

# Optimal antiplatelet pharmacotherapy guided by bedside genetic or functional TESTING in elective PCI patients: A pilot study: ONSIDE TEST pilot

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## Abstract

**Background:** Dual antiplatelet therapy (DAPT) is recommended after elective percutaneous coronary intervention (PCI) in stable coronary artery disease (SCAD) patients; however, still one-third of patients do not obtain adequate platelet inhibition that may result in increased cardiovascular risk. The aim of the ONSIDE TEST study is to evaluate the clinical impact of point-of-care genotyping- and platelet function-based personalized dual antiplatelet strategies in SCAD individuals undergoing PCI.

**Methods:** Fifty patients were randomized to one of the three study arms: 1) genotyping, 2) platelet function testing (PFT) and 3) control. Patients were tested with point-of-care Spartan RX CYP2C19 System (group 1) and VerifyNow P2Y<sub>12</sub> assay (group 2). In cases of inadequate response to clopidogrel, a loading dose of prasugrel was administered before PCI. The main clinical endpoint is the incidence of periprocedural myocardial injury (PMI).

**Results:** Five (32%) patients in the genotyping arm and two (13%) in the in the PFT arm were identified as poor clopidogrel metabolizers. The periprocedural platelet reactivity was significantly lower in the genotyping (80 ± 49.0 PRU) and PFT (36.5 ± 47 PRU) arms as compared to the control arm (176 ± 67.8 PRU),  $p = 0.01$  and  $p = 0.03$ , respectively. PMI appeared in 17 (37%) patients of the entire study population.

**Conclusions:** Personalized DAPT results in an improved platelet inhibition. Apart from genotyping and aggregometry, it is feasible to integrate into everyday clinical practice PMI rates which are relevant when comparing different strategies. (Cardiol J 2017; 24, 3: 284–292)

**Key words:** platelet aggregation inhibitors, platelet testing, clopidogrel, prasugrel, pharmacotherapy individualization

## Introduction

Percutaneous coronary interventions (PCI) with the implantation of new-generation drug-eluting stents (DES) or bioresorbable scaffolds improves symptoms, reduces the risk for recurrent ischemic events and improves quality of life in patients with stable coronary artery disease (SCAD) [1–3] and verified ischemia. However, procedure-

related complications including stent thrombosis, distal embolization and vessel dissection still occur and may lead to peri-procedural myocardial injury or infarction with an elevation of cardiac enzymes (i.e. creatine kinase muscle-brain [CK-MB], cardiac troponin T [cTnT] and I [cTnI]) in 20–30% of patients [4–6]. Dual antiplatelet therapy (DAPT) has proved to reduce these subsequent risks, although the efficacy of the currently recommended

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pharmacotherapy regime in SCAD, i.e. clopidogrel plus aspirin, is characterized by a large variability in the response of individual patients expressed by low platelet inhibition identified in 22–43% of the population [7–9]. By means of platelet function testing and genotyping, it is possible to identify patients who do not adequately respond to DAPT [10, 11]. In PCI patients treated with clopidogrel carriage of even one reduced-function CYP2C19 allele (\*2), there is an apparent association with a significantly increased risk of major adverse cardiovascular events (MACE), particularly stent thrombosis [11]. Hypothetically these individuals might be suitable candidates for more potent antiplatelet agents (prasugrel, ticagrelor) that are characterized by even stronger platelet inhibition and an ability to overcome high on-treatment platelet reactivity [12, 13]. The new generation rapid, easy-to-use, point-of-care diagnostic testing-systems appear to be a promising solution with the potential to present advantages of advanced genotyping and platelet function testing (PFT) into everyday clinical practice. To date, this personalized approach to periprocedural DAPT, although appealing, it has been difficult to implement in routine practice due to technical and logistic circumstances. In addition, results of previous large clinical trials focusing on hard clinical endpoints did not support the concept of individualization of antiplatelet therapy in low risk populations with SCAD.

