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Optimal antiplatelet therapy for prevention of gastrointestinal injury evaluated by ANKON magnetically controlled capsule endoscopy: Rationale and design of the OPT-PEACE trial

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Background Gastrointestinal injury is a common complication in patients treated with antiplatelet agents after percutaneous coronary intervention (PCI). However, the effects of different antiplatelet regimens on the incidence and severity of gastrointestinal injury have not been well studied, principally due to the lack of a low-risk sensitive and accurate detection system.

Trial design OPT-PEACE is a multicenter, randomized, double-blind, placebo-controlled trial. Gastrointestinal injury will be evaluated with the ANKON magnetically controlled capsule endoscopy system (AMCE), a minimally invasive approach for detecting mucosal lesions in the stomach, duodenum and small intestine. Patients without AMCE-detected gastrointestinal erosions, ulceration or bleeding after drug-eluting stent implantation are enrolled and treated with open-label aspirin (100 mg/d) plus clopidogrel (75 mg/d) for 6 months. Thereafter, 480 event-free patients will undergo repeat AMCE and are randomly assigned in a 1:1:1 ratio to receive aspirin plus clopidogrel, aspirin plus placebo or clopidogrel plus placebo for an additional 6 months. A final AMCE is performed at 12 months. The primary endpoint is the incidence of gastric or intestinal mucosal lesions (erosions, ulceration, or bleeding) within 12 months after enrollment.

Conclusions OPT-PEACE is the first study to investigate the incidence and severity of gastrointestinal injury in patients receiving different antiplatelet therapy regimens after stent implantation. This trial will inform clinical decision-making for personalized antiplatelet therapy post-PCI. (Am Heart J 2020;228:8-16.)

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is the cornerstone for prevention of atherothrombosis after percutaneous coronary intervention (PCI) in patients with coronary artery disease.[1,2] However, antiplatelet therapy (APT) may have serious adverse consequences, the most common of which is gastrointestinal mucosal injury with ulceration and bleeding.[3,4] The frequency of gastrointestinal complications increases with increasing duration of DAPT.[3] Trials in patients treated with contemporary drug-eluting stents (DES) have demonstrated that shortened DAPT regimens reduce the risk of major bleeding with (in most studies) similar ischemic risk.[5-9] However, the optimal duration of DAPT remains controversial, and the true impact of prolonged DAPT on gastrointestinal injury is unknown. In addition, proton pump inhibitors (PPI), which may reduce gastrointestinal bleeding,[10] have been inconsistently used and reported in prior studies. Although replacing DAPT with aspirin or clopidogrel monotherapy may prevent recurrent bleeding,[11] in most prior studies major bleeding rates have been low and the absolute risk reductions of routine abbreviated DAPT regimens have been small.

Gastrointestinal injury (erosion, ulceration or subclinical bleeding) likely occurs with much greater incidence than overt bleeding, and may be a sensitive surrogate of antiplatelet agent safety. However, studies examining the risk of APT on gastrointestinal injury have not been performed due to the invasive nature of

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endoscopy. Moreover, gastroenterologists may decline to perform gastroscopy in patients on DAPT given the bleeding risk. Finally, upper endoscopy can only detect lesions in the stomach and duodenum, as it does not visualize the remainder of the small intestine. Thus, the extent to which a shortened DAPT strategy reduces primary gastrointestinal mucosal injury (with or without overt bleeding) and whether aspirin or clopidogrel monotherapy is safer are unknown.

ANKON® magnetically controlled capsule endoscopy (AMCE) is a minimally invasive, active controlled system capable of visualizing the stomach and entire small intestine. Patient acceptance of AMCE is higher than standard endoscopy as the procedure involves only swallowing a small capsule endoscope. Discontinuation of antiplatelet drugs during AMCE is not necessary. Previous studies have confirmed that the sensitivity and specificity of AMCE for the detection of focal lesions of the gastrointestinal tract are similar compared with standard endoscopy.[12-15] We are therefore performing a double-blind, placebo-controlled randomized trial examining the incidence of gastrointestinal injury evaluated by AMCE in patients treated with a 12-month DAPT regimen versus a 6-month DAPT regimen followed by 6 months of aspirin monotherapy or clopidogrel monotherapy after DES implantation.

