

Study design and rationale for Optimal antiplatelet pharmacotherapy guided by bedside genetic or functional TESTING in elective percutaneous coronary intervention patients (ONSIDE TEST): a prospective, open-label, randomised parallel-group multicentre trial (NCT01930773)

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Abstract

Background and aim: High platelet reactivity (HPR) and presence of CYP2C19 loss-of-function alleles are associated with higher risk for periprocedural myocardial infarction in clopidogrel-treated patients undergoing percutaneous coronary intervention (PCI). It is unknown whether personalised treatment based on platelet function testing or genotyping can prevent such complications.

Methods: The ONSIDE-TEST is a multicentre, prospective, open-label, randomised controlled clinical trial aiming to assess if optimisation of antiplatelet therapy based on either phenotyping or genotyping is superior to conventional care. Patients will be randomised into phenotyping, genotyping, or control arms. In the phenotyping group, patients will be tested with the VerifyNow P2Y₁₂ assay before PCI, and patients with a platelet reactivity unit greater than 208 will be switched over to prasugrel, while others will continue on clopidogrel therapy. In the genotyping group, carriers of the *2 loss-of-function allele will receive prasugrel for PCI, while wild-type subjects will be treated with clopidogrel. Patients in the control arm will be treated with standard-dose clopidogrel. The primary endpoint of the study is the prevalence of periprocedural myocardial injury within 24 h after PCI in the controls as compared to the phenotyping and genotyping group. Secondary endpoints include cardiac death, myocardial infarction, definite or probable stent thrombosis, or urgent repeat revascularisation within 30 days of PCI. Primary safety outcome is Bleeding Academic Research Consortium (BARC) type 3 and 5 bleeding during 30 days of PCI.

Summary: The ONSIDE TEST trial is expected to verify the clinical utility of an individualised antiplatelet strategy in preventing periprocedural myocardial injury by either phenotyping or genotyping.

Trial registration: ClinicalTrials.gov: NCT01930773.

Key words: antiplatelet therapy, high platelet reactivity, bedside testing, CYP2C19*2 allele polymorphism, clopidogrel, prasugrel, percutaneous coronary interventions, stable coronary artery disease

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INTRODUCTION

Optimal antiplatelet pharmacotherapy has a major impact on the post-procedural outcomes related to percutaneous coronary intervention (PCI). Currently it involves a combination of aspirin and a P2Y₁₂-inhibitor. Dual antiplatelet therapy should be continued for at least one month after bare metal stent implantation, and up to six months in cases of drug-eluting stents in interventions for stable angina [1, 2].

Although adding clopidogrel to aspirin monotherapy reduced the risk of ischaemic events in the elective PCI setting, response to clopidogrel is highly heterogeneous and depends on individual clinical characteristics and on the genetically determined enzymatic activity of the cytochrome P450 enzyme system. Inadequate platelet inhibition and consequential high platelet reactivity (HPR) is associated with an increased risk of stent thrombosis and recurrent myocardial infarction (MI) in clopidogrel-treated patients after PCI. Similar to this, many reports have shown that patients with loss-of-function alleles are at higher risk for ischaemic events [3].

Administration of more potent antiplatelet agents, i.e. prasugrel or ticagrelor allows HPR to be overcome in most individuals who do not respond adequately to clopidogrel, identified either by genotyping or phenotyping [4–6]. However, clinical evidence from previously conducted trials on individualised antiplatelet therapy in stable disease remains inconclusive and requires further exploration [7, 8]. Moreover, phenotyping and genotyping have never been compared in a head-to-head manner in trials of personalised antiplatelet therapy.

Our aim is to evaluate whether tailored P2Y₁₂-inhibitor therapy by either bedside platelet or genetic testing may be superior to conventional approach in reducing the risk of periprocedural MI in stable angina patients undergoing PCI. This surrogate endpoint has been shown to correlate with survival and is relatively frequent among patients with stable coronary artery disease (CAD) [9]. Here we present the rationale and design of Optimal antiplatelet pharmacotherapy guided by bedside genetic or functional TESTING in elective PCI patients (ON-SIDE TEST) — a prospective, open-label, randomised parallel-group multicentre trial.