Nevertheless, the more potent P2Y<sub>12</sub> inhibitors successful implementation into the clinical practice of PCI in an acute coronary syndrome setting remains vastly unexplored among patients undergoing elective PCI, and are also at risk of periprocedural ischaemic complications. In the era of a wide access to the best-in-class DES it may be not feasible to conduct a study evaluating prasugrel or ticagrelor among stable angina subjects that would be powered for clinical endpoint. Thus, an approach to demonstrate the impact of antiplatelet therapy modification on myocardial injury expressed by biomarker leakage might constitute an efficient option to address this issue.

Given this background, the ONSIDE TEST project was initiated (Optimal aNtiplatelet pharmacotherapy guided by bedSIDE genetic or functional TESTing in elective PCI patients) — an investigator-initiated, phase IV, multicenter, prospective, open-label, randomized controlled clinical trial (NCT01930773), aimed to assess the efficacy of point-of-care genotyping and PFT in patients with SCAD undergoing elective PCI. In this pilot paper initial single-centre results of interim analysis

of the first 50 patients was reported. This initial interim analysis was pre-specified to assess the feasibility of integrating the rapid point-of-care PFT and genotyping into the routine PCI practice, as well as to evaluate the safety of more potent antiplatelet drug administration among patients with stable angina.

## Methods

### Selection of patients

The ONSIDE TEST Pilot study included patients treated at the Invasive Cardiology Unit of the 1<sup>st</sup> Department of Cardiology, Medical University of Warsaw (Poland). Patients with stable coronary disease, between 18 and 75 years of age scheduled for an elective PCI with stent implantation were invited to participate in the study. The exclusion criteria comprised elevation of concentrations of myocardial necrosis enzyme at baseline, anticipated administration of glycoprotein IIb/IIIa inhibitors, usage of rotational atherectomy, intervention in chronic total occlusion or bifurcation lesions, low platelet count ( $< 70,000/\mu\text{L}$ ), high bleeding risk, coronary artery bypass surgery in last 3 months, severe chronic renal failure (estimated glomerular filtration rate  $< 30 \text{ mL/min}$ ), requirement for oral anticoagulation (warfarin, dabigatran, apixaban, rivaroxaban etc.), history of stroke or transient ischemic attack, weight  $< 60 \text{ kg}$ , known bleeding diathesis, hematocrit of  $< 30\%$  or  $> 52\%$  and pregnancy [14].

### Financing and bioethics approval

The trial was sponsored by an independent research grant obtained from the Young Scientists Club 30 of the Polish Cardiac Society. The protocol was approved by the Bioethics Committee of the Medical University of Warsaw (Poland) in compliance with the Declaration of Helsinki.

### Endpoints

The primary efficacy outcome measure was the incidence of periprocedural myocardial injury defined as elevation of troponin I  $> 1 \times 99^{\text{th}}$  percentile upper limit of norm (ULN), but  $< 5 \times 99^{\text{th}}$  percentile ULN or elevation of troponin I  $> 5 \times \text{ULN}$  in the absence of angiographic or imaging findings of ischemia. The secondary outcome measures were maximum level of CK-MB elevation within 24 h after PCI, maximum troponin elevation within 24 h after PCI, the prevalence of periprocedural myocardial infarction, prevalence of periprocedural myocardial biomarker leak was understood as any

increase of myocardial necrotic enzymes above ULN. The periprocedural myocardial infarction was defined as troponin elevation  $5 \times > 99^{\text{th}}$  percentile ULN and one of the following: 1) chest pain exceeding 20 min; 2) ischemic ST changes or new pathological Q waves; 3) angiographic evidence of flow limiting complication; or 4) imaging evidence of myocardial ischemia. The safety endpoints included the risk of Bleeding Academic Research Consortium (BARC)-defined type 3 (clinical, laboratory, and/or imaging evidence of bleeding, with healthcare provider responses) and type 5 (fatal) bleeds happening within 7 and 30 days of PCI; and the rate of cardiac death, myocardial infarction, definite or probable stent thrombosis or urgent repeat revascularization within 30 days [15].

