Randomized evaluation of ticagrelor monotherapy after 3-month dual-antiplatelet therapy in patients with acute coronary syndrome treated with new-generation sirolimus-eluting stents: TICO trial rationale and design

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Abstract Background Ticagrelor monotherapy after short-term dual-antiplatelet therapy (DAPT) may optimize ischemic and bleeding risks, particularly for acute coronary syndrome (ACS) patients, because its strategy is less potent than ticagrelor-based DAPT but more potent than aspirin or clopidogrel monotherapy.

Methods The TICO randomized open-label trial will evaluate whether ticagrelor monotherapy following 3-month DAPT is superior to 12-month ticagrelor-based DAPT in terms of net adverse clinical events (NACE) including efficacy and safety in ACS patients treated with ultrathin bioresorbable polymer sirolimus-eluting stents (BP-SES). Patients undergoing BP-SES implantation for ACS treatment will be randomized in a 1:1 fashion to the (1) ticagrelor monotherapy group after 3-month DAPT; or the (2) 12-month DAPT group. The primary endpoint is NACE within 12 months of percutaneous coronary intervention, which includes major adverse cardiac and cerebrovascular events (MACCE) plus major bleeding as defined by Thrombolysis in Myocardial Infarction. MACCE includes the composite of all-cause death, myocardial infarction, stent thrombosis, stroke, and target vessel revascularization. Secondary endpoints included each component of the primary endpoint.

Conclusions The TICO trial is an ongoing trial evaluating the efficacy and safety of ticagrelor monotherapy following 3-month DAPT exclusively in ACS patients treated with uniform BP-SES. It may provide novel insights regarding the need for adjusted use of DAPT for rebalancing risk–benefit in current practice and changing from the conventional concept of aspirin maintenance to a ticagrelor-based regimen in the management of ACS. (Am Heart J 2019;212:45-52.)

Background

Regarding antiplatelet therapy for patients with acute coronary syndrome (ACS), the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial demonstrated the superiority of 12-month dual-antiplatelet therapy (DAPT) including clopidogrel plus aspirin over aspirin alone.[1] The concept of 12-month DAPT has been successively applied in trials evaluating new potent P2Y12 inhibitors, such as prasugrel and ticagrelor, including the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction (TRITON–TIMI) 38 and the Study of Platelet Inhibition and Patient Outcomes (PLATO).[2,3] Based on these trials, the current guidelines recommend DAPT using potent antiplatelet agents in ACS treatment, especially ticagrelor for 12 months and at least 6 months in selected patients.[4,5] However, a ticagrelor-based DAPT strategy up to 12 months can increase bleeding risks even in a high thrombotic risk population of ACS patients.[6] On the contrary, according to the Safety of 6-month Duration of Dual Antiplatelet Therapy After Acute Coronary

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Table 1. Recent randomized trials evaluating short-term dual-antiplatelet therapy duration for patients with acute coronary syndrome

Trials	SMART-DATE[7]	REDUCE[10]	DAPT-STEMI[11]
No. of patients	2712	1496	870
Experimental vs control regimen*	6-month DAPT vs 12-month DAPT	3-month DAPT vs 12-month DAPT	6-month DAPT vs 12-month DAPT
Use of new potent P2Y12 inhibitor	19%	59%	58%
Type of DES	EES (Xience prime), ZES (Resolute Integrity), BES (Biomatrix Flex)	Bioabsorbable polymer-based metallic DES with luminal CD34+ antibody coating	ZES (Resolute Integrity)
Primary endpoint/ Hypothesis	MACCE (all-cause mortality, myocardial infarction and cerebrovascular events) at 18 months/Non-inferiority	Composite of all-cause death, MI, stroke, TVR, or bleeding (BARC 2, 3, or 5) at 12 months/Non-inferiority	All-cause mortality, MI, any revascularization, stroke, TIMI major bleeding at 18 months/ Non-inferiority
Key findings	6-month DAPT (4.7%) was non-inferior to 12-month DAPT (4.2%).	3-month DAPT (8.2%) was non-inferior to 12-month DAPT (8.4%).	6-month DAPT (4.8%) was non-inferior to 12-month DAPT (6.6%).

