BMJ Open

Prospective multicentre open-label randomised controlled trial of 3-month versus 12-month dual antiplatelet therapy after implantation of the new generation biodegradable polymer sirolimus TARGET-eluting coronary stent: protocol of the TARGET DAPT trial

Hongbo Yang,[1] Feng Zhang,[1] Ji'e Yang,[1] Ming Zheng,[2] Ruifen Cao,[2] Yuxiang Dai,[1] Chenguang Li,[1] Kang Yao,[1] Juying Qian,[1] Junbo Ge ,[1] for the TARGET DAPT trial investigators

To cite: Yang H, Zhang F, Yang J, *et al*. Prospective multicentre open-label randomised controlled trial of 3-month versus 12-month dual antiplatelet therapy after implantation of the new generation biodegradable polymer sirolimus TARGET-eluting coronary stent: protocol of the TARGET DAPT trial. *BMJ Open* 2019;**9**:e033774. doi:10.1136/bmjopen-2019-033774

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-033774).

HY, FZ and J'eY contributed equally.

Received 25 August 2019
Revised 12 November 2019
Accepted 21 November 2019

For numbered affiliations see end of article.

Correspondence to
Dr Junbo Ge;
jbge@zs-hospital.sh.cn

ABSTRACT

Introduction Dual antiplatelet therapy (DAPT) with aspirin and thienopyridine is required after placement of coronary stents to prevent thrombotic complications. However, current recommendation for duration of DAPT remains controversial. Firehawk is a biodegradable polymer applied to recessed abluminal grooves, sirolimus target-eluting stent associated with early excellent healing response and almost complete strut coverage, as well as possibly reduced myocardial ischaemic events. But the optimal DAPT duration for such a new generation stent is less known. Therefore, the present trial seeks to evaluate the safety and efficacy of 3-month versus 12-month DAPT in broad patients receiving Firehawk stents.

Methods and analysis The TARGET DAPT study is designed to access the benefits and risks of short-term (3 months) versus long-term (12 months) DAPT in preventing stent thrombosis or major adverse cardiovascular and cerebrovascular events in subjects undergoing percutaneous coronary intervention for the treatment of coronary artery obstructive lesions. The TARGET DAPT trial is a large, prospective, multicentre, randomised (1:1) non-inferiority clinical trial that will enrol 2446 subjects treated with Firehawk stents. The primary endpoint is net adverse clinical and cerebral events, a composite of all-cause death, myocardial infarction, cerebral vascular accident and major bleeding (BARC 2,3 or 5) at 18 months clinical follow-up postindex procedure.

Ethics and dissemination Ethics approval was obtained from the Ethics Committee of Zhongshan Hospital, Shanghai. The reference number is B2018-146R. Study findings will be made available to interested participants. Study results will be submitted for publication in a peer-reviewed journal. Also the protocol will be submitted and approved by the institutional Ethics Committee at each participating clinical centre.

Trial registration NCT03008083

Strengths and limitations of this study

- This study will evaluate the safety and efficacy of 3-month versus 12-month dual antiplatelet therapy (DAPT) in broad patients receiving Firehawk stents.
- This study is the first public clinical study to investigate shortening duration of DAPT in China, which will provide evidence to generate antiplatelet strategy for Chinese people.
- This study undertaken in China limits its generalisability to other populations.

INTRODUCTION

Compared with bare-metal stent, drug-eluting stent (DES) has significantly reduced the risks of in-stent restenosis and target lesion revascularisation.[1 2] However, two major problems of DES implantation are stent thrombosis (ST) and in-stent restenosis, which are associated with death and myocardial infarction (MI). Delayed vessel healing after DES implantation is reported to be associated with higher rates of ST, making dual antiplatelet therapy (DAPT) even more important for DES era.[3] Previously, studies demonstrated that MI events occurred less in long-term DAPT than short-term DAPT.[4 5] With the development of stents and eluting drugs, ST was limited

to <1.0% through 2 years.[6 7] However, prolonged DAPT might be associated with several shortcomings, including bleeding complications, patients' poor compliance and high costs. Plenty of studies concerned with the duration of DAPT.[8–18] Some of them tried to determine whether P2Y12 inhibitor monotherapy after 1–3 months of DAPT is non-inferior to 12 months of DAPT in patients undergoing percutaneous coronary intervention (PCI). And the results indicated that short-term DAPT was non-inferior to the 12-month therapy at 1 year.[9 11 15–17] In addition, the recent STOPDAPT-2,[15] SMART-CHOICE[16] and TWILIGHT[17] studies demonstrated that short-term DAPT could effectively decrease bleeding complications. It may reduce patients' costs and improve patients' compliance. Therefore, following elective stent implantation 6-month instead of 12-month DAPT consisting of thienopyridine plus aspirin is recommended by European Society of Cardiology/European Association for Cardio-Thoracic Surgery in 2018.[19]