METHODS

Rationale for platelet function testing

Clopidogrel is an oral thienopyridine that irreversibly inhibits the P2Y₁₂ adenosine diphosphate receptor. One major limitation of clopidogrel is the large inter-individual variability in the achieved level of platelet inhibition between patients, resulting in an unpredictable antiplatelet effect during fixed-dose treatment. As a consequence, approximately 20–30% of CAD patients of the Caucasian population demonstrate high on-treatment platelet reactivity, which is associated with higher risk for stent thrombosis, MI, and cardiovascular mortality according to evidence from more than 25,000 patients [10, 11]. Most of the evidence is based on the results with

the VerifyNow P2Y₁₂ assay (Accumetrics, San Diego, CA), which measures platelet agglutination to fibrinogen-coated polystyrene droplets activated by adenosine diphosphate [12, 13] and provides results as platelet reactivity units (PRU). Several prior studies confirmed that patients with HPR, measured by the VerifyNow, have higher risk for periprocedural myonecrosis [14, 15].

Prasugrel is a potent, third-generation antiplatelet agent that shows faster onset of action and more potent inhibition of the P2Y₁₂ receptor. The clinical result of the more rapid and more potent platelet inhibition by prasugrel has been demonstrated in the TRITON TIMI 38 trial, in which prasugrel reduced the risk of cardiovascular death, MI, or stroke by 19% compared to clopidogrel in acute coronary syndrome (ACS) patients undergoing PCI. However, this benefit was accompanied by a higher risk for bleeding. Therefore, prasugrel may be a good candidate to overcome HPR in patients undergoing PCI and can be used in selected cases with stable CAD [16].

Rationale for genotyping of clopidogrel-treated patients

Clopidogrel activation by cytochrome P450 requires a two-step oxidation process, determined mostly by the activity of the CYP2C19 isoenzyme. Notably, a significant proportion of patients carry loss-of-function polymorphisms in CYP2C19, most commonly *2 (rs4244285) [17]. Individuals with loss-of-function alleles have lower levels of active metabolite and have less potent platelet inhibition on-clopidogrel, resulting in higher prevalence of HPR [18, 19]. The clinical implication of such single nucleotide polymorphisms translates into a higher risk of mortality and stent thrombosis, with most of the data available for the *2 loss of function (LOF) allele [18–20]. A prior study has shown that overcoming HPR in *2 carriers by increasing the dose of clopidogrel is not effective [21, 22]. On the contrary, switching clopidogrel to prasugrel in heterozygous and homozygous loss-of-function carriers results in adequate platelet inhibition comparable to non-carriers [6].

Rationale for bedside testing

Even the most precise and advanced diagnostic methods are useless if they are not implemented in everyday clinical practice. Barriers comprise costs, poor logistics, high level of complexity for the operator, low accessibility, and little or no standardisation of the respective testing method. Traditional models of centralised hospital laboratories provide high-speed and high-throughput capabilities at reasonable pricing; however, they are associated with prolonged time from sample collection to final result. The bedside approach accelerates patient care decision-making, reduces errors, and promotes patient safety by eliminating process steps and handoffs. Most PCIs are performed in the acute coronary setting, which requires rapid reaction and quick therapeutic decisions. Delays in reperfusion lead to increased risk of mortality, myocardial

injury, and heart failure. Stable CAD patients are usually admitted to the hospital for a short stay, even as a one-day admission, which drastically restricts the number of additional diagnostic tests performed before the PCI. Bedside testing is the most rational mode of assessment. The estimation of platelet function before PCI allows identification of individuals at risk and pursuing essential clinical action, i.e. optimisation of pharmacotherapy.

Rationale for a comparison of genotyping and phenotyping

Prior studies confirmed that both genotyping for CYP2C19 *2 alleles and platelet function testing for HPR predicts a higher risk for ischaemic events in patients undergoing PCI. Both tests have possible advantages and disadvantages: for example, genotyping can be performed in clopidogrel-naïve patients, genotype is constant, but LOF alleles are only responsible for a minority in variability in clopidogrel effect, and platelet function testing is faster. Therefore, it would be important to compare these two approaches in the personalised antiplatelet approach. So far, platelet function testing has not been compared in a prospective study in a head-to-head manner.

Study objectives

The primary objective of the study is to test whether optimisation of P2Y₁₂-inhibition based on either phenotyping or genotyping is able to reduce the risk of periprocedural MI compared to conventional care in patients undergoing elective PCI.

Study population and eligibility criteria

The ONSIDE TEST is an investigator-initiated, phase IV, multicentre, prospective, open-label, randomised controlled clinical trial involving investigational centres in Poland and Hungary. This study is registered with ClinicalTrials.gov, number NCT01930773. The investigators obtained independent research grants from non-commercial sources.