### Study design

Patients who agreed to participate in the study and signed written informed consent were randomized using an electronic randomization tool for iPhone [Randomizer for Clinical Trial, MEDSHARING, Fontenay Sous Bois, France] to three arms: 1) phenotyping arm, 2) genotyping arm and 3) control arm [16]. All patients were on aspirin 75 mg daily and on clopidogrel 75 mg daily or received a loading dose of clopidogrel 600 mg at least 6 h before testing. Patients in the phenotyping arm had their platelet reactivity checked using the point-of-care VerifyNow P2Y<sub>12</sub> assay (Accumetrics, San Diego, US). Results were available within 5 min, values above the cutoff point of 208 platelet reactivity units (PRU) indicated inadequate platelet inhibition and a mandatory loading dose of prasugrel 60 mg was administered followed by a daily dose of 10 mg; other patients continued on clopidogrel. In the genotyping arm, the poor responders to clopidogrel were identified by the rapid, point-of-care Spartan RX CYP2C19 System (Spartan Bioscience Inc., Ottawa, Canada). Carriers of at least one copy of the CYP2C19\*2 received a loading dose of prasugrel 60 mg with a following 10 mg daily [14].

### Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics, version 21.0 (IBM, New York). The statistical analysis was based on an intention-to-treat population Shapiro-Wilk test which was used to check for normal distribution of continuous variables. Continuous variables were presented as mean  $\pm$  one standard deviation (SD) or median depending on distribution. Groups were compared with t-Student or Mann-Whitney tests, respectively. Nominal variables were shown as percentage or

frequencies, and compared using the Fisher's exact test. P-values lower than 0.05 were considered as statistically significant.

## Results

Overall 50 patients, who were scheduled for an elective PCI with stent implantation were randomized between December 2012, and November 2014. Four patients had to be excluded from the final analysis: two received ticagrelor before platelet function testing and two withdrew the informed consent. This was a high-risk population as per clinical characteristic with excessive prevalence of diabetes (39%), hypertension (70%), hyperlipidemia (70%), heart failure (37%), history of smoking (93%), or previous myocardial infarction (59%). Before admission most patients were on clopidogrel (76%) and all on aspirin. There were no significant differences in the baseline clinical characteristics between the three study arms (Table 1).

The bedside testing was performed in all patients  $8 \pm 1.2$  h before PCI. Genotyping took 60 min and the test had to be repeated for 2 patients due to inconclusive results. The mean PFT time was 4 min. Nurses or physicians performed all tests and no input from trained laboratory staff was needed.

The genotyping revealed that 15 (32.6%) patients had at least one copy of the loss-of-function (CYP2C19\*2) allele, of those 2 (4.3%) were homozygous. At baseline, in the entire population the mean PRU was  $157.5 \pm 73.55$ , 11 (24%) patients had high on-treatment platelet reactivity according to the prespecified cutoff value of PRU  $> 208$  (Table 2). Based on the point-of-care testing 5 (32%) patients in the genotyping arm and 2 (13%) patients in the PFT arm were identified as poor clopidogrel metabolizers and received loading dose of prasugrel at least 2 h before the scheduled PCI. No patient in the control arm was given prasugrel regardless of the geno-/phenotyping profile.

During the PCI most patients received 1 DES (83%) in left anterior descending artery (46%) (Table 3). Lesion preparation with predilatation was performed in 98% of cases; a balloon post-dilatation was done in 1 of 5 patients. There were no major differences in terms of the procedural characteristics, except a numerically longer time of total vessel occlusion during intervention in the control group (Table 3).

