Design and rationale of the Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen (MASTER DAPT) Study

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Background The optimal duration of antiplatelet therapy in high–bleeding risk (HBR) patients with coronary artery disease treated with newer-generation drug-eluting bioresorbable polymer-coated stents remains unclear.

Design MASTER DAPT (clinicaltrial.gov NCT03023020) is an investigator-initiated, open-label, multicenter, randomized controlled trial comparing an abbreviated versus a standard duration of antiplatelet therapy after bioresorbable polymer-coated Ultimaster (TANSEI) sirolimus-eluting stent implantation in approximately 4,300 HBR patients recruited from ≥100 interventional cardiology centers globally. After a mandatory 30-day dual-antiplatelet therapy (DAPT) run-in phase, patients are randomized to (*a*) a single antiplatelet regimen until study completion or up to 5 months in patients with clinically indicated oral anticoagulation (experimental 1-month DAPT group) or (*b*) continue DAPT for at least 5 months in patients without or 2 in patients with concomitant indication to oral anticoagulation, followed by a single antiplatelet regimen (standard antiplatelet regimen). With a final sample size of 4,300 patients, this study is powered to assess the noninferiority of the abbreviated antiplatelet regimen with respect to the net adverse clinical and major adverse cardiac and cerebral events composite end points and if satisfied for the superiority of abbreviated as compared to standard antiplatelet therapy duration in terms of major or clinically relevant nonmajor bleeding. Study end points will be adjudicated by a blinded Clinical Events Committee.

Conclusions The MASTER DAPT study is the first randomized controlled trial aiming at ascertaining the optimal duration of antiplatelet therapy in HBR patients treated with sirolimus-eluting bioresorbable polymer-coated stent implantation. (Am Heart J 2019;209:97-105.)

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High–bleeding risk (HBR) patients represent up to 45% of the patients with coronary artery disease (CAD) undergoing stent implantation, depending on the setting and bleeding risk definition.[1]

The European and American guidelines endorse by consensus the assessment of bleeding risk to inform the decision making on duration of antiplatelet therapy in patients undergoing percutaneous coronary intervention (PCI) and suggest a shorter than average antiplatelet therapy duration in patients fulfilling at least 1 HBR criterion.[2,3] However, only few studies have so far focused on HBR patients receiving stent implantation[4-9]; no dedicated randomized controlled trial (RCT) has assessed the optimal antiplatelet therapy regimen in HBR patients undergoing PCI, whereas pivotal antiplatelet therapy duration studies have excluded patients with 1 or more HBR criteria.[2,3,10] Therefore, the optimal antiplatelet therapy duration in HBR patients receiving coronary stenting remains uncertain.

HBR and type of coronary stent

The Zotarolimus-Eluting Endeavor sprint stent in Uncertain DES candidates (ZEUS), which compared any commercially available thin-strut bare metal stent (BMS) or Zotarolimus-eluting Endeavor Sprint stent (E-ZES) at the time of PCI, was the first randomized controlled study that included, among others, patients with HBR features.[4-6] It included a total of 1,606 participants, and a total of 828 patients fulfilled 1 or more HBR criteria, of whom 425 (51.3%) were aged >80 years, 311 (37.6%) had clinical indication to oral anticoagulant (OAC), 113 (13.6%) reported previous or recent bleeding requiring hospitalization or medical attention, 95 (11.5%) presented bleeding diathesis, 68 (8.2%) had known anemia, and 25 (3.0%) were in the need for chronic treatment with steroids or nonsteroidal anti-inflammatory drugs. In this selected high-risk patient population, the study protocol mandated 30-day dual-antiplatelet therapy (DAPT) irrespective of the stent type. HBR patients derived benefits in terms of reductions of major adverse cardiac events (MACE), myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis (ST) when treated with E-ZES as compared to BMS. More recently, the Prospective Randomized Comparison of the BioFreedom Biolimus A9 Drug-Coated Stent versus the Gazelle Bare-Metal Stent in Patients at High Bleeding Risk (LEADERS FREE) trial was designed to evaluate the efficacy and safety of the polymer-free Biolimus A9–coated stent as compared with a BMS in HBR patients, with a 1-month regimen of DAPT in both groups.[7,8] Definition of HBR differed from that used in the ZEUS trial and also included patients who were otherwise considered by the investigator to be candidates for implantation of a BMS instead of a drug-eluting stent owing to the perceived need to terminate DAPT at 1 month. In a total of 2,466 patients, a polymer-free Biolimus A9–coated stent was superior to a BMS with respect to the primary safety and efficacy end points when used with a 1-month course of DAPT, owing to lower TVR and MI rates.[8,11]