*DAPT includes aspirin plus P2Y12 inhibitor including clopidogrel, ticagrelor, or prasugrel at the discretion of the physician. Aspirin monotherapy was continued after mandatory DAPT period. BES, biolimus-eluting stent; DAPT, dual-antiplatelet therapy; DES, drug-eluting stent; EES, everolimus-eluting stent; MACCE, major adverse cardiac and cerebrovascular event; TIMI, Thrombolysis in Myocardial Infarction; MI, myocardial infarction; PCI, percutaneous coronary intervention; TVR, target-vessel revascularization; ZES, zotarolimus-eluting stent.

Syndromes (SMART-DATE) trial, short-term DAPT followed by aspirin monotherapy had a higher incidence of myocardial infarction (MI) driven by spurt of events just after DAPT termination.[7] Ticagrelor elicits more potent platelet inhibition than aspirin or clopidogrel, and a shorter duration of DAPT is known to be associated with reductions in bleeding risk.[4,8] In this sense, a strategy of short-term DAPT followed by ticagrelor monotherapy may optimize ischemic and bleeding risks, particularly for ACS patients. The GLOBAL LEADERS study recently reported the clinical use of an experimental, ticagrelor-based treatment strategy including 1-month DAPT followed by 23-month ticagrelor monotherapy, compared with a current-day intensive DAPT for 12 months followed by aspirin monotherapy, in patients undergoing percutaneous coronary intervention (PCI). Although it failed to demonstrate superiority in all patients with stable angina or ACS, the experimental treatment led to a significant reduction in major bleeding events in the subgroup of patients with ACS.[9]

There is insufficient evidence regarding the optimal DAPT duration of potent antiplatelet agents in the post-clopidogrel era, particularly for ACS patients, although the recent randomized SMART-DATE, REDUCE, and DAPT STEMI trials focused on DAPT duration for ACS patients (Table 1).[7,10,11] In the SMART-DATE study, specific P2Y12 inhibitors were not recommended, while new potent P2Y12 inhibitors were used in only 19%.[7] According to the preliminary data presented in the late-breaking clinical trial session in the Transcatheter Cardiovascular Therapeutics 2017 (TCT 2017) scientific meeting, new potent P2Y12 inhibitors were used in 59% and 58% in the REDUCE and DAPT STEMI trials, respectively.[12,13]

The multicenter, randomized, open-label trial of Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome (TICO) trial evaluates whether ticagrelor monotherapy following 3-month DAPT is superior to 12-month ticagrelor-based DAPT in terms of net adverse clinical events (NACE) for patients with ACS treated with ultrathin bioresorbable polymer sirolimus-eluting stents (BP-SES) (Orsiro; Biotronik AG, Bülach, Switzerland).

Study design

Objectives and hypothesis

The TICO trial (ClinicalTrials.gov identifier: NCT02494895) is a multicenter prospective randomized open-label clinical trial in Korea. It will test the superiority of 3-month DAPT with ticagrelor plus aspirin followed by 9-month ticagrelor monotherapy in comparison to 12-month DAPT with ticagrelor and aspirin. We will assess the incidence of NACE at 12 months as a primary endpoint to weigh overall risk in clinical practice considering both ischemic and bleeding adverse events after PCI with BP-SES in ACS patients. Secondary objective is to assess whether our experimental strategy may lead to a difference in the incidence of major ischemic or bleeding events.

Study organization and funding

This trial is investigator-initiated with grant support from AstraZeneca (Cambridge, UK) and Biotronik (Bülach, Switzerland). Other than financial sponsorship, the companies played no role in the study or decision to publish. The executive committee has a pivotal role with overall responsibility for the concept, design, and execution of the study progress in accordance with scientific, medical, ethical, and practical elements. The committee will convene a meeting to ensure the good execution and management of the study's progress, execution, and management and take charge of data management including its acquisition, security, analysis,

Table 2. Inclusion and exclusion criteria

Inclusion criteria

1. Age ≥19 years
2. Patients who received bioresorbable polymer sirolimus-eluting stent implantation to treat acute coronary syndrome
3. Provision of informed consent