The study includes stable CAD patients between 18 and 75 years of age scheduled for an elective PCI with stent implantation, based on coronary angiography. The exclusion criteria are ACS, any elevation of myocardial necrosis enzymes at screening, planned administration of glycoprotein IIb/IIIa inhibitors for PCI, PCI for chronic total occlusions, lesions with extensive calcifications requiring rotational atherectomy, low platelet count (< 70 000/ μ L), high bleeding risk, coronary artery bypass surgery in the previous three months, severe chronic renal failure (estimated glomerular filtration rate < 30 mL/min), requirement for oral anticoagulation (warfarin, dabigatran, apixaban, rivaroxaban, etc.), history of stroke or transient ischaemic attacks, weight < 60 kg, known bleeding diathesis, haematocrit of < 30% or > 52%, and pregnancy.

Randomisation, patient flow, and study intervention

Patients who fulfil all inclusion criteria and none of the exclusion criteria, and who sign informed consent will be randomised with an electronic randomisation tool for iPhone [Randomizer for Clinical Trial, MEDSHARING, Fontenay Sous Bois, France] into three arms: 1) phenotyping arm, 2) genotyping arm, and 3) control arm [23].

Phenotyping arm

In the phenotyping arm, treatment decisions are based on the test results of the VerifyNow P2Y₁₂ assay. Patients who are not on long-term pretreatment with clopidogrel before PCI (at least five days on 75 mg clopidogrel) will receive a loading dose of 600 mg of clopidogrel after angiography just after randomisation. Platelet function testing will be performed at least 6 h after 600 mg loading dose, or after coronary angiography in patients adequately pretreated with clopidogrel. The cutoff point of 208 PRU will be used to identify patients with HPR. Those with values above this threshold will receive a loading dose of 60 mg of prasugrel. The PCI will be performed 1–2 h after prasugrel loading to allow the drug to reveal its full potency [24]. Directly before the procedure, platelet function testing will be repeated to evaluate the current on-prasugrel platelet reactivity. After PCI, patients will be treated for seven days with 10 mg of prasugrel daily. Consecutive choice of P2Y₁₂ inhibitor will be at the discretion of a primary care physician or cardiologist based on individual patient characteristics, clinical scenario, drug availability, and economic capabilities. At this time point a switch to clopidogrel is allowed. Patients without HPR will go to the PCI procedure on standard 75 mg clopidogrel therapy.

Genotyping arm

The genotyping arm will be tested using a bedside cheek swab Spartan RX CYP2C19 System (Ottawa, Ontario, Canada). Homozygous and heterozygous carriers of loss-of-function polymorphism *2 (poor metabolisers), in whom the metabolism of prodrug to active clopidogrel is impaired, will receive a loading dose of 60 mg of prasugrel 1–2 h before PCI. Directly before the procedure, platelet function testing will be performed to evaluate the current on-prasugrel platelet reactivity. After PCI, patients with *2 LOF alleles will be treated for seven days with a daily dose of 10 mg prasugrel. Subjects with wild-type alleles will be loaded with clopidogrel, if naïve, or will continue the clopidogrel therapy according to pretreatment. Although the loss-of-function *3–*8 alleles' polymorphisms are also associated with poor clopidogrel metabolism, they will not be assessed in this study as their frequency is < 1% in the general population and such additional analysis would significantly increase the overall cost [25].