Finally, 1,200 patients aged 75 years or older have been included in the short duration of DAPT with Synergy II Stent in Patients Older Than 75 Years Undergoing Percutaneous Coronary Revascularization (SENIOR) trial which compared everolimus-eluting Synergy stent with BMS followed by 1- or 6-month DAPT duration in stable or unstable CAD patients, irrespective of the stent type.[9] At 12 months, the primary end point—a composite of all-cause mortality, MI, and ischemia-driven target lesion revascularization (TLR)—occurred in 16.4% of patients treated with the BMS and 11.6% among those treated with Synergy, a 29% relative reduction in risk (RR 0.71; 95% CI 0.52-0.94). There was no statistically significant difference in the risk of death, stroke, or MI at 12 months, nor was there any difference in the risk of bleeding, but TLR was higher with BMS as compared to Synergy.[9]

Therefore, current evidence[4,6,8,9] suggests that BMS should no longer be considered the device of choice in HBR patients undergoing PCI even if a relatively short BMS-like DAPT duration is anticipated. Accordingly, the European Society of Cardiology DAPT focused update recommended the use of drug-eluting stent over BMS irrespective of the planned DAPT duration with a class I level of evidence A.[2]

Investigational aspirin-free antithrombotic regimens after coronary stent implantation

Multiple studies have so far investigated the safety and efficacy of dropping aspirin shortly after coronary stent implantation, mainly in patients who have concomitant indication to OAC. A recent meta-analysis pooled 4 randomized trials including 5,317 patients assessing the strategy of DAT versus triple antithrombotic therapy (TAT) mainly in atrial fibrillation patients following PCI.[12] Compared with patients in the TAT arm, patients in the DAT arm demonstrated a 47% relative reduction in the risk of Thrombolysis in Myocardial Infarction major or minor bleeding [4.3% vs 9.0%; HR 0.53, 95% CrI 0.36-0.85]. There was apparently no difference with respect to composite or individual ischemic end points. However, the uncertainty around the point estimates for MI and ST entailed the possibility that a DAT regimen may still be associated to 2- or 3-fold higher risk of events as compared to TAT, respectively.

Moreover, the only study which limited TAT duration to 6 months and which mandated the use of the same type of OAC in both study arms did not observe an excess of bleeding events in the long-term TAT group (ISAR-TRIPLE). This observation raises the question of whether a strategy based on few months of TAT followed by a single antiplatelet therapy in conjunction with an OAC

may provide the best compromise to limiting bleeding and events while offering full ischemic protection shortly after intervention.

The most recent GLOBAL LEADERS trial is the largest trial so far testing 1 month of DAPT (aspirin with ticagrelor) versus standard DAPT after stent implantation. The trial failed to show a superiority of this new treatment strategy with respect to the primary end point of death or new Q-wave MI. Yet, it provided reassurance over the safety of new tested antiplatelet regimen. In this study, patients with concomitant indication to OAC were excluded.[13]

HBR and DAPT duration

There is no dedicated RCT assessing the optimal DAPT duration in patients at HBR. Moreover, many, if not all, available DAPT studies formally excluded these patients.

In a post hoc analysis of the Prolonging Dual Antiplatelet Treatment After Grading Stent- Induced Intimal Hyperplasia Study (PRODIGY), it was observed that patients at HBR according to the CRUSADE score treated with a 24-month DAPT experienced a 3-fold higher risk of major bleeding and a 5-fold risk of red blood cell transfusion as compared with a 6-month therapy, without clear evidence of benefit.[14,15] The number of patients needed to treat for harm in the HBR group was as low as 17 and 15 for major bleeding and red blood cell transfusion, respectively, which was lower than corresponding figures in the unselected patient cohort, suggesting that long-term DAPT has a narrow therapeutic window and high potential for harm in this selected HBR patient population. More recently, it was observed that among patients deemed at HBR based on PRECISE-DAPT, prolonged (ie, 12 months or longer) DAPT regimen was associated with no ischemic benefit but a remarkable bleeding burden as compared to 3- or 6-month DAPT, leading to a number needed to treat for harm of 38.[16] Conversely, longer treatment duration in patients without HBR was associated to a marginal or even no increase of bleeding and a significant reduction of the composite ischemic end point, with a significant interaction terms between HBR status according to the PRECISE-DAPT score and anticipated treatment benefits and risks.[16]

