in the TARGET-FIRST trial.[9,10,17,18] It is important to note that none of these trials enrolled

Table 2. Primary and Secondary Outcomes at 11 Months after Randomization (Intention-to-Treat Population).*

Outcome	P2Y12-Inhibitor Monotherapy (N=961)	Dual Antiplatelet Therapy (N=981)	Hazard Ratio (95% CI)	P Value
	no. of patients (%)			
Primary outcome: net adverse clinical and cerebrovascular events†	20 (2.1)	21 (2.2)	—	0.02
Secondary outcome: individual components of the primary outcome				
Death from any cause	4 (0.4)	2 (0.2)	2.04 (0.37–11.14)	—
Myocardial infarction	7 (0.7)	10 (1.1)	0.72 (0.27–1.88)	—
Stent thrombosis, definite or probable	1 (0.1)	0	—	—
Stroke	3 (0.3)	2 (0.2)	1.53 (0.26–9.18)	—
BARC type 3 or 5 bleeding‡	7 (0.7)	7 (0.7)	1.02 (0.36–2.91)	—
Type 3a	1 (0.1)	1 (0.1)	—	—
Type 3b	6 (0.6)	3 (0.3)	—	—
Type 3c	0	3 (0.3)	—	—
Main secondary outcome: BARC type 2, 3, or 5 bleeding§	25 (2.6)	54 (5.6)	0.46 (0.29–0.75)	0.002
Other secondary outcomes				
Death from cardiovascular causes	3 (0.3)	2 (0.2)	1.53 (0.26–9.16)	—
Patient-oriented composite outcome¶	43 (4.5)	71 (7.2)	0.61 (0.42–0.89)	—
Major adverse cardiovascular events‖	15 (1.6)	16 (1.6)	— **	—
Device-oriented composite outcome: target-lesion failure††	10 (1.1)	8 (0.8)	1.28 (0.50–3.23)	—
Ischemia-driven revascularization of target lesion	5 (0.5)	6 (0.6)	0.85 (0.26–2.79)	—
Ischemia-driven revascularization of target vessel	7 (0.7)	7 (0.7)	1.02 (0.36–2.91)	—

* The percentages of patients with events were calculated as Kaplan–Meier estimates of the incidence at 11 months after randomization (335 days). The P value for the primary outcome was for noninferiority, and the P value for the main secondary outcome was for superiority.

† Net adverse clinical and cerebrovascular events were defined as a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding (defined by the Bleeding Academic Research Consortium [BARC] as a bleeding event of type 3 or 5).

‡ Type 3a indicates overt bleeding with a decrease in the hemoglobin level of 3 to 5 g per deciliter or the use of transfusion. Type 3b indicates overt bleeding with a decrease in the hemoglobin level of more than 5 g per deciliter, the occurrence of cardiac tamponade, surgical intervention (nonminor), or the use of intravenous vasoactive agents. Type 3c indicates intracranial bleeding, intraspinal bleeding, or vision-threatening intraocular bleeding.

§ BARC type 2, 3, or 5 bleeding indicates clinically relevant bleeding, which ranges from overt bleeding for which medical attention is warranted (type 2) to fatal bleeding (type 5).

¶ This outcome was defined as a composite of death from any cause, myocardial infarction, definite or probable stent thrombosis (according to Academic Research Consortium criteria), stroke, ischemia-driven repeat revascularization, or BARC type 2, 3, or 5 bleeding.

‖ Major adverse cardiovascular events (also known as MACE) were defined in this trial as a composite of death from cardiovascular causes, myocardial infarction, or ischemia-driven revascularization of the target vessel.

** The difference between the groups in the restricted mean survival time was –1.3 days (95% CI, –3.6 to 0.9).

†† Target-lesion failure was defined as a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven revascularization of the target lesion.

only patients with acute myocardial infarction — a clinical context in which thrombotic involvement may substantially affect both the patient's prognosis and the efficacy of antithrombotic strategies.

Another distinctive feature of our trial was that the choice of P2Y12 inhibitor was at the discretion of the investigator, although the use of a potent P2Y12 inhibitor was recommended; a

potent P2Y12 inhibitor was used in more than 90% of the patients. Although the overall incidence of ischemic events during the trial appeared to be low, this finding may reflect the effectiveness of modern stent technology, a high incidence of procedural success, adherence to evidence-based medical therapy, and the low-risk patient population enrolled in the trial. Taken together, our trial provides targeted evidence regarding the noninferiority of early cessation of aspirin at 1 month as compared with continued dual antiplatelet therapy for a low-risk European patient population treated with modern PCI strategies and optimized medical therapy.