The periprocedural platelet reactivity was significantly lower in the genotyping ( $80 \pm 49.0$  PRU) and phenotyping ( $36.5 \pm 47.0$  PRU) arms

**Table 1.** Baseline clinical characteristics.

	Genotyping (n = 16)	Aggregometry (n = 16)	Control (n = 14)
Age [years]	61.2 ± 10.2	61 ± 6.54	63.5 ± 5.64
Female gender	7 (44%)	6 (38%)	5 (36%)
Height [cm]	170.5 ± 6.42	171.7 ± 9.35	170.9 ± 6.66
Weight [kg]	84.8 ± 13.41	87.1 ± 18.76	85.5 ± 16.14
Body mass index [kg/m <sup>2</sup> ]	31.7 ± 5.92	28.4 ± 2.56	25.3 ± 3.36
<b>Cardiac risk factors</b>			
Symptomatic stable CAD:	16 (100%)	11 (69%)	11 (79%)
CCS 1	5 (29.4%)	5 (35.7%)	7 (46.7%)
CCS 2	8 (47.1%)	4 (28.6%)	5 (33.3%)
CCS 3	4 (23.5%)	2 (14.3%)	0 (0%)
Hypertension	11 (69%)	10 (63%)	11 (79%)
Diabetes mellitus	7 (44%)	4 (25%)	7 (50%)
Hyperlipidemia	13 (82%)	10 (63%)	9 (65%)
Atrial fibrillation	1 (7%)	3 (19%)	3 (22%)
Heart failure (NYHA II–III)	5 (32%)	6 (38%)	6 (43%)
LVEF [%]	45 ± 16.9	44 ± 15.8	50 ± 11.7
COPD	1 (7%)	2 (13%)	2 (15%)
Smoking status	13 (82%)	16 (100%)	14 (100%)
Habitual smoker	4 (25%)	6 (38%)	4 (29%)
Ex-smoker	9 (57%)	10 (63%)	10 (72%)
Non-smoker	3 (19%)	0 (0%)	0 (0%)
Previous myocardial infarction	9 (57%)	11 (69%)	7 (50%)
Anterior wall	1 (7%)	5 (32%)	3 (22%)
Lateral wall	2 (13%)	1 (7%)	0 (0%)
Inferior wall	5 (32%)	5 (32%)	3 (22%)
Posterior wall	1 (7%)	0 (0%)	1 (8%)
Previous PCI	9 (57%)	9 (57%)	7 (50%)
<b>Laboratory</b>			
CK-MB [ng/mL]	0.60 (0.35–1.25)	1.05 (0.62–1.97)	1.60 (0.65–2.65)
Troponin I [ng/mL]	0.002 (0.000–0.009)	0.007 (0.000–0.019)	0.014 (0.000–0.022)
Creatinine [mg/dL]	0.9 ± 0.20	1.0 ± 0.20	1.0 ± 0.32
eGFR [mL/min/1.73 m <sup>2</sup> ]	57 (49–59)	59 (51–60)	58 (51–60)
Red blood cells [10 <sup>6</sup> /μL]	4.6 ± 0.35	4.7 ± 0.51	4.8 ± 0.384
Hamoglobin [g/dL]	14.5 ± 0.97	14.6 ± 1.22	14.2 ± 1.14
Platelets [10 <sup>3</sup> /μL]	241 ± 68.9	245 ± 79.8	219 ± 80.3
INR	1.00 ± 0.069	1.00 ± 0.055	0.98 ± 0.055
APTT [s]	27 ± 2.2	32 ± 3.7	29 ± 2.4
AST [U/L]	21.5 ± 5.92	23.9 ± 6.54	24.8 ± 7.52
ALT [U/L]	29.7 ± 11.67	33.1 ± 12.95	45.62 ± 67.126
<b>Baseline pharmacotherapy</b>			
Aspirin	16 (100%)	13 (82%)	14 (100%)
Clopidogrel	14 (88%)	12 (75%)	9 (65%)
Statin	16 (100%)	13 (82%)	13 (93%)
Beta-blocker	16 (100%)	12 (75%)	12 (86%)
ACE-I or ARB	15 (94%)	12 (75%)	12 (86%)
Calcium channel blocker	1 (7%)	1 (7%)	0 (0%)
Proton pump inhibitor	5 (32%)	8 (50%)	7 (50%)