Ultimaster (TANSEI) stent

The Ultimaster (TANSEI) coronary stent system consists of a cobalt-chromium BMS platform featuring thin struts (80 μm).[17-19] The Ultimaster (TANSEI) platform is coated with sirolimus (3.9 μg/mm stent length) in a matrix with bioresorbable, poly(DL-lactide-co-caprolactone) polymer. A thin biocompatible, bioresorbable gradient coating is intended to reduce polymer cracking and delamination on the hinges of the stent. Within 3 to 4 months, the polymer is metabolized through the hydrolysis of DL-lactide and caprolactone into carbon dioxide and water. Because of an abluminal (outside surface) coating, the dose of drug was reduced as compared to stents coated both endo- and abluminally. Furthermore, coating only the abluminal surface leaves the luminal side of the stent free from drug and polymer, as such enhancing endothelial coverage.[20]

The Ultimaster (TANSEI) stent is the only sirolimus-eluting stent having received CE mark labeling for 1-month DAPT duration in HBR population. More precisely, the instruction for use indicates that DAPT after implantation of Ultimaster (TANSEI) stent can be discontinued earlier in case of clinical need (ie, HBR) but not before 1 month.

Methods

Study design and population

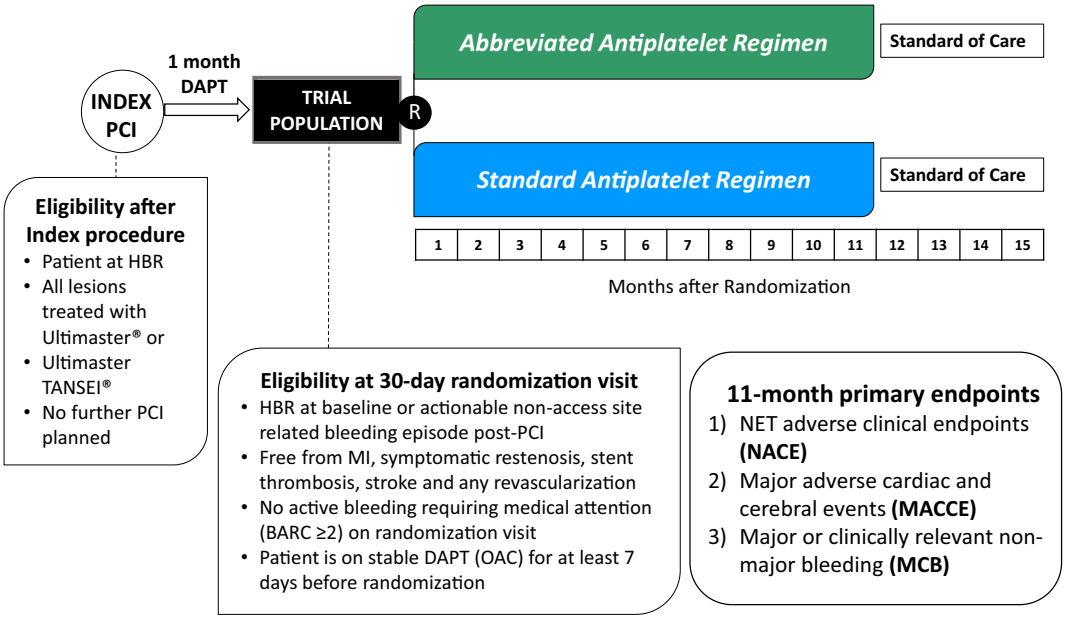
The MAnagement of high bleeding risk patients post bioresorbable polymer coated STEnt implantation with an abbReviated versus standard DAPT regimen (MASTER DAPT, clinicaltrial.gov NCT03023020) is an investigator-initiated, open-label, multicenter, randomized trial comparing an abbreviated (experimental arm) versus a standard (control group) duration of antiplatelet therapy after bioresorbable polymer-coated Ultimaster or Ultimaster TANSEI sirolimus-eluting stent implantation regardless of PCI indication in approximately 4,300 HBR patients recruited from ≥100 interventional cardiology centers across the globe. After a mandatory 30-day DAPT run-in phase, patients are randomized to (*a*) a single antiplatelet regimen until study completion or up to 5 months in patients with clinically indicated OAC (experimental 1-month DAPT group) or (*b*) continue DAPT for at least 5 months in patients without or for at least 2 months in patients with concomitant indication to OAC, followed by a single antiplatelet regimen (standard antiplatelet regimen) (Figures 1 and 2). Eligible patients are aged 18 or more, with at least 1 HBR criterion (Table I) and with all intended coronary lesions successfully treated with Ultimaster or Ultimaster TANSEI stent without flow-limiting angiographic complications which require prolonged prescription of DAPT at operator's discretion. In addition, all staged PCIs (if any) must be completed, and no further PCI should be planned.