Exclusion criteria

1. Age >80 years
2. Increased risk of bleeding due to
   1) Any prior event of hemorrhagic stroke;
   2) Ischemic stroke, dementia, or impairment of central nervous system within a year;
   3) Traumatic brain injury or brain surgery within the past 6 months;
   4) Known intracranial tumor;
   5) Documented or suspected aortic dissection;
   6) Internal bleeding within the past 6 weeks;
   7) Active bleeding or bleeding diathesis;
   8) Anemia (hemoglobin ≤8 g/dL) or thrombocytopenia (platelet count <100,000/μL); and
   9) Major surgery or traumatic injury resulting in any impairment of physical activity within the past 3 weeks
3. Need for oral anticoagulation therapy
4. Current or potential pregnancy
5. Life expectancy <1 year
6. Currently treated with strong CYP3A4 inhibitors
7. Moderate to severe hepatic dysfunction (Child-Pugh class B or C)
8. Increased risk of bradycardia-related symptoms

CYP3A4, cytochrome P450 3A4.

and reporting. The study adheres to the ethical principles of the Declaration of Helsinki, and its protocol was approved by the institutional review board at each participating center.

Study population, randomization, and follow-up

Patients who underwent BP-SES implantation for ACS treatment will be eligible for study enrollment. ACS includes unstable angina defined as typical symptoms, including recurrent episodes at resting or with minimal effort and occurrence of severe angina initiated or aggravated within 4 weeks, and MI defined as the presence of clinical symptoms, electrocardiographic changes, or abnormal imaging findings of MI combined with an increase in creatine kinase myocardial band fraction above the upper normal limit or an increase in troponin-T or troponin-I to greater than the 99th percentile of the upper normal limit unrelated to revascularization.[14] Inclusion and exclusion criteria are presented in Table 2. Allocation of the treatment and study procedures including baseline measurements will be started after each patient voluntarily provides informed consent. For obtaining informed consent from eligible patients who are able to fully comprehend the study purpose and processes without verbal and written language constraints, the study may seek to only enroll patients of Korean nationality and ethnicity.

Randomization and assignment will be done after PCI. Patients will be randomized in a 1:1 fashion to (1) the ticagrelor monotherapy group after 3-month DAPT or (2) the 12-month DAPT group. All DAPT treatments comprised a combination of aspirin and ticagrelor. A web-response permuted-block randomization (mixed blocks of 4 or 6) at each participating site will be used to allocate random assignment stratified by the presence of diabetes mellitus and ST-elevation myocardial infarction.[15,16] Loading doses of aspirin 300 mg and ticagrelor 180 mg will be given if the patient is not taking aspirin or ticagrelor at the time of PCI. Aspirin 100 mg once and ticagrelor 90 mg twice, which had been considered as a standard of care in the management of ACS in Korea at the start of this study, will be prescribed for daily maintenance.[17,18] After a 3-month DAPT treatment consisting of ticagrelor and aspirin, the aspirin will be discontinued for the ticagrelor monotherapy group and continued in the 12-month DAPT group in an open-label design. Concomitant use of other antiplatelet agents or anticoagulants will not be allowed. Other medical treatments will be left at the physician's discretion, but guideline-directed medical therapy will be strongly encouraged to allow for a patient's individual condition (e.g. control of hypertension or diabetes mellitus, prescription of high-intensity statin, cessation of cigarette smoking, optimal pharmacologic treatment for heart failure).

At baseline, angiographic, procedural, electrocardiographic, echocardiographic, and laboratory findings will be assessed. The collection of each participant's general health status, current medication, and adverse or endpoint-related events is performed at baseline and during 3, 6, 9, and 12 months of follow-up after PCI. Serial follow-up of laboratory study will be performed at 3 and 12 months, and HbA1c will be evaluated at baseline and 12 months in diabetic patients. At the time point around 2 weeks at 3 months and around 1 month at 6, 9, and 12 months, patients are obligated to attend outpatient appointments or to be contacted by telephone.

Study endpoint

The primary endpoint is NACE within 12 months of PCI, which includes major adverse cardiac and cerebrovascular events (MACCE) plus major bleeding according to the Thrombolysis in Myocardial Infarction (TIMI) definition. MACCE includes the composite of all-cause death, MI, stent thrombosis, stroke, and target vessel revascularization (TVR). Secondary endpoints will include each component of the primary endpoint (Table 3).