Study design and methods

Study objectives and hypothesis

The principal hypothesis of the trial is that following 6 months of DAPT, antiplatelet monotherapy with aspirin or clopidogrel between 6 and 12 months after DES implantation is superior to 12 months of DAPT for preventing gastrointestinal injury detected by AMCE. Thus, the primary study objective is to determine the risks of 12 months of DAPT vs a 6 months of DAPT followed by 6 months of aspirin monotherapy or clopidogrel monotherapy on gastrointestinal mucosal injury after DES implantation. The secondary objective is to evaluate the feasibility and safety of AMCE as a method for detecting gastrointestinal mucosal injury and bleeding in patients receiving APT.

In addition, an exploratory objective is to establish a gastrointestinal mucosal injury scoring system that may identify patients at future risk for clinical gastrointestinal bleeding during long-term APT. For this purpose, 2 previously developed scoring systems will be used to assess the degree of mucosal injury observed by AMCE: (1) The modified Lanza score (MLS),[16] and (2) a separate 5-point scoring system[17] (Table I).

Table I. Scoring systems to assess gastrointestinal mucosal injury

I. The modified Lanza score to assess gastric mucosal injury

Category	Score
No erosion	0
1–2 erosions localized in the gastric antrum, body or bottom	1
3–5 erosions localized in one area of the stomach	2
Erosions localized in 2 different areas of the stomach (total 6–9 lesions)	3
Gastric ulcer or ≥ 10 erosions	4

II. Five-point scoring system to assess intestinal mucosal injury

Category	**Score**
Normal	0
Petechiae/red spot (demarcated, usually circular, area of crimson mucosa with preservation of villi)	1
Small number of erosions (1–4 erosions)	2
High number of erosion (>4 erosions)	3
Mucosal breaks (large erosion and/or ulcer)	4

Study organization

OPT-PEACE is a multicenter, randomized, double-blind, placebo-controlled trial. The trial organization and key committees appear in the Appendix. The investigator team at each center consists of cardiologists and gastroenterologists or endoscopists. Executive and steering committees are responsible for the medical, scientific, and operational conduct of the study. The executive committee is responsible for the integrity of data analysis and reporting of results. An independent clinical events committee will adjudicate all cardiovascular and gastrointestinal events. Endoscopic images will be analyzed by an independent core laboratory.

An independent data safety monitoring board (DSMB) will review unblinded interim data at regular intervals. The data to be reviewed will consist of gastrointestinal mucosa lesions, all bleeding, major adverse cardiovascular events, stent thrombosis as well as other serious adverse events, in order to identify potential safety issues. Based on the safety data, the DSMB may advise the Steering Committee if, in their view, the randomized data provide evidence that may warrant early termination for either efficacy or safety. All final decisions regarding trial modifications rest with the Executive Committee.

The OPT-PEACE trial is approved by the institutional ethics committee of the General Hospital of Northern Theater Command and is conducted in accordance with the Declaration of Helsinki. The study is registered at Clinicaltrials.gov (Identifier: NCT03198741).

The OPT-PEACE trial is supported by the China national key R&D project (contract no. 2016YFC1301300, 2016YFC1301303) and an investigator-initiated grant by ANKON Medical Technologies (Shanghai, China). The company is not involved in the study design, study processes, including site selection and management, data collection and analysis or decision to submit for publication. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final

Table II. Study enrollment criteria

Inclusion criteria (all must be present)*:

1) Adult patients with age 18–80 years;
2) Presentation with silent ischemia, stable angina, or non-ST-segment elevation acute coronary syndrome with GRACE score< 140 at admission;
3) PCI with implantation of contemporary drug-eluting stent(s)** during the present admission;
4) Complete revascularization (successful PCI treatment of all epicardial coronary lesions with diameter stenosis >70% or intermediate lesions with FFR ≤0.80);
5) Planned DAPT with aspirin and clopidogrel for at least 6 months;
6) Agreement to comply with all study procedures;
7) Written informed consent provided.