Detailed inclusion and exclusion criteria are shown in Table II. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study; all study analyses, the drafting and editing of the paper, and its final contents.

Screening phase

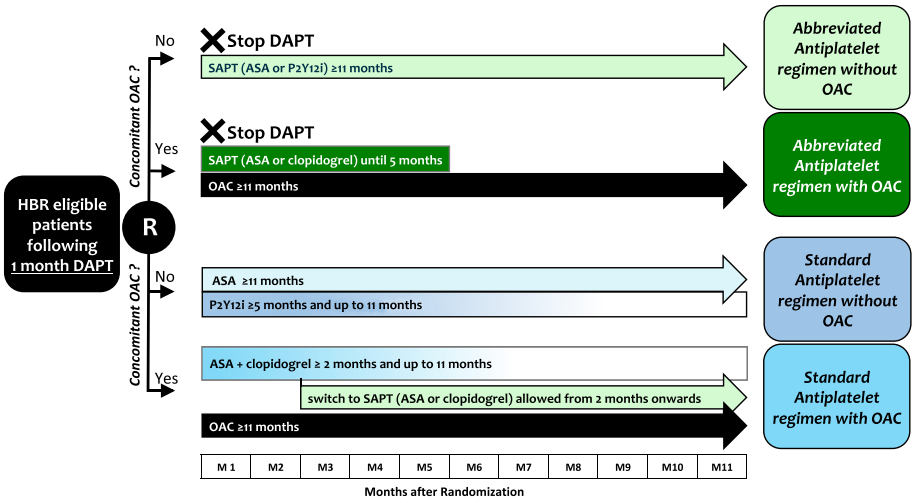
Patients are screened for inclusion from immediately after the *index procedure*—defined as either a single procedure or the last installment in planned staged procedure—and up to 1-month randomization visit, occurring between 30 and 44 days thereafter. Consenting

Figure 1



Study design and key features. Patient selection starts immediately after index PCI, and patients can be consented at any time between the index PCI and the 1-month randomization visit. After index PCI, DAPT is mandatory for 1 month. During the randomization visit, eligibility is reassessed, and if met, the patient is randomized to an abbreviated or a standard antiplatelet regimen.

Figure 2



Treatment in the experimental and control arm. In patients randomized to an abbreviated antiplatelet regimen without OAC, a single antiplatelet agent (SAPT; either ASA or P2Y12i) is continued until 11 months postrandomization. In patients requiring OAC, an SAPT (either ASA or clopidogrel) is continued until 5 months postrandomization, and OAC is prescribed until at least 11 months postrandomization. In patients randomized to a standard antiplatelet regimen without OAC, aspirin is continued until at least 11 months postrandomization. The P2Y12 inhibitor being taken at the time of randomization is continued for at least 5 months postrandomization and up to 11 months postrandomization. In patients requiring OAC, aspirin and clopidogrel are continued for at 2 months after randomization and up to 11 months postrandomization. Thereafter, a single antiplatelet (SAPT; either aspirin or clopidogrel) is continued up to 11 monthspost randomization. OAC is continued until at least 11 months postrandomization.