Cardiac death is defined as death due to MI, cardiac perforation or pericardial tamponade, an arrhythmia or conduction abnormality, stroke within 30 days of the procedure or related to the procedure, death due to a procedural complication, and any case of death in which a cardiac cause cannot be excluded as adjudicated by a clinical endpoints committee.[19] Stent thrombosis is defined as definite or probable stent thrombosis by the definition of the Academic Research Consortium.[19] An acute cerebrovascular event resulting in death or neurological deficit >24 hours or the presence of acute

Table 3. Study endpoint

Primary endpoint
Net clinical adverse events (NACE), defined as major adverse cardiac and cerebrovascular events (MACCE)* plus major bleeding as defined by TIMI within 12 months of the index procedure
*MACCE is a composite endpoint of all-cause death, MI, stent thrombosis, stroke, and target vessel revascularization
Secondary endpoint
Each component of primary endpoint
Cardiac or non-cardiac death
Stent thrombosis (definite or probable)
Any bleeding (TIMI minor or major)
Other composite events
MACCE
Cardiac death or MI
Cardiac death, MI, stent thrombosis, or target vessel revascularization

TIMI, Thrombolysis in Myocardial Infarction; MI, myocardial infarction.

infarction demonstrated by imaging studies will be defined as a stroke.[20] TVR is defined as a repeat PCI or bypass surgery of the target vessel with either of the following: (1) angiographic diameter stenosis >50% by quantitative coronary angiographic analysis with symptoms or objective evidence of ischemia; or (2) angiographic diameter stenosis >70% by quantitative coronary angiographic analysis with symptoms of ischemia. Routine follow-up angiography is not recommended.[21] Major bleeding was defined as overt clinical bleeding associated with a hemoglobin drop of >5 g/dL or a hematocrit drop of >15% (absolute) according to TIMI bleeding criteria.[22,23] Post-hoc analysis will be needed to evaluate other composite endpoints, including or excluding relevant events, in order to determine the scope of the use of a composite endpoint as a primary outcome.

An independent clinical endpoints committee blinded to the primary result of the trial and treatment assignment before locking of the database is responsible for categorizing each adverse event including the ischemic and bleeding events.

Sample size calculation

This study is designed to compare 3-month DAPT treatment followed by ticagrelor monotherapy to standard treatment with 12-month DAPT at the patient level. We hypothesize that ticagrelor monotherapy may be sufficient to prevent thromboembolic events from 3 months after PCI in patients with ACS and reduce bleeding risk compared to reference 12-month DAPT treatment. Based on the PLATO trial, we anticipate that 18% of patients in a reference treatment arm will reach the primary endpoint.[3] Considering nearly comparable incidences of major bleeding and ischemic events among patients presenting ACS in the PLATO trial and the improved efficacy of new generation drug-eluting stent (DES), reduction in bleeding risk may gain increasing importance for better net clinical benefit in the contemporary DES era. With assumption that the 3-month DAPT followed by ticagrelor monotherapy will reduce primary endpoint by 25% (expected event rate, 13.5%), a total of 1528 patients are required for each group considering a 5% 2-sided α error rate, 90% power, and 10% of follow-up loss. Therefore, we will enroll a total of 3056 patients (Figure 1).