Exclusion criteria (all must be absent):
1) Presentation with STEMI;
2) Left main disease (diameter stenosis >30%);
3) Any prior coronary stent implantation during the last year prior to the index procedure;
4) Implantation of first-generation drug-eluting stents or bioabsorbable scaffolds during the index procedure;
5) Implantation of >4 stents during the index procedure;
6) Any prior stent thrombosis;
7) Any active gastrointestinal bleeding or ulcers, or prior gastrointestinal bleeding or ulcers within the last 24 months;
8) Prior gastrointestinal tract or abdominal surgery other than simple procedures which would not change the gastrointestinal tract anatomy, such as polyp removal, cholecystectomy or appendectomy;
9) Contraindications to the AMCE test, including suspected or known gastrointestinal obstruction, stenosis, fistula, diverticula, etc; presence of gastrointestinal obstruction symptoms such as pain or dysphagia; inoperative conditions or refusal to undergo abdominal surgery if required (ie, if the capsule will not pass and cannot be removed by endoscopy);
10) Severe hemorrhoids (phase 3–4 according to guidelines of American Society of Colon and Rectal Surgery);
11) LVEF <0.40 on admission by echocardiography;
12) Renal dysfunction (eGFR <30 ml/min/1.73m^2);
13) Active hepatitis or ALT >3 times upper limits of normal at admission;
14) Uncontrolled severe hypertension (>180/110 mmHg);
15) Hemoglobin <100 g/L;
16) Platelet count <100 × 10^9/L;
17) Planned use of a proton pump inhibitor, gastric mucosa protectant or any other antacid agent after study enrollment ;
18) Required use of oral anticoagulation (warfarin or other factor II or factor X inhibitors);
19) Inability to take 12-month DAPT for any reason;
20) Mandatory use of >6-month DAPT;
21) Any comorbidity with estimated survival time< 12 months (eg, progressive cancer, chronic obstructive lung disease, etc);
22) Any contraindication to MRI examination, including implantation of an MRI-incompatible pacemaker, defibrillator, or other ferromagnetic material, etc;
23) Pregnant or plan to be pregnant within 1 year;
24) Any condition that may interfere with any study procedures, such as dementia, immobility, alcohol use, etc;
25) Planned surgery within 1 year;
26) Taking iron supplement;
27) Participating in any other clinical trial of an investigational drug or device that has not met its primary endpoint.

* Patients who are unable to comply with the baseline AMCE test, or in whom a suboptimal baseline AMCE test result is obtained (inadequate visualization of the upper GI tract for any reason) are excluded from the study. The analysis population will consist of the modified intention-to-treat (ITT) population, consisting of all patients with an evaluable AMCE test at baseline.

** Contemporary DES refers to DES with thin cobalt-chromium or platinum-chromium struts, with a durable or biodegradable polymer eluting a rapamycin-analogue antiproliferative agent. The current major DES available in China market include: EXCEL and EXCEL 2 (JW Medical System, Weihai, China), Tivoli(Essen Technology, Beijing, China), Endeavor Resolute (Medtronic Inc, Minnesota, USA), FireHawk (MicroPort Medical (Group) Co, Ltd, Shanghai, China), BuMA (SinoMedical, China), Xience V (Abbott, Abbott Park, Illinois, USA), Xience Prime (Abbott Laboratories, Abbott Park, Illinois, USA), Promus Element and Synergy (Boston Scientific, Massachusetts, USA)].

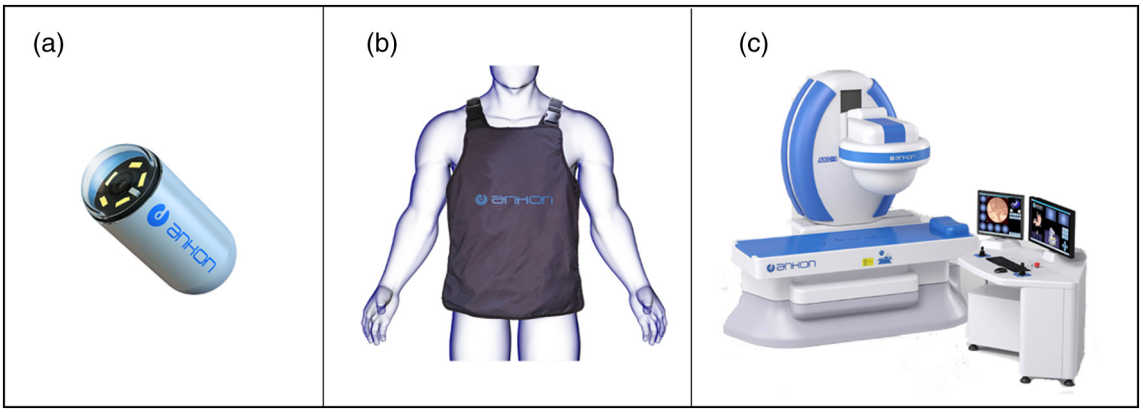
contents. None of the authors have any financial or other relationships with ANKON Medical Technologies.