Data are presented as count and percentage (%) or mean ± standard deviation; CAD — coronary artery disease; CCS — Canadian Cardiovascular Society; NYHA — New York Heart Association; LVEF — left ventricular ejection fraction; COPD — chronic obstructive pulmonary disease; PCI — percutaneous coronary intervention; CK-MB — creatine kinase muscle-brain; eGFR — estimated glomerular filtration rate; INR — international normalized ratio; APTT — activated partial thromboplastin time; AST — aspartate aminotransferase; ALT — alanine aminotransferase; ACE-I — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker

**Table 2.** Platelet function, genotype and pharmacotherapy.

	Genotyping (n = 16)	Aggregometry (n = 16)	Control (n = 14)
<b>Before testing</b>			
Baseline pharmacokinetic response, platelet reactivity [PRU]	160.5 ± 61.36	138.4 ± 87.7	177.5 ± 67.8
High platelet reactivity, PRU > 208	2 (13%)	5 (32%)	4 (29%)
CYP2C19*2 carrier (heterozygote)	5 (32%)	4 (25%)	4 (29%)
CYP2C19 carrier (homozygote)	1 (7%)	0 (0%)	1 (8%)
<b>After testing</b>			
Switch to prasugrel	5 (32%)	2 (13%)	0 (0%)

Data are presented as count and percentage (%) or mean ± standard deviation; PRU — platelet reactivity units

**Table 3.** Procedural characteristics.

	Genotyping (n = 16)	Aggregometry (n = 16)	Control (n = 14)
<b>Lesion location</b>			
Left main	0 (0%)	1 (7%)	0 (0%)
Left anterior descending artery	7 (44%)	8 (50%)	6 (43%)
Circumflex artery	3 (19%)	2 (13%)	4 (29%)
Right coronary artery	3 (19%)	3 (19%)	1 (8%)
<b>Number of stents</b>			
One	11 (69%)	12 (75%)	11 (79%)
Two	5 (32%)	4 (25%)	3 (22%)
Drug eluting stent	14 (88%)	13 (82%)	11 (79%)
Bare metal stent	2 (13%)	3 (19%)	3 (22%)
Direct stenting	0 (0%)	1 (7%)	0 (0%)
Stent postdilatation	3 (19%)	3 (19%)	3 (22%)
Total length of stent [mm]	27.1 ± 13.79	26.1 ± 14.01	28.8 ± 23.18
Total vessel occlusion time [s]	79 ± 40.1	102 ± 53.6 <sup>#</sup>	68 ± 23.4 <sup>#</sup>
Periprocedural pain	1 (7%)	1 (7%)	1 (8%)
Intravascular ultrasound	1 (7%)	1 (7%)	0 (0%)
Optical coherence tomography	1 (7%)	1 (7%)	0 (0%)
<b>Periprocedural pharmacotherapy</b>			
Unfractionated heparin [10 <sup>3</sup> units]	6.9 ± 2.34	8.1 ± 1.94)	8.0 ± 1.73
Abciximab	1 (7%)	0 (0%)	0 (0%)
Eptifibatide	1 (7%)	0 (0%)	0 (0%)
Good angiographic result (TIMI 3)	15 (94%)	16 (100%)	13 (93%)

Data are presented as count and percentage (%) or mean ± standard deviation; <sup>#</sup>p = 0.066

as compared to the control arm (176 ± 67.8 PRU), (p = 0.01 and p = 0.03, respectively).