Statistical analysis plan

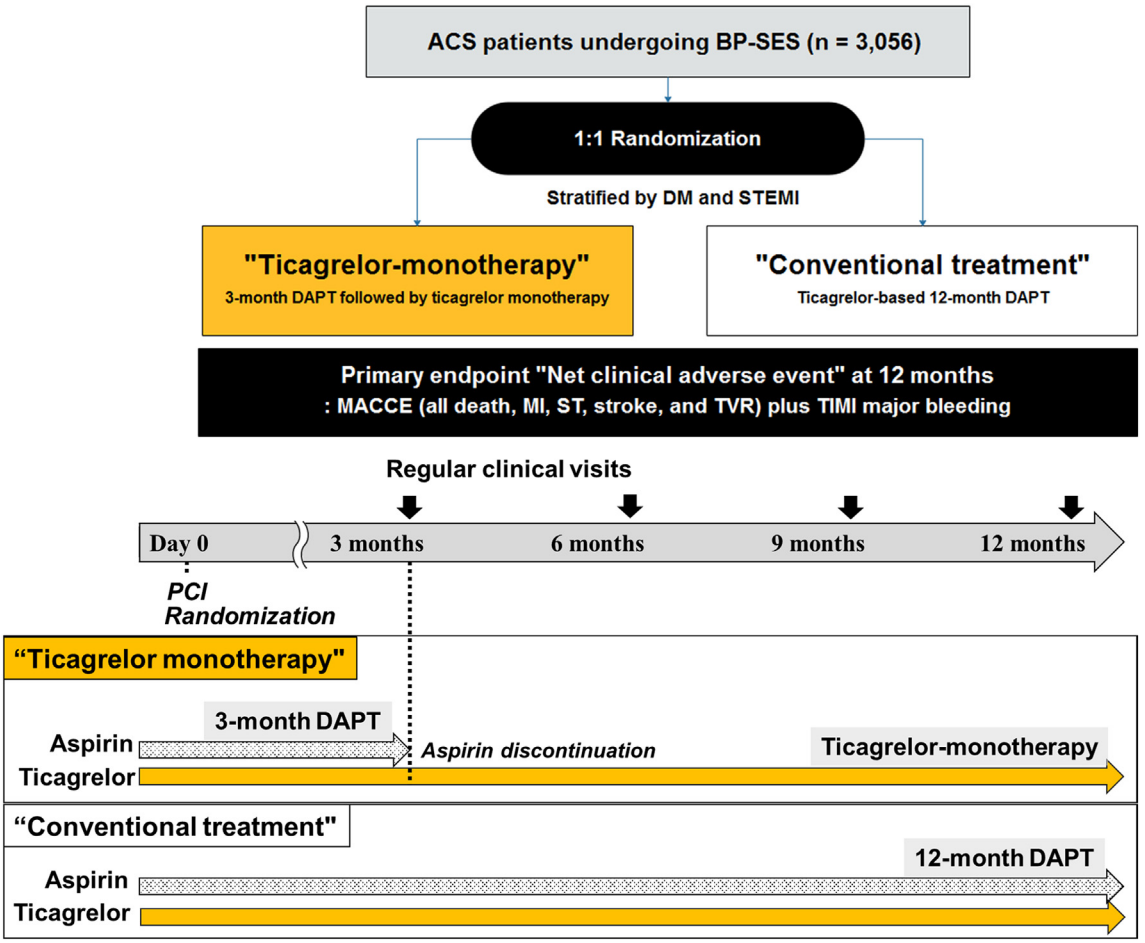
A major comparison of the 2 treatment strategies will be performed primarily in an intention-to-treat manner in addition to a per-protocol analysis. Categorical data of demographic, medication, angiography, and procedural characteristics will be described as number (percentage). Continuous variables will be expressed as mean ± standard deviation or median (interquartile range) for normal or skewed distributions, respectively. Baseline characteristics will be compared between the treatments using the chi-square or Fisher's extract test for categorical variables and Student's t-test or the Mann–Whitney U test (unless normally distributed) for continuous variables. The cumulative incidence of primary and secondary endpoints will be estimated at 12 months and Kaplan–Meier curves for time-to-event analysis will be plotted from the time of the index procedure to the occurrence of the first event of interest.

The primary analysis of endpoints will be conducted using a Cox proportional-hazard model. A pre-specified landmark analysis of the primary endpoint will also be performed from 3 to 12 months since treatment during the first 3 months is the same in both groups. A subgroup analysis will be also conducted for clinically relevant factors such as age, sex, comorbidities, lesion or procedural characteristics, and other risk indicators. A 2-sided test will be used for all hypotheses testing at a 5% significance level.

Safety monitoring

The Data and Safety Monitoring Board (DSMB), in conjunction with the executive committee responsible for ensuring participant safety, will act in an advisory capacity to monitor participant safety; evaluate the study progress; review procedures for maintaining data

Figure 1



Schematic study design and flow diagram of the TICO trial.BP-SES ultrathin bioresorbable polymer sirolimus-eluting stents; DAPT dual antiplatelet therapy; DM diabetes mellitus; MACCE major adverse cardiac and cerebrovascular event; MI myocardial infarction; PCI percutaneous coronary intervention; ST stent thrombosis; STEMI ST-elevation myocardial infarction; TIMI Thrombolysis in Myocardial Infarction; TVR target vessel revascularization.

confidentiality; and perform the data collection, management, and analyses. A regular DSMB meeting will be held twice annually, either in person or by teleconference call to discuss study progress; ensure good execution of the study procedure, data quality, and security; and review any participant-related safety issues. Although there was no interim analysis originally planned, the DSMB has the authority to discontinue the study process and to review the relevant events during the trial if any safety issue occurs.