Study population and AMCE procedure

Patients with either stable coronary artery disease or low-risk acute coronary syndromes without ST-segment elevation (GRACE score <140) after complete coronary revascularization with at least 1 but not more than 4 contemporary DES will be considered for enrollment. Clinical inclusion and exclusion criteria are listed in Table II. Patients meeting all entry criteria will provide informed written consent and then undergo a screening AMCE examination 30–120 hours after successful PCI.

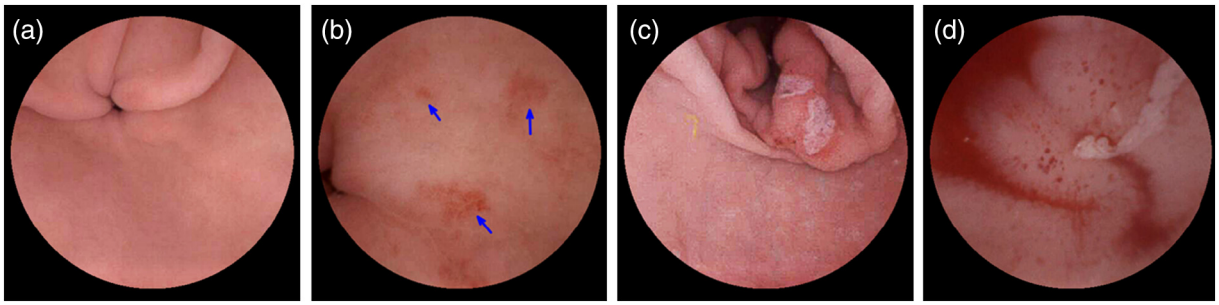
The AMCE system is composed of a magnetic navigation control system, a portable data recorder and a capsule position detector (Figure 1). The capsule endoscope (known as an endoscopic robot) has a length of 27 mm and a diameter of 11 mm and contains a permanent magnet (Figure 1A). It provides a 140° viewing angle, a 30 mm depth of field and operates for at least 10 hours after ingestion. The activated capsule is swallowed into the digestive tract and continually records the condition of digestive tract mucosa at 2 frames per second. After reaching the gastric cavity, the endoscopic capsule is navigated by the external magnetic control system to visualize all aspects of the stomach (the cardia, fundus, angulus, antrum, and pylorus). The controller

Figure 1



ANKON magnetically controlled capsule endoscopy system. a) capsule endoscope; b) portable data recorder; c) magnetic navigation control system.

Figure 2



Representative examples of gastrointestinal mucosal images captured by ANKON magnetically controlled capsule endoscopy. a) normal; b) erosions (blue arrows); c) ulcers with fibrin coating; d) bleeding.

allows movements of 2 mm and changes in viewing angle of 3°. The dimensions of any visualized lesions are measured by the ANKON ESNavi software. Representative examples of normal and abnormal gastric and intestinal findings are shown in Figure 2. Multicenter randomized studies have demonstrated that the AMCE system provides 93.4% accuracy in diagnosis of focal lesions in the stomach compared with standard gastroscopy.[12,13]

Subjects do not eat or drink any colored liquid or syrup after 8 PM the day before AMCE examination. On the following morning the subject is administered 10 ml of simethicone (Menarini Group, Florence, Italy) as a defoaming agent to clean the stomach cavity 40 minutes before the examination, and drinks water (~500–1000 mL) until feeling stomach fullness. During examination, if the gastric cavity is not filled with sufficient liquid to enable navigation of the capsule, the subject will drink additional water.

After the whole stomach is examined, subjects continue to wear the portable recorder for visualization of the duodenum and small intestine. The capsule is ultimately excreted. Standard magnetic resonance imaging procedures are prohibited before capsule excretion. If the capsule is not found to be excreted within 2 weeks after examination, the subject returns to the hospital for detection of the capsule by a position detector or abdominal x-ray to confirm whether the capsule is still in the body. If it is, endoscopy may be performed to remove the capsule.

Those undergoing successful screening AMCE exam (visualization of the entire upper gastrointestinal tract and small intestine) and with no sites of erosion, ulceration or bleeding will be enrolled in the trial. Consented patients

Table III. Randomization ineligibility criteria at 6 months.