The benefit of P2Y12-inhibitor monotherapy with respect to bleeding was accompanied by a low incidence of key ischemic-outcome events, including death from any cause, myocardial infarction, stroke, and stent thrombosis. The incidence of stent thrombosis was particularly low, reinforcing the safety of this approach among patients who had been carefully selected for low ischemic risk. Our results align with and contribute to the growing body of evidence that supports tailored antiplatelet strategies that are based on individual bleeding and ischemic-risk profiles. Our findings contrast with those of the STOPDAPT-2 ACS (Short and Optimal Duration of Dual Antiplatelet Therapy after Everolimus-Eluting Cobalt-Chromium Stent-2 in Patients with an Acute Coronary Syndrome) trial,[11] in which 1 month of dual antiplatelet therapy was not noninferior to 12 months of dual antiplatelet therapy. However, in the STOPDAPT-2 ACS trial, the completeness of revascularization was unknown and recurrent ischemic events were often linked to untreated lesions rather than to stent failure. Our trial suggests that when complete revascularization is achieved with the use of a latest-generation stent platform, the justification for extended dual antiplatelet therapy in low-risk patients may differ from current practice because residual anatomical ischemic risk has already been addressed.

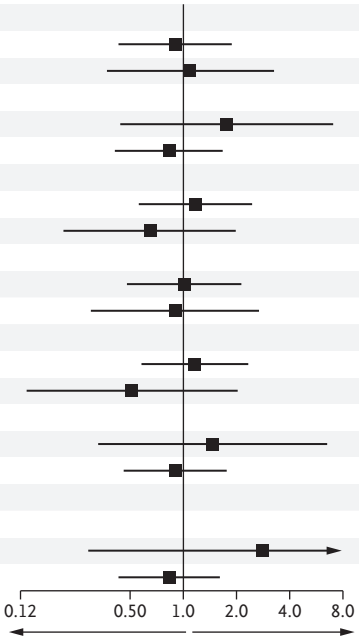
Our trial required complete revascularization within a narrow window of time after the index PCI in order to eliminate the possibility of residual high-grade or flow-limiting lesions being present at the time of randomization to ensure a consistent anatomical baseline across the trial population. Although most of the patients had single-vessel disease, which is consistent with a low residual ischemic risk, this uniform revascularization strategy enabled a reliable evaluation of the balance between ischemic protection and bleeding risk and of the effect of early antiplatelet de-escalation. The results of previous trials such as the COMPLETE (Complete vs. Culprit-Only Revascularization to Treat Multi-Vessel Disease after Early PCI for STEMI) trial[19] showed the benefits of complete revascularization; however, the timing of complete revascularization in the COMPLETE trial could have occurred up to 45 days after the index PCI, and the trial involved higher-risk patients. Our findings should be interpreted in the specific context of early, anatomically complete revascularization in a carefully selected population and may not be directly generalizable to the broader, more heterogeneous populations studied previously.

Our trial has limitations that merit consideration. First, although the noninferiority criterion was formally met, the observed effect size was smaller than anticipated. The lower-than-expected incidence of primary-outcome events led to an increase in the relative inferiority margin. Second, although noninferiority was shown in the intention-to-treat and as-treated analyses (Table S18 and Fig. S3), it was not shown in the per-protocol analysis (Tables S19, S20, and S21 and Fig. S4). The per-protocol analysis may have had reduced statistical power owing to the reduced sample size; nonetheless, it showed a similar direction of treatment effect with no safety signals and with a favorable bleeding outcome. Third, the trial was not powered to detect between-group differences in rare events such as stent thrombosis, stroke, and death from cardiovascular causes. Although the assumed incidence of events was based on previous trials and feasibility data, the observed incidence was lower. This finding may reflect a population free from early adverse events, with high procedural success, low ischemic risk, and excellent adherence to therapy that involved the widespread use of potent P2Y12 inhibitors, contemporary stents, and optimized secondary prevention. Fourth, the focus on patients who completed 1 month of dual antiplatelet therapy without major events and underwent complete revascularization may limit generalizability to higher-risk patients or more complex populations with myocardial infarction.

A fifth limitation is that the open-label design could have introduced bias; however, blinded adjudication of major events mitigates this concern.

A Primary Outcome (net adverse clinical and cerebrovascular events)

Subgroup	P2Y12-Inhibitor Monotherapy	Dual Antiplatelet Therapy	Hazard Ratio for Primary Outcome (95% CI)
	no. of events/no. (%)		
Age			
<75 yr	13/848 (1.5)	15/875 (1.7)	0.90 (0.43–1.88)
≥75 yr	7/113 (6.2)	6/106 (5.7)	1.09 (0.37–3.26)
Sex			
Female	6/223 (2.7)	3/197 (1.5)	1.76 (1.44–7.04)
Male	14/738 (1.9)	18/784 (2.3)	0.83 (0.41–1.67)
Indication for PCI			
NSTEMI	15/479 (3.1)	13/484 (2.7)	1.17 (0.56–2.45)
STEMI	5/482 (1.0)	8/497 (1.6)	0.65 (0.21–1.98)
No. of vessels affected			
Single	14/754 (1.9)	14/767 (1.8)	1.02 (0.48–2.13)
Multiple	6/207 (2.9)	7/214 (3.3)	0.90 (0.30–2.68)
No. of lesions affected			
Single	17/735 (2.3)	15/751 (2.0)	1.16 (0.58–2.33)
Multiple	3/226 (1.3)	6/230 (2.6)	0.51 (0.13–2.03)
Diabetes mellitus			
Yes	4/135 (3.0)	3/146 (2.1)	1.46 (0.33–6.51)
No	16/826 (1.9)	18/835 (2.2)	0.90 (0.46–1.76)
P2Y12 inhibitor			
Clopidogrel	1/46 (2.2)	0/53 (0)	—
Prasugrel	3/209 (1.4)	1/196 (0.5)	2.81 (0.29–26.98)
Ticagrelor	16/706 (2.3)	20/731 (2.7)	0.83 (0.43–1.61)