The Firehawk stent is a balloon-expandable L605 cobalt-chromium stent with a strut thickness of 86 µm. Biodegradable polylactic acid polymers containing sirolimus were eluted in the abluminal grooves on the outside surface of the stent. The sirolimus density is 0.30 µg/mm², and 90% of the drug releases over 90 days.[20] The unique design reduces polymer exposure to the vessel wall and allows a timed and target drug release. The Firehawk stent is a thin-strut DES with the lowest drug and bioresorbable polymer load of all DES on the market.[21 22] Therefore, Firehawk stent is capable of inhibiting smooth muscle cell proliferation, maintaining early healing, promoting endothelial cell recovery and minimising inflammatory response. Recently, an authorised trial demonstrated that the safety and efficacy of the Firehawk stents were comparable to XIENCE everolimus eluting stents in all-comers population of coronary artery disease patients.[21] The percentage of covered struts was 99.9% and malapposed struts were <1.2% in Firehawk stents at 90 days based on optical coherence tomography.[23] Early excellent healing response and almost complete strut coverage suggested that 3-month DAPT after PCI might be safe for the Firehawk stents.

Therefore, TARGET DAPT trial is promising to provide more data in terms of safety and clinical impact of short-term (3 months) DAPT in patients treated with Firehawk stent. This is the first study of Firehawk stent to assess short-term duration of DAPT following biodegradable polymer sirolimus-eluting stents.

Methods and analysis

Study design and hypothesis

The TARGET DAPT trial was a prospective, multicentre, clinical randomised trial evaluating different durations of DAPT (aspirin plus clopidogrel/ticagrelor) in patients undergoing PCI with Firehawk implantation for treatment of coronary artery lesions. The objective of the TARGET DAPT study was to investigate the clinical implications of short-term (3 months) versus long-term (12 months) DAPT in real-world patients treated with Firehawk. The study hypothesis was that short-term (3 months) DAPT is non-inferior in clinical outcomes as compared with long-term (12 months) DAPT in patients undergoing Firehawk implantation, including a high-bleeding risk population.

Study population

The study population consisted of patients treated solely with Firehawk stents. Major exclusion criteria include subjects suffered from ST-segment Elevation Myocardial Infarction (STEMI), planned surgery necessitating discontinuation of antiplatelet therapy within the 18 months after enrollment, planned to undergo revascularisation within 18 months, previous PCI and specific lesions (left main, grafts and in-stent restenosis). A complete list of inclusion and exclusion criteria is detailed in table 1.

Randomisation

With written informed consent, patients meeting the eligible criteria were randomised in a 1:1 ratio to short-term (3 months) or long-term (12 months) DAPT in 40 clinical centres in China (figure 1). The enrollment and random assignment should be implemented within 4 hours after the index-procedure with a dedicated web-based system. The index-procedure time and randomisation time was recorded as network time in burning disc and stochastic system. Patients will be enrolled from December 2018 to December 2020. Treatment allocation was stratified by centres and presence of diabetes mellitus. A dedicated web-based system was used for conducting randomisation and electronic data capture throughout the study. Interventions were performed according to the current standard guidelines.

For patients who were not taking aspirin (100 mg/day) and P2Y12 inhibitor (clopidogrel 75 mg/day or ticagrelor 90 mg two times per day) routinely, a loading dose of aspirin (300 mg) and P2Y12 (clopidogrel 300 mg or ticagrelor 180 mg) is prescribed at least 4 hours prior to procedure. In our centre, patients with acute coronary syndrome (ACS) or at relatively high risk for ischaemic events will be recommended ticagrelor. Patients with stable coronary artery disease (CAD) or high bleeding risk will be recommended clopidogrel. About 80% of patients who underwent PCI received clopidogrel plus aspirin therapy, while 20% of patients received ticagrelor plus aspirin therapy. DAPT with aspirin 100 mg/day and clopidogrel 75 mg/day or ticagrelor 90 mg two times per day was continued according to randomisation scheme (3 or 12 months) after Firehawk stent implantation. All the enrolled patients will be maintained on 100 mg of aspirin indefinitely, regardless of allocated group. Clopidogrel or ticagrelor discontinuation complied with the randomisation, and 100 mg/day aspirin was recommended. This study is an open-label study. We will enhance telephone and interview follow-up to guarantee medication regimen according to the protocol.