Table I. HBR criteria

Post-PCI patients are at HBR if at least 1 of the following criteria applies:

1. Clinical indication for treatment with OAC for at least 12 m
2. Recent (<12 m) non–access-site bleeding episode(s), which required medical attention (ie, actionable bleeding)
3. Previous bleeding episode(s) which required hospitalization if the underlying cause has not been definitively treated (ie, surgical removal of the bleeding source)
4. Age equal or greater 75 y
5. Systemic conditions associated with an increased bleeding risk (eg, hematological disorders, including a history of current *thrombocytopenia* defined as a platelet count <100.00/mm^3 (<100 × 10^9/L) or any known coagulation disorder associated with increased bleeding risk
6. Documented *anemia* defined as repeated hemoglobin levels <11 g/dL or transfusion within 4 wk before inclusion
7. Need for chronic treatment with steroids or nonsteroidal anti-inflammatory drugs
8. Diagnosed malignancy (other than skin) considered at HBR including gastrointestinal, genitourethral/renal, and pulmonary
9. Stroke at any time or TIA in the previous 6 months
10. PRECISE-DAPT score* ≥25

* PRECISE DAPT score is a 5-item bleeding risk score, developed and externally validated to predict the out-of-hospital bleeding risk while on DAPT, which integrates prior bleeding, age, white blood cell count, creatinine clearance, and hemoglobin.[16] Further details about PRECISE DAPT and online calculator can be found at http://www.precisedaptscore.com/predapt/webcalculator.html.

Table II. Inclusion and exclusion criteria

Inclusion criteria

Inclusion criteria after index PCI

1. Age ≥18 y
2. At least 1 HBR criterion (listed above)
3. All coronary lesions are successfully treated with Ultimaster (TANSEI) stent
4. Free of any flow-limiting angiographic complications which required prolonged DAPT duration based on operator's decision
5. All stages of PCI are complete (if any), and no further PCI is planned

Inclusion criteria at 1-m randomization visit (30-44 d after qualifying index PCI)

1. At least 1 HBR criterion (listed above) or on the basis of post-PCI actionable non–access-site related bleeding episode
2. Uneventful 30-d clinical course (ie, new episode of acute coronary syndrome, symptomatic restenosis, ST, stroke, any revascularization requiring prolonged DAPT)
3. If not on OAC:
   a) Patient is on DAPT regimen of aspirin and a P2Y12 inhibitor;
   b) Patient with 1 type of P2Y12 inhibitor for at least 7 d
4. If on OAC:
   a) Patient is on the same type of OAC for at least 7 d;
   b) Patient is on clopidogrel for at least 7 d

Exclusion criteria

Patients are not eligible if any of the following applies:

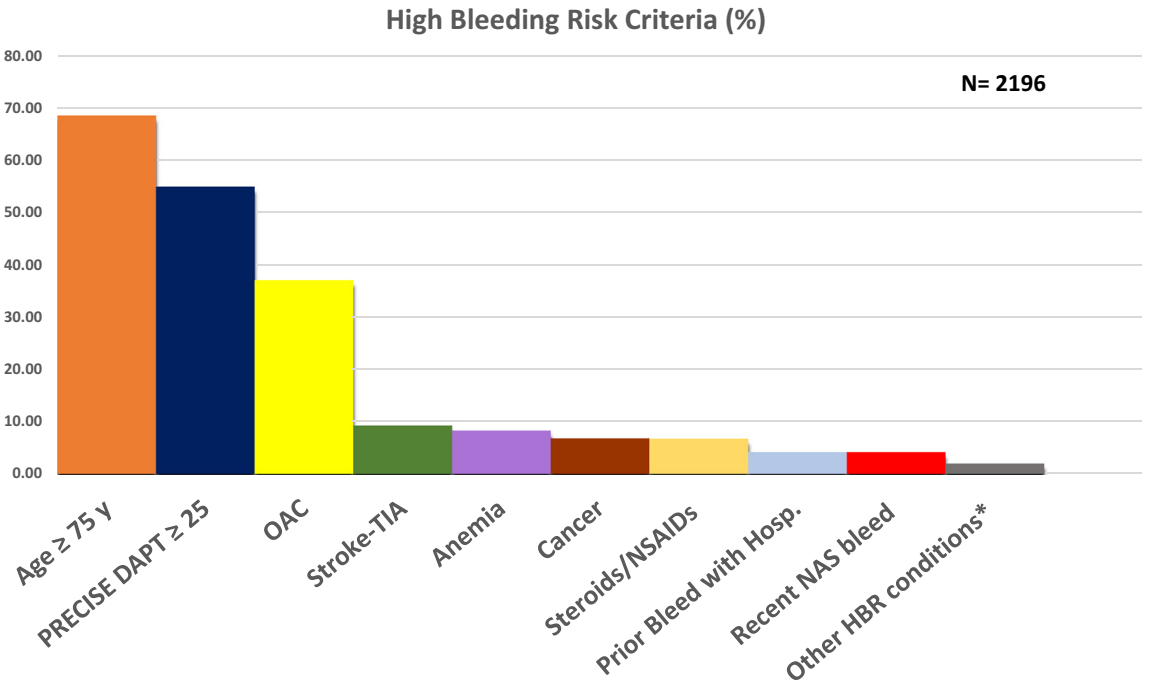
1. Treated with stent other than Ultimaster (TANSEI) stent within 6 m prior to index PCI
2. Treated for in-stent restenosis or ST at index PCI or within 6 m before
3. Treated with a bioresorbable scaffold at any time prior to index procedure
4. Incapable of providing written informed consent
5. Under judicial protection, tutorship, or curatorship
6. Unable to understand and follow study-related instructions or unable to comply with study protocol
7. Active bleeding requiring medical attention (BARC ≥2) on randomization visit
8. Life expectancy less than 1 y
9. Known hypersensitivity or allergy for aspirin, clopidogrel, ticagrelor, prasugrel, cobalt-chromium, or sirolimus
10. Any planned and anticipated PCI
11. Participation in another trial
12. Pregnant or breastfeeding women