1) Withdrawal of informed consent;
2) Lost to follow-up at 6 months;
3) Any event in the prior 6 months which in the opinion of the investigator results in the patient not being suitable for randomization of antiplatelet agent regimen either because of a) necessity to continue dual antiplatelet therapy (eg, *major* adverse cardiovascular or cerebrovascular event within the prior 6 months or need for repeat stenting), or b) inability to continue dual antiplatelet therapy (eg, bleeding, neoplasm, need for urgent surgery, etc within the prior 6 months);
4) Not presently taking both aspirin and clopidogrel, or any prior temporary discontinuation of aspirin or clopidogrel for ≥5 days;
5) Use of proton pump inhibitors or gastric mucosal protectants for more than 12 days, or for more than 4 continuous days in the 6 months prior to randomization*;
6) Unwillingness or inability to undergo the 6-month AMCE examination or the remainder of the study procedures, including the 12-month AMCE exam.

*Proton pump inhibitors or any other kind of gastric mucosal protectant agents may not be used after study enrollment unless a clear clinical indication has developed (eg, new gastrointestinal bleeding or ulcer disease). After randomization, gastric mucosa protectants may not be taken for more than 4 days continuously or in total for >10 days without a clear clinical indication.

in whom the baseline screening AMCE was not performed, was not evaluable or was positive (ie, erosion, ulceration or bleeding present) will be followed for 30 days only for safety surveillance.

Study treatments, randomization and follow-up

All enrolled patients with a negative screening AMCE examination will be treated with open-label aspirin (100 mg/d) plus clopidogrel (75 mg/d) for 6 months. Proton pump inhibitors or other gastric mucosal protectant agents may not be used after study enrollment unless a clear clinical indication has developed (eg, new gastrointestinal bleeding or documented ulcer). Eligibility for randomization (including medication adherence and the interval occurrence of adverse events) will be evaluated in this group at 6 months (±2 weeks). At this time patients free from interval major adverse ischemic or clinically overt bleeding events and otherwise without any exclusion criteria (Table III) will undergo a second AMCE examination before randomization. Patients successfully completing this exam are then randomly assigned in a 1:1:1 ratio to receive aspirin plus clopidogrel, aspirin plus clopidogrel-placebo or clopidogrel plus aspirin-placebo for an additional 6 months in a double blinded manner. The placebos of aspirin and clopidogrel, having an identical appearance to the original agents, were produced by a GMP certificated manufacturing company. All drugs (including placebos) were packaged and coded by a contract research organization. A final in-person visit will be performed at 6 months (±2 weeks) after randomization during to assess study medication adherence and adverse events, after which a third AMCE examination will be performed (Figure 3).

A *Helicobacter pylori* (HP) breath test will be performed after the screening AMCE exam to document HP infection status. HP eradication therapy is not mandatory but is allowed per physician discretion. Serum hemoglobin levels and assessment for occult fecal blood will be performed at baseline and every 2 months after enrollment, until withdrawal or termination of the study. Platelet function testing, including adenosine diphosphate-induced platelet aggregation by light transmission aggregometry and VerifyNow aspirin and P2Y12 testing assessment, will be performed at baseline screening, randomization and at the end of the study in first 102 enrolled patients (34 per group) as a platelet function substudy.