Table 1 Inclusion and exclusion criteria

Inclusion criteria	
Clinical	1. Age ≥18 years.
	2. Subjects (or legal guardians) understanding the testing requirements and procedures, and providing written informed consent.
	3. Subjects with symptomatic coronary artery disease or confirmed asymptomatic ischaemia.
	4. Target lesion should be a new lesion with visually estimated reference diameter ≥2.5 mm and ≤4.0 mm in autologous coronary artery.
	5. Subjects willing to accept PCI therapy and to implant Firehawk stent only.
	6. LVEF ≥30%.
	7. Subjects willing to accept the trial plan calls for all subsequent evaluations.
Exclusion criteria	
Clinical	1. Subjects with ST-segment elevation MI.
	2. Subjects having an organ transplant or waiting for an organ transplant.
	3. Subjects receiving chemotherapy or going to receive a chemotherapy within 30 days after PCI.
	4. Subjects undergoing chronic (over 72 hours) anticoagulant therapy (such as heparin and coumarin) other than acute coronary syndrome.
	5. Subjects with abnormal counts of platelet and WBC (investigator assesses clinical significance and combines it with normal reference range of laboratory)
	6. Subjects with confirmed or suspected liver disease, including hepatitis lab results.
	7. Subjects with elevated serum creatinine level >3.0 mg/dL or undergoing dialysis therapy.
	8. Subjects with active peptic ulcer, active GI bleeding or other bleeding diathesis or coagulopathy, or refused a blood transfusion.
	9. Subjects with CVA or TIA in the past 6 months, or with permanent nerve defects.
	10. Subjects undergoing any PCI treatment in target vessels within 12 months prior to baseline.
	11. Subjects planned to undergo PCI or CABG within 18 months after the baseline PCI.
	12. Subjects with a history of any coronary endovascular brachytherapy treatment previously.
	13. Subjects associated with drugs allergy (such as sirolimus, or structure-related compounds fluorinated polymers, thienopyridine or aspirin).
	14. Subjects being suffered from other serious illness (such as cancer, congestive heart failure), which may cause drop in life expectancy to <18 months.
	15. Subjects with a history of drug abuse (such as alcohol, cocaine, heroin, etc).
	16. Subjects planned to undergo any operations that may lead to confuse with the programme.
	17. Subjects participating in another study of drug or medical device which did not meet its primary endpoint.
	18. Subjects planning for pregnancy within 18 months after baseline.
	19. Pregnant or breastfeeding women.
Angiographic	1. Target lesions with the following criteria: left main, saphenous vein grafts or arterial grafts and in-stent restenosis.
	2. Unprotected left main coronary artery disease (diameter stenosis >50%).
	3. Protected left main coronary artery disease(diameter stenosis >50% and undergoing CABG) with target lesions located in left anterior descending artery and left circumflex artery.
	4. Additional lesions of clinical significance possibly needing interventional within 18 months after enrollment.

CABG, Coronary artery bypass grafting; CVA, cerebral vascular accident; GI, gastrointestinal; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack; WBC, white blood cell.

Study endpoints and follow-up

The primary endpoint is net adverse clinical and cerebral events (NACCE), a composite of all-cause death, MI, cerebral vascular accident (CVA) and major bleeding (BARC 2,3 or 5) at 18 months. The secondary endpoint is the overall cost-effectiveness of the 3-month DAPT group versus 12-month DAPT group at 18 months. The cost was composed of index procedure cost, antiplatelet cost and hospitalisation costs associated with net adverse clinical and cereberal events (NACCE) within 18 months. Other endpoints estimated in hospital, at 1, 3, 6, 12, 18, 24 and 36 months of follow-up include: (1) target vessel

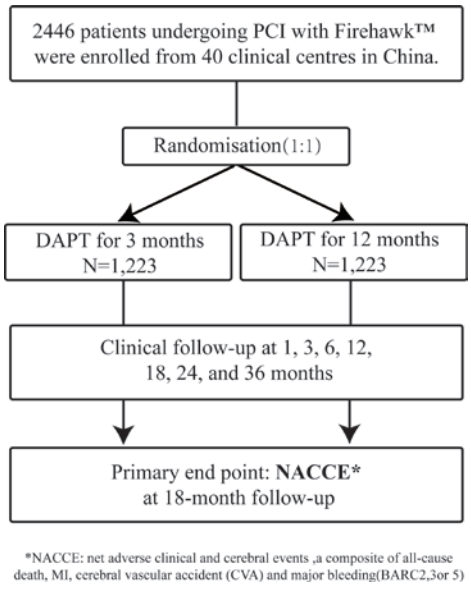

Figure 1 TARGET DAPT study design flow chart. DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention.