patients are entered into the electronic case report form and further reassessed for eligibility at the time of randomization (Figure 1). Patients experiencing spontaneous MI, symptomatic restenosis, ST, stroke, or any revascularization requiring prolonged DAPT after index PCI will be excluded. Similarly, patients with ongoing bleeding during the randomization visit are deemed ineligible. Adherence to only 1 type of DAPT (ie, avoiding switching among P2Y12 inhibitors) is required for at least 7 days prior to randomization. In addition, in patients with clinically indicated OAC, adherence to 1 type of OAC (ie, avoiding switching among OACs) and to DAPT in the form of aspirin and clopidogrel is protocol mandated for ≥7 days prior to randomization.

Randomization and treatment protocol

At randomization, occurring 30 to 44 days after index PCI, patients are centrally allocated in a 1:1 ratio to an

Figure 3



Distribution of HBR criteria among randomized patients.HBR criteria are not mutually exclusive, and many patients fulfill more than 1. *: Systemic condition associated with increased bleeding risk or any known coagulation disorders associated with increased bleeding risk.

abbreviated or standard antiplatelet regimen using secuTrial data capturing system available at https://secutrial.insel.ch/apps/WebObjects/ST21-productive-DataCapture.woa/wa/. The randomization sequence is computer generated and stratified per site by a history of acute MI within 12 months prior to index PCI and use of OAC.

Abbreviated antiplatelet regimen. In the experimental arm, the DAPT regimen is immediately discontinued after randomization followed by a single antiplatelet regimen (either aspirin or P2Y12 inhibitor at discretion of the treating physician) until study completion or up to 5 months in patients with clinically indicated OAC, which is continued until at least 11 months postrandomization (Figure 2).

Standard antiplatelet regimen. In the standard antiplatelet regimen arm, patients without clinically indicated OAC continue aspirin until 11 months postrandomization plus a P2Y12i inhibitor (ie, ticagrelor, prasugrel, or clopidogrel) for at least 5 and up to 11 months postrandomization, at the discretion of the treating physician (Figure 3).

In patients with clinically indicated OAC, aspirin and clopidogrel are continued for at least 2 and up to 11 months postrandomization, at the discretion of the treating physician. Thereafter, a single antiplatelet agent (aspirin or clopidogrel) is continued up to 11 months postrandomization. OAC prescribed before randomization is continued until 11 months (Figure 3).

In both study groups, switching among antithrombotics (ie, from one P2Y12 inhibitor to another or among OACs) is discouraged, unless dictated by a clinical and documented reason.