Discussion

Ticagrelor monotherapy after ticagrelor-based short DAPT for ACS management

Given the fact that potent antiplatelet drugs with strong platelet inhibitory action reduce thrombotic events in return for increased bleeding, the conventional 12-month DAPT strategy must be reconsidered in this post-clopidogrel era for ACS management. Sustained use of DAPT for 12 months with potent P2Y12 inhibitors leads to a more profound risk of major bleeding,[6,24] and a treatment strategy with DAPT potency de-escalation has been shown to be associated with favorable clinical outcomes.[25,26] The CURE study demonstrated that DAPT reduces early ischemic events but did not influence the risk of ischemic events after 3 months in patients following ACS.[1,27] It seems reasonable that the clinical importance of DAPT would be more profound during the early period after ACS. Ticagrelor, which strongly blocks ADP, also has an effect on thromboxane-mediated platelet activation,[28] and aspirin plays a minimal role in platelet inhibition in the presence of strong P2Y12 receptor blockage.[29] In our assumption, ticagrelor monotherapy would exert comparable effects on platelet inhibition

Table 4. Ongoing and recently finished randomized trials evaluating short-term DAPT followed by P2Y12 inhibitor monotherapy after DES implantation

Trials	TICO (NCT02494895)	TWILIGHT[30] (NCT02270242)	SMART-CHOICE[31] (NCT02079194)	GLOBAL-LEADERS[9] (NCT01813435)
Key inclusion criteria	ACS	Clinically/ angiographically high-risk	SCAD or ACS	SCAD or ACS
No. of patients	3056	9000	3000	15,968
Initiation	July 2015	July 2015	March 2014	June 2013
Experimental vs control regimen	3-month ticagrelor-based DAPT followed by ticagrelor monotherapy vs 12-month ticagrelor-based DAPT	3-month ticagrelor-based DAPT followed by ticagrelor monotherapy vs 15-month ticagrelor-based DAPT	3-month DAPT followed by any P2Y12 inhibitor monotherapy vs 12-month DAPT	1-month ticagrelor-based DAPT followed by ticagrelor monotherapy vs 12-month DAPT followed by aspirin monotherapy
Type of DES	Bioresorbable polymer SES (Orsiro; Biotronik, Bülach, Switzerland)	Any drug-eluting stent	Cobalt-chromium EES (Xience family, Abbott, Santa Clara, CA), platinum-chromium EES (Promus family or Synergy, Boston Scientific, Marlborough, MA), or bioresorbable polymer SES (Orsiro, Biotronik).	Biodegradable polymer biolimus A9-eluting stents (Biomatrix family, Biosensors Europe SA, Morges, Switzerland)
Primary endpoint/ Hypothesis	Net adverse clinical events at 12 months/Superiority	BARC bleeding type 2, 3, or 5 at 15 months/Superiority	Major adverse cardiac and cerebrovascular event at 12 months/Non-inferiority	All-cause mortality or new Q-wave myocardial infarction at 24 months/Superiority
Key findings	Not revealed yet	Not revealed yet	Not revealed yet	The experimental regimen (3.8%) did not demonstrated a superiority compared with the control regimen (4.4%; rate ratio 0·87 [95% CI 0·75–1·01]; $P = .07$]).

ACS, Acute coronary syndrome; *BARC*, Bleeding Academic Research Consortium; *DAPT*, dual-antiplatelet therapy; *EES*, everolimus-eluting stent; *SCAD*, stable coronary artery disease; *SES*, sirolimus-eluting stent.

irrespective of the use of aspirin for ACS patient after some period of extremely high risk of ischemia. It would have a benefit in lowering bleeding risk, which would be associated with better net clinical benefit. Therefore, ticagrelor monotherapy is expected to be more effective, while the withdrawal of aspirin may be beneficial and play a trivial role in platelet inhibition in the recent new antiplatelet era.