revascularisation; (2) target lesion revascularisation; (3) target vessel failure; (4) target lesion failure; (5) major adverse cardiac and cerebral events; (6) NACCE; (7) MI; (8) death (all-cause, cardiac, non-cardiac); (9) cardiac death/all MI; (10) major bleeding (BARC 2,3 or 5) (per the definition of Bleeding Academic Research Consortium); and (11) definite/probable ST (per the definition of Academic Research Consortium). We will perform secondary landmark analyses from 3 to 12 months and from 12 to 18 months. All patients will receive follow-up at 1, 3, 6, 12, 18, 24 and 36 months. Interview follow-up is set at 3, 12 and 18 months. Other timing follow-up could be interview or telephone follow-up.

Statistical design and analytic approach

Sample size calculations

Based on the event rates and previous data involving a real-world patient population treated with DES,[8 18 24–27] we predicted the NACCE rates of the 3-month DAPT group and the 12-month DAPT group to be at least 10.0% at 18 months after the index PCI. The non-inferiority margin is of 3.5%. We estimated that with a total of 2446 patients (1223 per group), the power of the study would be at 80.2% to detect non-inferiority with a 1-sided type I error rate of 0.025, assuming that 5% of patients would be lost to follow-up.

Statistical hypothesis and analysis

- H0 (null): $\mu_{group\ A} - \mu_{group\ B} \geq \delta$;
- H1 (alternative): $\mu_{group\ A} - \mu_{group\ B} < \delta$; (Non-inferior);

where $\mu_{group\ A}$ and $\mu_{group\ B}$ are the 18-month NACCE rates for the 3-month DAPT (test) and 12-month DAPT (control) groups, respectively, and δ is the non-inferiority margin. The intent-to-treat (ITT) population will be used for the primary analysis of the primary endpoint (NACCE at 18 months). The ITT population will also be used for the primary analysis of all secondary clinical endpoints. A secondary analysis of the primary endpoint and all others clinical endpoints will also be conducted in the per protocol population. A two-group Z test will be used to test the one-sided hypothesis of non-inferiority in proportions. If the p value from the one-sided Z test is <0.025, the 3-month DAPT (test) group will be concluded to be non-inferior to 12-month DAPT (control) group. This corresponds to the one-sided upper 97.5% confidence bound on the difference between treatment groups in 18-month NACCE rates (the 3-month DAPT – 12-month DAPT) being less than δ. Continuous variables were analysed using the Student's t-test or the Mann-Whitney U test, and categorical variables were compared using the $\chi 2$ test or Fisher's exact test, as appropriate. Cumulative event rates were estimated using the Kaplan-Meier methods and were compared by the log-rank test. Adjusted hazard rates were compared with multivariable Cox proportional hazards regression. All analyses were performed using SAS software version 9.2 or above (SAS Institute).

Study organisation

Study Steering Committee

The study Steering Committee is formed by the chairman and principal investigators of the study, representative(s) from the Sponsor and from the Clinical Research Organization (CRO). The study Steering Committee is responsible for managing the scientific aspects of the study (review and approval of the protocol and study design; review of trial progression and so on). The study Steering Committee interacts with the Sponsor and the CRO on study progress and related issues.

Data Safety Monitoring Board (DSMB)

DSMB is an independent committee whose members are not affiliated with any (interventional) cardiology site enrolling subjects into the trial, are not participating in the trial and will declare any conflicts of interest should they arise. Serious adverse events (events leading to serious disability or admission to hospital, life-threatening events or death) will be periodically reviewed and analysed by an independent DSMB. The composition, guiding policies and operating procedures governing the DSMB are described in a separate DSMB Charter. Based on safety data, the DSMB may recommend that the Steering Committee should modify or stop the clinical trial. All final decisions regarding clinical trial/investigation modifications, however, rest with the Steering Committee. All analyses are carried out aiming to protecting the safety of the trial participants. If the data at hand suggest a substantial safety concern about the study treatment strategy, the DSMB will carefully balance the observed risk profile against possible signs of improved efficacy.