Blinding and unblinding

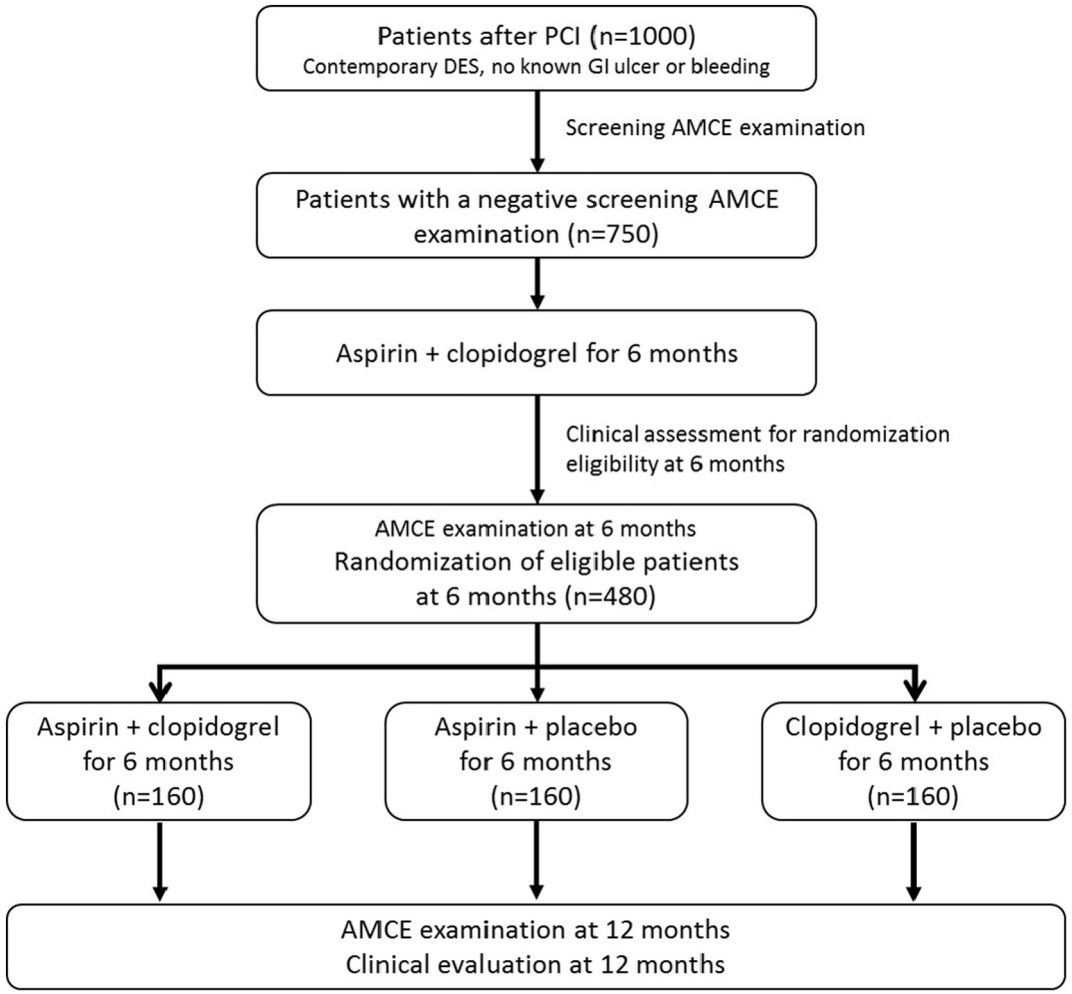
The study utilizes a double-blind design with matching placebo for aspirin and clopidogrel. The patients, study site research personnel, and treating physicians will not be aware of treatments received. In emergency situations the blind may be broken if absolutely necessary for the treating physician to provide optimal management.

Study endpoints and definitions

The primary and secondary endpoints are shown in Table IV. The primary endpoint is the incidence of gastric or intestinal mucosal injury occurring within 12 months after enrollment, defined as erosion, ulceration or bleeding[18,19] detected by either planned AMCE or clinically-driven endoscopy. Specifically, gastrointestinal erosion is defined as superficial mucosal breaks with a diameter of <5 mm. Gastrointestinal ulcer is defined as a mucosal break with a diameter ≥5 mm, typically covered with fibrin.

Secondary endpoints include the primary endpoint assessed between enrollment and 6 months, and between 6 and 12 months; clinically evident gastrointestinal hemorrhage[19]; gastrointestinal symptoms (graded by the severity and frequency of abdominal pain, bloating, acid regurgitation and eructation); any bleeding events as defined by the BARC definition (types 1–5)[20]; target lesion failure (TLF, defined as the composite of cardiac death, target-vessel myocardial infarction, or clinically-driven target lesion revascularization); net adverse clinical events (defined as the composite of TLF or BARC type 2–5 bleeding); and stent thrombosis according to the Academic Research Consortium (ARC) definite or probable criteria.[21]

Figure 3



Study flowchart. PCI: percutaneous coronary intervention; DES, drug-eluting stent; GI: gastrointestinal; AMCE: ANKON magnetically controlled capsule endoscopy.