To date, 3 randomized trials including the TICO trial are now ongoing to evaluate the role of P2Y12 monotherapy without aspirin after DES placement (Table 4),[30,31] and the GLOBAL LEADERS trial was recently reported.[9] Although the superiority of experimental regimen with short DAPT followed by P2Y12 monotherapy was not determined in the study, its greater benefit in terms of lowering bleeding risk was demonstrated among subgroups with patients receiving ticagrelor-based regimen or those with ACS. However, the GLOBAL LEADERS trial recruited a wide-spectrum of patients including stable coronary artery disease (>50% of all enrolled patients) and evaluated the role of extended use (>12 months) of ticagrelor monotherapy unlike the TICO trial; the TICO trial only included ACS patients and excluded the patients with stable angina. The TICO trial will answer whether ticagrelor monotherapy results in sufficient anti-ischemic effect and reduced bleeding risk among ACS patients during 12 months after PCI.

Short DAPT duration for ACS patients treated with new-generation DES

A long-term DAPT duration (>12 months) has been adopted as the standard treatment for managing patients with ACS undergoing PCI. Although previous trials suggested the potential advantages in favor of short-term DAPT with a lower bleeding risk and a comparable ischemic risk, even in patients with ACS, evidence of short-term DAPT use for the management of ACS, especially that <6 months, remains insufficient. Two large-scale randomized trials, the Real Safety and Efficacy of 3-Month Dual Antiplatelet Therapy following Endeavor Zotarolimus-Eluting Stent Implantation (RESET) and Optimized Duration of Clopidogrel Therapy Following Treatment with the Zotarolimus-Eluting Stent in Real-World Clinical Practice (OPTIMIZE), comparing 3- and 12-month DAPT after PCI, demonstrated no statistical difference in primary endpoints including ischemic and bleeding events, even in the ACS subset.[32,33] However, both studies included a limited number of patients with ACS and had inadequate power to demonstrate the differences among them. In addition, these studies did not focus on the ACS subset; they included only subgroup analyses. The SMART-DATE, REDUCE, and DAPT STEMI trials evaluated the optimal DAPT duration, especially for ACS patients.[7,10-13] However, these studies did include

only substantial patients with clopidogrel-based DAPT (Table 1). In contrary to these trials evaluating short-term DAPT, the Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin–Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial showed that long-term therapy with ticagrelor at a dose of 60 mg twice daily added to low-dose aspirin reduces the risk of major adverse cardiovascular events among stable patients with a history of myocardial infarction.[34] Thus, in the post-clopidogrel era, randomized clinical trials are needed to evaluate the optimal duration of DAPT using new potent antiplatelet agents and the role of new antiplatelets as mono-antiplatelet therapy. Therefore, in the TICO trial, different from these trials, aspirin instead of P2Y12 inhibitors will be discontinued.

Although short DAPT duration is known to lead to a higher risk of ischemic events in both ACS and non-ACS patients, the causal significance is significantly attenuated by the use of second-generation DES.[8] Thus, the improvement of stent characteristics may reduce the risk of subsequent ischemic events and the need for long-term DAPT as well. The TICO trial will exclusively enroll patients undergoing PCI with a single type of stent, BP-SES, showing both efficacy and safety through various clinical trials,[35-37] to eliminate potential confounding factors introduced by the combined use of multiple different types of DES.

Current status of the TICO trial

The TICO trial enrolled the first patient in August 2015 and the last patient in October 2019: a total of 3056 patients were finally enrolled at the 38 participating sites. All participants were allocated to the trial groups during index hospitalization after an ACS event. The completion of the study follow-up is projected for October 2019, and the trial results are expected to be reported until the first quarter of 2020.

Summary

The ongoing TICO trial is evaluating the efficacy and safety of ticagrelor monotherapy following 3-month DAPT exclusively in ACS patients treated with BP-SES. The study will ultimately suggest optimal antiplatelet treatment after ACS in patients treated with the latest-generation DES, BP-SES. It may provide novel insights regarding the need to adjust DAPT use to rebalance the risk–benefit ratio in current practice and change from a conventional concept of aspirin maintenance to a ticagrelor-based regimen in the management of ACS.

Conflict of interest

The authors declare no disclosures or conflicts of interest.

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