B Main Secondary Outcome (BARC type 2, 3, or 5 bleeding)

Subgroup	P2Y12-Inhibitor Monotherapy	Dual Antiplatelet Therapy	Hazard Ratio for Main Secondary Outcome (95% CI)
	no. of events/no. (%)		
Age			
<75 yr	18/848 (2.1)	49/875 (5.6)	0.41 (0.24–0.68)
≥75 yr	7/113 (6.2)	5/106 (4.7)	1.40 (0.50–3.94)
Sex			
Female	8/223 (3.6)	8/197 (4.1)	0.87 (0.33–2.31)
Male	17/738 (2.3)	46/784 (5.9)	0.46 (0.27–0.76)
Indication for PCI			
NSTEMI	18/479 (3.8)	23/484 (4.8)	0.83 (0.46–1.51)
STEMI	7/482 (1.5)	31/497 (6.2)	0.28 (0.14–0.59)
No. of vessels affected			
Single	22/754 (2.9)	49/767 (6.4)	0.45 (0.27–0.73)
Multiple	3/207 (1.4)	5/214 (2.3)	1.25 (0.38–4.09)
No. of lesions affected			
Single	21/735 (2.9)	46/751 (6.1)	0.49 (0.30–0.81)
Multiple	4/226 (1.8)	8/230 (3.5)	0.67 (0.24–1.89)
Diabetes mellitus			
Yes	3/135 (2.2)	7/146 (4.8)	0.67 (0.22–2.05)
No	22/826 (2.7)	47/835 (5.6)	0.50 (0.30–0.81)
P2Y12 inhibitor			
Clopidogrel	1/46 (2.2)	0/53 (0)	—
Prasugrel	9/209 (4.3)	19/196 (9.7)	0.48 (0.22–1.03)
Ticagrelor	15/706 (2.1)	35/731 (4.8)	0.50 (0.28–0.87)

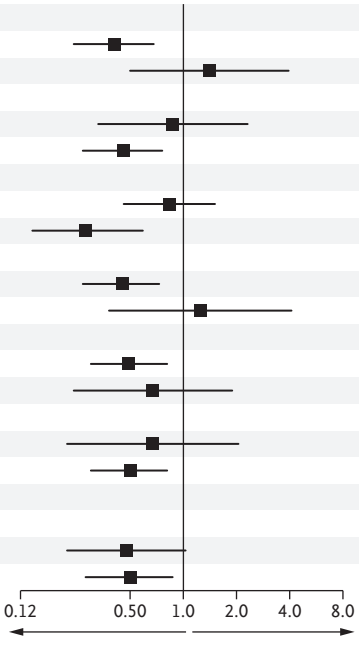


Figure 3 (facing page). Primary and Main Secondary Outcomes in Prespecified Subgroups.

Panel A shows the subgroup analysis of net adverse clinical and cerebrovascular events, defined as a composite of death from any cause, myocardial infarction, stent thrombosis, stroke, or major bleeding (defined by the BARC as a bleeding event of type 3 or 5) (the primary outcome). The arrow on the confidence interval bar indicates that upper boundary of the confidence interval is off the scale. Panel B shows the subgroup analysis of BARC type 2, 3, or 5 bleeding (clinically relevant bleeding) (the main secondary outcome). NSTEMI denotes non–ST-segment elevation myocardial infarction, PCI percutaneous coronary intervention, and STEMI ST-segment elevation myocardial infarction.

Sixth, the subgroup analyses of the primary and secondary outcomes were exploratory, were based on small numbers, and should be interpreted cautiously. Seventh, the exclusive use of a single-stent platform may limit extrapolation of the results to other types of devices. Eighth, no platelet-function testing or genotyping was performed in the small percentage of patients (5.1%) treated with clopidogrel. Finally, the trial population was highly selected, reflecting strict inclusion and exclusion criteria, a mandated narrow window for anatomically complete revascularization (within 7 days), and a low overall incidence of events. Indeed, a substantial percentage of enrolled patients (13.5%) were excluded before randomization, largely owing to early clinical events, incomplete revascularization, or site-level discretion. Modest baseline imbalances between patients who had undergone randomization and those who had not were noted, but none of the imbalances meaningfully affected the heterogeneity of the treatment effect.

The results of this trial showed that, among low-risk patients with acute myocardial infarction who had undergone complete revascularization and had subsequently received 1 month of dual antiplatelet therapy, P2Y12-inhibitor monotherapy was noninferior to continued dual antiplatelet therapy with respect to the occurrence of adverse cardiovascular or cerebrovascular events and resulted in a lower incidence of bleeding events at 1 year than dual antiplatelet therapy.

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