The periprocedural myocardial injury appeared in 17 (37%) patients of the entire study population. There were no statistically significant differences in terms of the periprocedural myocardial injury in

the control, aggregometry and genotyping groups (35.7%, 37.5%, and 40%, respectively, p = 0.97) (Table 4). The median peak CK-MB elevation within 24 h after PCI was 2.0 ng/mL. Seven patients in the control arm, 9 in the phenotyping arm and 5 in the genotyping arm had CK-MB above the median.

**Table 4.** Main study outcomes.

	Genotyping (n = 16)	Aggregometry (n = 16)	Control (n = 14)	P: Gen vs. Agg*	P: Agg vs. Con*	P: Gen vs. Con*
Pharmacokinetic response 30 min after PCI [PRU]	80.3 ± 49	36.5 ± 47	177.5 ± 67.8	0.39	<b>0.01</b>	<b>0.03</b>
Periprocedural myocardial injury	40.0%	37.5%	35.7%	1.00	1.00	1.00
Peak CK-MB elevation [ng/mL]	1.3 (0.7–4.2)	2.4 (1.1–4.1)	2.1 (1.1–3.5)	0.82	0.72	0.85
Periprocedural MI [cTnl > 5 × ULN + symptoms]	6.3%	0.0%	0.0%	0.31	1.00	0.34
Periprocedural myocardial biomarker leak [cTnl or CK-MB > 1 × ULN]	80.0%	81.3%	75.0%	1.00	1.00	1.00
Peak Tnl elevation [ng/mL]	1.73 (0.41–3.16)	1.92 (0.82–5.99)	1.54 (0.54–5.00)	0.33	0.36	0.32
BARC 3 or 5 bleeding (within 7 days)	0.0%	12.5%	0.0%	0.16	0.17	1.00
Cardiac death, MI, stent thrombosis, revascularization (within 30 days)	6.3%	0.0%	0.0%	0.31	1.00	0.34

Data are presented as count and percentage (%), median and interquartile range or mean ± standard deviation; Agg — aggregometry; Gen — genotyping; PCI — percutaneous coronary intervention; PRU — platelet reactivity units; CK-MB — creatine kinase muscle-brain; MI — myocardial infarction; cTnl — cardiac troponin I; ULN — upper normal limit; BARC — Bleeding Academic Research Consortium

The median peak troponin elevation within 24 h was 0.19 ng/mL. Seven patients in the control arm, 8 in the phenotyping arm and 8 in the genotyping arm had CK-MB above the median. There were no differences in the prevalence of periprocedural myocardial infarction, myocardial biomarker leak, and risk of major bleeding and MACE at the 30-day follow-up. Main study outcomes are presented in Table 4.

## Discussion

In research of the literature, this is the first study aiming to compare two point-of-care testing methods in a head-to-head manner with standard care in patients undergoing elective PCI for SCAD. The present report confirmed safety and feasibility of personalized point-of-care strategy in this patient population. Previous studies have assessed only one type point-of-care testing and did not evaluate the platelet inhibition before and during PCI. It is worth underlining that the presented results are based on one third of the planned population and should be examined carefully. In the present study no differences were found in terms of peak CK-MB within 24 h after PCI between the three study populations. There are no other studies that would assess the myocardial injury in relation to type of antiplatelet drug used. However there is evidence that higher platelet reactivity during PCI

is related to periprocedural myonecrosis [17] and worse prognosis [18–25].

There was a significantly stronger platelet inhibition in the genotyping and PFT groups as expressed by the PRU values than in the control group. This is in line with pharmacodynamic data from the Testing platelet Reactivity In patients undergoing elective stent placement on clopidogrel to Guide alternative therapy with prasugrel (TRIGGER PCI) study that demonstrated the efficacy of prasugrel in overcoming HTPR on clopidogrel in patients with SCAD [12].