All antiplatelet or anticoagulant treatment options are to be dosed according to the corresponding authorization for use and locally approved regimens. Daily doses of allowed antiplatelet regimens include 75-162 mg for aspirin, 75 mg for clopidogrel, 90 mg for ticagrelor bid, and 10 mg for prasugrel or 5 mg in patients weighting <60 kg or who are >75 years old. In Japan, prasugrel is approved and prescribed at a dose of 3.75 mg.

Daily doses of allowed OACs include apixaban 5 mg bid or apixaban 2.5 mg bid, if at least 2 among age ≥80 years, body weight ≤60 kg or serum creatinine level ≥1.5 mg/dL (or 133 mol/L); dabigatran 150 mg bid or 110 mg bid; edoxaban 60 mg or 30 mg if creatinine clearance is 30-50 mL/min or body weight ≤60 kg or there is concomitant use of verapamil or quinidine or dronedarone; rivaroxaban 20 mg or 15 mg qd if creatinine clearance 30-49 mL/min.

Finally, the dose intensity of vitamin K antagonist is monitored with a target international normalized ratio in

the lower part of the recommended target range, in keeping with guideline recommendations.[2]

Follow-up visits

Scheduled follow-up visits occur at 60 (±14), 150 (±14), 335 (±14), and 420 (±14) days postrandomization. All follow-up visits are preferably scheduled on-site. If the patients are unable or unwilling to visit the outpatient clinic, the scheduled visit can be replaced by telephone call except for the randomization and the 1-year visits. At each visit, self-reported adherence to study and nonstudy medications is collected together with the assessment of any cardiac or cerebrovascular ischemic or bleeding occurrences or any serious adverse event.

Study end points

This study has 3 co-primary end points, including (1) *net adverse clinical end points* (NACE) defined as the composite of all-cause death, MI, stroke, and Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding events; (2) *major adverse cardiac and cerebral events* (MACCE) defined as a composite of all-cause death, MI, and stroke; and (3) *major or clinically relevant nonmajor bleeding* (MCB) defined as a composite of types 2, 3, and 5 BARC bleeding events.

The secondary end points include the individual components of the 3 co-primary end points; the composite of cardiovascular death, MI, and stroke; the composite of cardiovascular death, MI definite or probable ST, any revascularization, transient ischemic attack, and bleeding events adjudicated according to not only the validated BARC classification[21] but also the Thrombolysis in Myocardial Infarction as well as Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) classifications.

The main analyses evaluate the occurrence of the primary end points between randomization and 11 months thereafter. Secondary analyses include the occurrence of primary end points between randomization and 15 months and other secondary end points at any time frames throughout study duration. All primary and secondary end point definitions are shown in the supplementary appendix. All primary and secondary end points are adjudicated by an independent clinical event committee (CEC) who will be blinded to randomized treatment allocation.

Statistical considerations

Main analysis of the primary end points is conducted on the full analysis set of all randomized patients according to the intention-to-treat principle based on CEC-adjudicated end points.

Rates of primary end points are estimated as the cumulative incidence from the date of randomization to 335 days (11 months) after randomization by Kaplan-Meier methods. *Rate differences* are defined as the rate in the abbreviated antiplatelet minus that in the standard antiplatelet arms.

The study is designed to test the following hypotheses: (1) an abbreviated antiplatelet regimen is noninferior to standard antiplatelet in terms of NACE, (2) an abbreviated antiplatelet regimen is noninferior to standard antiplatelet in terms of MACCE, and (3) an abbreviated antiplatelet regimen is superior to standard antiplatelet in terms of MCB. These hypotheses are tested in a hierarchical order, preserving type 1 error rate.

Based on conservative assessments of the previous evidence,[4,6-8,14,15] the event rates of NACE, MACCE, and MCB in the standard antiplatelet group are assumed to be, respectively, 12%, 8%, and 6.5% at 1 year.

Noninferiority of the abbreviated antiplatelet regimen in terms of NACE is declared if the 95% CI of the rate differences excludes 3.6%. Noninferiority of the abbreviated DAPT regimen in terms of MACCE is declared if the 95% CI of the rate differences excludes 2.4%.