The primary endpoint will be assessed in the 12-month DAPT group compared to the pooled 6-month DAPT plus 6-month aspirin and clopidogrel monotherapy groups. Secondary endpoints will also be assessed in these groups. The primary endpoint and all secondary endpoints will also be compared across the 3 groups, and for all single group versus group comparisons (12-month DAPT vs 6-month DAPT plus 6-month aspirin monotherapy; 12-month DAPT vs 6-month DAPT plus 6-month clopidogrel monotherapy; and 6-month DAPT plus 6-month aspirin monotherapy versus 6-month DAPT plus 6-month clopidogrel monotherapy).

Subgroup analyses

The primary and secondary endpoints will be also analyzed in the following clinically relevant pre-specified subgroups: age (65-year cut-off), sex, diabetes mellitus, chronic kidney disease (eGFR 60 mL/min/1.73m^2 cut-off), acute coronary syndrome, prior history of gastrointestinal bleeding (24 month cut-off), HP infection status, and DAPT duration prior to randomization (>6 months vs ≤6 months). Stratum-specific odds ratios or hazard ratios with 95% confidence intervals will be calculated for each subgroup using either logistic or Cox proportional hazards models as appropriate. Formal interaction testing will be performed using the subgroup × treatment allocation as an additional term in the multivariable models.

Sample size determination and adjustment

The cumulative incidence of the primary endpoint of gastric or intestinal mucosal lesions within 12 months is

Table IV. Study endpoints.

Primary endpoint*
The incidence of gastric or intestinal mucosal injuries within 12 months after enrollment, defined as erosion, ulceration or bleeding detected by planned AMCE or clinically-driven endoscopy.
Secondary endpoints
1) The incidence and severity of gastric and intestinal mucosal lesions during the first 6 months after study enrollment (prior to randomization);
2) The incidence and severity of gastric and intestinal mucosal lesions after randomization (ie, between 6 months and 12 months after study enrollment);
3) The incidence of clinically evident gastrointestinal hemorrhage attributed to the upper GI tract (or of unknown origin) during 6 months after study enrollment (prior to randomization);
4) The incidence of clinically evident gastrointestinal hemorrhage attributed to the upper GI tract (or of unknown origin) after randomization (ie, between 6 months and 12 months after study enrollment);
5) The incidence of clinically evident gastrointestinal hemorrhage attributed to the upper GI tract (or of unknown origin) during 12 months after study enrollment;
6) Gastrointestinal symptoms (pain, nausea/vomiting, dysphagia, other) during the 12 months after enrollment;
7) All bleeding (BARC types 1–5) during the 12 months after enrollment;
8) The incidence of target lesion failure (TLF; cardiac death, target-vessel MI, or clinically-driven target lesion revascularization), during the 12 months after enrollment;
9) The incidence of net adverse clinical events (NACE, defined as TLF or BARC type 2–5 bleeding) during the 12 months after enrollment;
10) The incidence of stent thrombosis (ARC definite, probable, or definite/probable) during the 12 months after enrollment.

* Patients will be *evaluable* for the primary endpoint if either: a) an AMCE test is performed at 12 months (±2 weeks) and is either positive (whether or not the entire GI tact is visible) or is negative with complete visualization of the GI tract; OR b) if a 6-month AMCE test was done and was positive, even if a 12-month test was not done; OR c) if overt GI bleeding occurred anytime during the 12-month follow-up and an AMCE or endoscopy test was positive.

estimated to be 47% in patients who received 12 months of DAPT and 30% in those treated with either aspirin or clopidogrel monotherapy beginning at 6 months after enrollment.[22,23] With a 2:1 ratio in patients treated with either aspirin or clopidogrel monotherapy after 6-month DAPT versus DAPT for 12 months, 384 evaluable patients (256 and 128 respectively) provide 90% power to detect a 17% absolute risk reduction (36% relative risk reduction) with a 2-sided type I error of 0.05. Assuming 20% loss of evaluable primary endpoint outcome assessments due to patient withdrawal, loss to follow-up between 6 and 12 months or suboptimal AMCE visualization of the GI tract at 12 months, 480 patients are planned to be randomized. Assuming that an additional 10% of enrolled patients will not be randomized at 6 months because of adverse clinical events, non-compliance with antiplatelet therapy or lost to follow-up or withdrawal, 534 patients were initially planned to be enrolled after baseline screening. Finally, assuming that 10% of patients who undergo a screening AMCE examination will be excluded due to gastrointestinal ulcer or bleeding, approximately 593 patients were initially planned to be consented and undergo the screening AMCE examination.