The number of heterozygous carriers of the CYP2C19\*2 allele observed in this study confirms the observations from previous studies [11, 26–28]. It should be noted that in the genotyping group there was a numerically higher rate of periprocedural myocardial injury than in the control group. Nevertheless, it was mainly driven by procedural mechanical complications (severe artery dissection) and thus, cannot be directly associated with inadequate response to antiplatelet agents.

The data from randomized clinical trials confirmed that stronger platelet inhibition in acute coronary syndrome patients treated with PCI reduces the rate of ischemic events, with an increase in risk of bleeding complications [29–32]. However, such an association has been less apparent in patients with stable angina [33].

Dual antiplatelet tailored strategy based on bedside aggregometry was previously studied

by Collet et al. [34], however in the Assessment by a Double Randomization of a Conventional Antiplatelet Strategy versus a Monitoring-guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption versus Continuation One Year after Stenting (ARCTIC) trial pre-PCI intensification of P2Y<sub>12</sub> and glycoprotein IIb/IIIa inhibition when monitoring with VerifyNow P2Y<sub>12</sub> aggregometry revealed a poor response to clopidogrel did not show any improvement in ischemic or safety outcomes with a strategy of monitoring and drug adjustment as compared with a conventional treatment strategy [34]. Similarly, the TRIGGER PCI study, comparing prasugrel vs. clopidogrel in the low risk population of patients screened with the VerifyNow assay after elective uncomplicated angioplasty with DES implantation was stopped prematurely for futility [12]. In the group of 236 patients with complete 6-month follow-up only one primary endpoint of cardiac death or myocardial infarction had occurred, accounting for an incidence of 0.4%. As the rate of MACE in the population of SCAD patients is minimal in the era of new generation DES, it might not be feasible to perform an appropriately sized study assessing clinical endpoints with sufficient statistical power. Having evidence for a gradual increase in mortality risk with each increment of CK-MB plasma concentration after PCI [35–37], it appears that an approach involving assessment of surrogate endpoint (i.e. myocardial injury) might be more efficacious in verification of tailored antiplatelet therapy hypothesis in low-risk populations. Nevertheless, the threshold beyond which biomarker elevations are clinically significant still needs to be determined, presumably with the employment of high-resolution imaging to verify the extent of myonecrosis [38, 39]. The plasma levels of myocardial injury biomarkers were comparable in all three-study arms in this study. However, the study is still ongoing and will continue until 362 subjects are randomized, according to the already reported sample size analyses.

Notably, the present investigation provided also novel data on the prevalence of periprocedural myocardial infarction in the elective PCI patient population, that might also constitute additional reference for other investigators, as the evidence on the incidence of periprocedural myocardial injury among SCAD patients undergoing invasive treatment remains unsatisfactory.

Finally, in this pilot study, it was also confirmed that the feasibility and convenience of point-of-care testing methods in the assessment of response to

antiplatelet therapy in patients undergoing elective PCI. Both phenotyping and genotyping could have been performed by a physician or nurse subsequent to a short training and the results could have been achieved quickly, especially in cases of aggregometry.

### Limitations of the study

The main limitation of this study is a small number of enrolled patients. Another limitation is a potential lack of sensitivity of the primary endpoint, which may be driven by the incidence of periprocedural technical complications apart from adequate platelet inhibition. However, the approach enclosing exclusion of periprocedural myocardial infarction from the study endpoint analysis has already proved to be ineffective [12] and the optimal antiplatelet therapy might potentially attenuate ischemic complications of PCI. Furthermore, a limitation of this trial is also its open-label design, which was the consequence of numerous interventions occurring over the course of this study.

### Conclusions

In the present study, individualization of antiplatelet therapy on the basis of point-of-care platelet function testing by switching to prasugrel in SCAD patients with high on-clopidogrel platelet reactivity resulted in a consistent decrease in platelet reactivity, achieving a level similar to that observed in clopidogrel responsive subjects. This pilot study confirms feasibility of bedside genotyping and phenotyping testing in everyday clinical practice.

**Conflict of interest:** None declared

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