Events Adjudication Committee (EAC)

EAC is an independent committee comprised of interventional cardiologists who are not participants in the study. The EAC is responsible for the categorisation of

death, MI, CVA and bleeding based on the definitions in the protocol. Prior to any EAC activity, a EAC Charter will be developed, which will describe the events to be adjudicated, the minimum amount of data required and the algorithm followed in order to classify the events.

Patient and public involvement

Patients and the public are not involved in the design or conduct of the study or the outcome measures, and no attempt will be made to assess the burden of intervention on the patients themselves. To further facilitate the recruitment of patients and inform patients and their partners, advertisement of this study will be done by posters in the wards. All participants are asked if they want to be informed about the results of the study during the informed consent procedure. If required, they will receive a summary of the results.

ETHICS AND DISSEMINATION

Printed informed consent and detailed information about the study will be offered to all patients before randomization. All information and data of this trial are encrypted and stored in an online database accessible only to main researchers and administrators. Patients primarily enrolled have rights to withdraw at any time point and the reasons will be documented. If patients in short-term group decided to withdraw, traditional 12-month DAPT would be adopted. The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request. The findings of the study will be disseminated at (inter) national conferences and published in peer-reviewed journals.

The TARGET DAPT Study is a randomised, open-label, parallel group, clinical trial designed to provide a definitive efficacy and safety comparison of 3-month versus 12-month duration of DAPT after PCI with the new generation biodegradable polymer sirolimus TARGET-eluting coronary stent.

TRIAL STATUS

Recruitment was started in January 2019 and is estimated to be completed in December 2023.

Author affiliations
[1]Department of Cardiology, Zhongshan Hospital, Fudan University; Shanghai Institute of Cardiovascular Diseases, Shanghai, China
[2]Shanghai MicroPort Medical Group Co, Ltd, Shanghai, China

Acknowledgements The authors extend their thanks to all participating centres, hospitals and researchers in the TARGET DAPT study.

Collaborators Jincheng Guo, Wei Yang, Xi Su, Liansheng Wang, Biao Xu, Yizu Yuan, Jianhong Tao, Yitong Ma, Jianan Wang, Zhaofen Zheng, Yanqing Wu, Chunyu Zeng, Zheng Zhang, Zhixiong Zhong, Liyue Wang, Yaojun Zhang, Yong Xia, Xiwen Zhang, Yawei Xu, Guidong Xu, Hong Jiang, Yujie Zhou

Contributors JG initiated the study. HY, FZ, J'eY, MZ, RC and JQ contributed to planning and design. HY, FZ and J'eY drafted the study protocol and design. All authors are involved in the design of the study. HY, FZ, J'eY, YD, CL and KY perform statistical analysis and are responsible for daily research management and communications through clinical centres. JG is the supervisor of the project. All authors read and approved the final manuscript.

Funding This study was sponsored by Shanghai MicroPort Medical Co., Ltd., Shanghai, China. The role of the sponsor includes study design, overseeing, logistic support, and review of study reports. Contact: Ming Zheng, MD (86)(10)66513642-6229 mzheng@microport.com

Competing interests JG has received research grants and speaker fees from MicroPort. HY and FZ have received speaker fees from MicroPort. MZ and RC are Microport employees.

Patient consent for publication Not required.

Ethics approval This study complied with the Declaration of Helsinki regarding investigation in humans and its protocol was submitted and approved by the institutional Ethics Committee at each participating clinical centre. The study protocol and other associated documents have been approved by the Ethics Committee of Zhongshan Hospital, Shanghai. The reference number is B2018-146R

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Junbo Ge http://orcid.org/0000-0002-9360-7332