With 2 × 2,050 evaluable patients, this study has >90% power to detect noninferiority of abbreviated antiplatelet for NACE, >80% power to detect noninferiority of abbreviated antiplatelet on MACE, and >90% to detect superiority of the abbreviated antiplatelet arm on MCB assuming a 35% relative risk reduction with nominal 5% type I error preserved by the sequential hierarchical testing. To compensate for 5% attrition rate, 2 × 2,150 patients are being randomized.

Predefined subgroup analyses

Prespecified subgroup analyses of the 3 primary and major secondary end points entail stratification on the need for OAC at the time of randomization, history of acute MI within 12 months prior to randomization, acute coronary syndrome as indication to index PCI, PRECISE-DAPT or DAPT scores, gender, age, diabetes mellitus, and the fulfillment of each inclusion criterion.

Study organization, timelines, and conclusions

This study is an investigator-driven clinical trial sponsored by European Cardiovascular Research Institute and supported by an unrestricted research grant from TERUMO Corporation, Tokyo, Japan. The Executive Committee (ExC) is responsible for scientific content and oversight of the study and oversees publication. The Steering Committee is comprised of the ExC and national/regional lead investigators. The Operational Committee is responsible for executing and implementing study procedures under the supervision of the ExC. The Data Monitoring Committee is an independent, multidisciplinary board composed of 3 members who are not directly involved in the conduct of the trial and is responsible for ensuring the safety of the patients participating in the clinical study. The Data Monitoring Committee members will seriously consider

recommending early termination of the trial when the abbreviated DAPT regimen would show a statistically significant increased rate of (cardiovascular) mortality or of MACCE, provided the latter is not counterbalanced by a reciprocal reduction in the rate of major bleeding. An independent, multidisciplinary, and blinded CEC is responsible for the adjudication of all investigator-reported as well as electronically triggered potential end points events from the electronic case report form. Independent study monitoring and site management are performed by Cardiovascular European Research Center (Massy, France), Cardialysis (Rotterdam, the Netherlands), and CV Quest (Tokyo, Japan). Data management, central data review, and statistical analyses will be conducted by an independent academic Clinical Trial Unit located in Bern, Switzerland. The first study patient was randomized in April 2016, and enrolment is projected to reach completion by Q4 2019. At 10th December 2018, 2,196 patients were randomized, and their distribution according to each HBR criterion is shown in Figure 3.

MASTER DAPT is the first dedicated randomized clinical trial aiming at investigating the optimal duration of antiplatelet therapy in patients with HBR features after bioresorbable polymer-coated stent implantation.

Disclosures

Dr Valgimigli reports grants from The Medicines Company and Terumo during the conduct of the study, personal fees from AstraZeneca, grants and personal fees from Terumo, personal fees from Abbott Vascular, personal fees from Bayer, personal fees from Amgen, personal fees from Cardinal health, personal fees from Biosensors, personal fees from Abbott Vascular, and personal fees from Daiichi Sankyo, outside the submitted work.

Dr Smits reports grants from Terumo, during the conduct of the study; grants and personal fees from Abbott Vascular, grants from St Jude Medical, and personal fees from Medinol, outside the submitted work.

Dr Vranckx reports personal fees from Daiichi Sankyo, personal fees from Bayer Health care, and personal fees from Biosensors, outside the submitted work.

Dr Onuma reports having been a member of advisory board of Abbott.

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Dr Spaulding reports personal fees from Terumo, during the conduct of the study; personal fees from Medtronic, personal fees from Stentys, personal fees from Boehringer, and personal fees from Amgen, outside the submitted work.

Dr Chevalier reports personal fees from Terumo, grants and personal fees from Medtronic, personal fees from Cordis, and personal fees from Biotronik, during the conduct of the study.

Dr Hildick-Smith reports Advisory for Terumo.

Dr Roffi reports institutional research grants from Terumo, Abbott Vascular, Medtronic, Boston Scientific, and Biotronik, outside the submitted work.

Dr Schultz reports grants and personal fees from Abbott Vascular and personal fees from Merck Sharp & Dome, outside the submitted work.

Dr Lesiak reports personal fees from Terumo and personal fees from AstraZeneca, outside the submitted work.

Dr James reports grants and personal fees from Astra Zeneca, grants and personal fees from Bayer, and grants and personal fees from Jansen, outside the submitted work.

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The other authors have nothing to disclose.

Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2018.10.009.

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