Among the first 200 patients enrolled, ~25% had gastrointestinal injury at baseline by screening AMCE (despite clinically absent bleeding or gastrointestinal complaints). Of those who passed the initial exam, only ~65% were eligible for randomization; 17% of patients were noncompliant with the 6-month repeat AMCE exam, and new gastrointestinal ulceration or bleeding was found on the 6-month AMCE examination in 18% of patients. The study sample size was adjusted accordingly so 1000 patients will be screened by AMCE at baseline, with 750 patients enrolled and followed to the 6-month randomization eligibility period to achieve the 480 patient randomized goal (Figure 3).

Trial status

The first patient was enrolled in OPT-PEACE trial on July 13, 2017. Between July 2017 and July 2019, a total of 1028 patients were screened by AMCE examination, 749 of whom were formally enrolled in 29 sites. Among these, 638 patients underwent AMCE at 6 months, and 505 were randomized. At present, 12-month clinical follow-up and AMCE examination has been completed in 380 patients. Due to the COVID-19 pandemic, some follow-up visits have had to be postponed for 1 to 3 months. Those patients were prescribed open-label antiplatelet therapy after their study medication depletion. Subgroup analysis will be performed in patients in whom follow-up was complete vs incomplete or otherwise affected by the COVID-19 pandemic. The primary endpoint is expected to be reported in the fourth quarter of 2020.

Conclusions

The OPT-PEACE trial is the first randomized study to investigate gastrointestinal endoscopic outcomes in patients receiving different APT regimens after PCI. The trial will provide new insights regarding the frequency, severity and clinical implications of subclinical and clinical gastrointestinal injury after PCI. This randomized, double-blind, placebo-controlled study will also investigate the pros and cons of

different antiplatelet regimens beyond 6 months (continued DAPT vs clopidogrel monotherapy vs aspirin monotherapy between 6 and 12 months) after PCI, which will be informative for clinical decision-making on personalized APT. In addition, the OPT-PEACE study will provide useful insights as to the safety of AMCE as a noninvasive method for detecting gastrointestinal mucosal injury in patients receiving APT.

Declaration of competing interest

Drs. Yi Li, Xiaozeng Wang, Dan Bao, Zhuan Liao, Jing Li, Xiao Han, Heyang Wang, Kai Xu, Zhaoshen Li and Yaling Han have no competing interests to declare. Dr. Gregg W. Stone has received speaker or other honoraria from Cook, Terumo, QOOL Therapeutics and Orchestra Biomed; has served as a consultant to Valfix, TherOx, Vascular Dynamics, Robocath, HeartFlow, Gore, Ablative Solutions, Miracor, Neovasc, V-Wave, Abiomed, Ancora, MAIA Pharmaceuticals, Vectorious, Reva, Matrizyme, Cardiomech; and has equity/options from Ancora, Qool Therapeutics, Cagent, Applied Therapeutics, Biostar family of funds, SpectraWave, Orchestra Biomed, Aria, Cardiac Success, MedFocus family of funds, Valfix.

Appendix A. OPT-PEACE organization and participating investigators

Principal Investigator: Yaling Han (China).

Co-Principal Investigators: Zhaoshen Li (China), Xiaozeng Wang (China), Gregg W. Stone (USA).

Steering committee:

Yaling Han (Chair), Department of cardiology, General hospital of Northern Theater Command, Shenyang, China; Xiaozeng Wang, Department of cardiology, General hospital of Northern Theater Command, Shenyang, China; Zhaoshen Li, Digestive Endoscopy Center, Department of Gastroenterology, Shanghai Changhai Hospital, Second Military Medical University, Shanghai, China; Zhuan Liao, Digestive Endoscopy Center, Department of Gastroenterology, Shanghai Changhai Hospital, Second Military Medical University, Shanghai, China; Gregg W. Stone, Icahn School of Medicine at Mount Sinai, New York, US.

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Data safety monitoring board:

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Clinical event adjudication committee:

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Contract Research Organization: ExcellentCRO Co, Ltd, Shenyang, China.

Image core laboratory: Digestive Endoscopy Center, Department of Gastroenterology, Shanghai Changhai Hospital, Second Military Medical University, Shanghai, China.

Data analysis center: YuKang Pharmaceutical Technology Co, Ltd, Shenyang, China.

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