REFERENCES

1 Moses JW, Leon MB, Popma JJ, *et al*. Sirolimus-Eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315–23.
2 Stone GW, Ellis SG, Cox DA, *et al*. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221–31.
3 Mauri L, Hsieh W-hua, Massaro JM, *et al*. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med* 2007;356:1020–9.
4 Mauri L, Kereiakes DJ, Yeh RW, *et al*. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *N Engl J Med* 2014;371:2155–66.
5 Hahn J-Y, Song YB, Oh J-H, *et al*. 6-Month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial. *Lancet* 2018;391:1274–84.
6 Brener SJ, Kirtane AJ, Stuckey TD, *et al*. The impact of timing of ischemic and hemorrhagic events on mortality after percutaneous coronary intervention. *JACC: Cardiovascular Interventions* 2016;9:1450–7.
7 Kandzari DE, Koolen JJ, Doros G, *et al*. Ultrathin Bioresorbable polymer sirolimus-eluting stents versus thin durable polymer everolimus-eluting stents. *J Am Coll Cardiol* 2018;72:3287–97.
8 Gwon H-C, Hahn J-Y, Park KW, *et al*. Six-Month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the efficacy of Xience/Promus versus Cypher to reduce late loss after stenting (excellent) randomized, multicenter study. *Circulation* 2012;125:505–13.
9 Valgimigli M, Campo G, Monti M, *et al*. Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. *Circulation* 2012;125:2015–26.
10 Feres F, Costa RA, Abizaid A, *et al*. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: the optimize randomized trial. *JAMA* 2013;310:2510–22.
11 Stefanini GG, Byrne RA, Serruys PW, *et al*. Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and leaders randomized trials. *Eur Heart J* 2012;33:1214–22.
12 Kim B-K, Hong M-K, Shin D-H, *et al*. A new strategy for discontinuation of dual antiplatelet therapy: the reset trial (real safety and efficacy of 3-month dual antiplatelet therapy following endeavor zotarolimus-eluting stent implantation). *J Am Coll Cardiol* 2012;60:1340–8.

13 Kandzari DE, Barker CS, Leon MB, *et al*. Dual antiplatelet therapy duration and clinical outcomes following treatment with zotarolimus-eluting stents. *JACC: Cardiovascular Interventions* 2011;4:1119–28.
14 Park S-J, Park D-W, Kim Y-H, *et al*. Duration of dual antiplatelet therapy after implantation of drug-eluting stents. *N Engl J Med* 2010;362:1374–82.
15 Watanabe H, Domei T, Morimoto T, *et al*. Effect of 1-Month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI. *JAMA* 2019;321:2414–27.
16 Hahn J-Y, Song YB, Oh J-H, *et al*. Effect of P2Y12 inhibitor monotherapy vs dual antiplatelet therapy on cardiovascular events in patients undergoing percutaneous coronary intervention. *JAMA* 2019;321:2428–37.
17 Mehran R, Baber U, Sharma SK, *et al*. Ticagrelor with or without aspirin in high-risk patients after PCI. *N Engl J Med Overseas Ed* 2019;381:2032–42.
18 Frigoli E, Smits P, Vranckx P, *et al*. 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. *Am Heart J* 2019;209:97–105.
19 Neumann F-J, Sousa-Uva M, Ahlsson A, *et al*. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J* 2019;40:87–165.
20 Gao R-L, Xu B, Lansky AJ, *et al*. A randomised comparison of a novel abluminal groove-filled biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: clinical and angiographic follow-up of the target I trial. *EuroIntervention* 2013;9:75–83.
21 Lansky A, Wijns W, Xu B, *et al*. Targeted therapy with a localised abluminal groove, low-dose sirolimus-eluting, biodegradable polymer coronary stent (target all Comers): a multicentre, open-label, randomised non-inferiority trial. *The Lancet* 2018;392:1117–26.
22 Dudek D, Dziewierz A, Stone G, *et al*. The year in cardiology 2018: coronary interventions. *Eur Heart J* 2019;40:195–203.
23 Baumbach A, Lansky AJ, Onuma Y, *et al*. Optical coherence tomography substudy of a prospective multicentre randomised post-market trial to assess the safety and effectiveness of the Firehawk cobalt-chromium coronary stent (rapamycin target-eluting) system for the treatment of atherosclerotic lesions: target all Comers. *EuroIntervention* 2018;14:1121–8.
24 Brener SJ, Kirtane AJ, Stuckey TD, *et al*. The impact of timing of ischemic and hemorrhagic events on mortality after percutaneous coronary intervention: the ADAPT-DES study. *JACC Cardiovasc Interv* 2016;9:1450–7.
25 Valgimigli M, Patialiakas A, Thury A, *et al*. Zotarolimus-Eluting versus bare-metal stents in uncertain drug-eluting stent candidates. *J Am Coll Cardiol* 2015;65:805–15.
26 Ariotti S, Adamo M, Costa F, *et al*. Is bare-metal stent implantation still justifiable in high bleeding risk patients undergoing percutaneous coronary intervention?: a Pre-Specified analysis from the Zeus trial. *JACC Cardiovasc Interv* 2016;9:426–36.
27 Urban P, Meredith IT, Abizaid A, *et al*. Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med* 2015;373:2038–47.