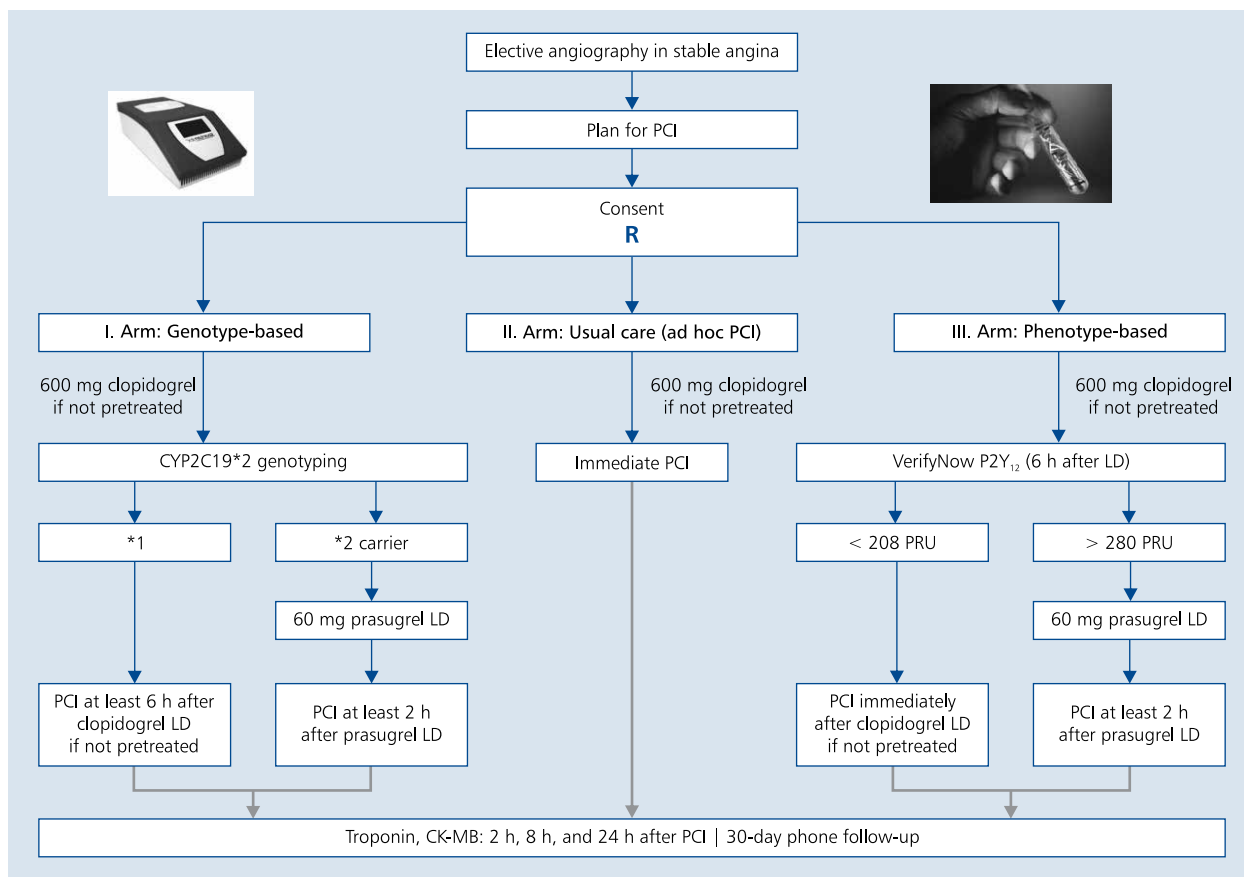


Figure 1. Optimal aNtiplatelet pharmacotherapy guided by bedSIDE genetic or functional TESTING in elective PCI patients (ONSIDE TEST) — study design diagram; CK-MB — creatine kinase muscle brain; LD — loading dose; PCI — percutaneous coronary intervention; PRU — platelet reactivity unit; R — randomisation

Control arm

Patients randomised to the control arm will follow the conventional pathway receiving standard doses of clopidogrel (75 mg daily) and proceed without any additional testing as indicated by the current European Society of Cardiology guidelines on the management of stable CAD [16]. A flow chart of the study is provided in Figure 1.

Monitoring of myocardial injury

The trials in stable CAD conducted so far, such as TRIGGER-PCI, assessed hard clinical endpoints. The incidence of major adverse cardiac event in this particular population and especially in the in the era of modern drug eluting stents is low and requires very large cohort of patients to evaluate. Therefore, a more appealing approach is to assess a surrogate endpoint that clearly correlates with long-term clinical outcomes, such as periprocedural myonecrosis biomarkers. We will measure troponin I and creatine kinase muscle brain (CK-MB) before PCI to exclude patients with baseline myocardial injury or infarction. Blood samples will be drawn at prespecified intervals: 2 h, 8 h, and 24 h after PCI, to detect the rise in cardiac enzymes. Periprocedural myocardial injury

is defined as elevation of troponin I > 1× 99th percentile upper limit of norm (ULN), but < 5× 99th percentile ULN or elevation of troponin I > 5× ULN in the absence of angiographic or imaging findings of ischaemia. Periprocedural MI will be recognised in patients with troponin elevation 5× > 99th percentile ULN and one of the following: 1) chest pain for longer than 20 min, 2) ischaemic ST changes or new pathological Q waves, 3) angiographic evidence of a flow limiting complication, or 4) imaging evidence of myocardial ischaemia [26].

Moreover, MI associated with stent thrombosis will be diagnosed after its detection by coronary angiography or autopsy in the setting of myocardial ischaemia together with a rise of troponin levels with at least one value > 99th percentile ULN [26].

Periprocedural myocardial biomarker leak is defined as a troponin or CK-MB elevation greater than 1× of the ULN within 24 h of elective PCI.

Study outcomes

Primary outcomes. The primary outcome measure is the prevalence of periprocedural myocardial injury within 24 h

after PCI in the genotyping and the phenotyping groups as compared to the controls.

Secondary outcomes. The secondary endpoints include:

- maximum level of CK-MB elevation within 24 h after PCI;
- maximum troponin elevation within 24 h after PCI;
- mean PRU during PCI;
- prevalence of inadequate platelet inhibition during PCI (PRU > 208);
- prevalence of periprocedural MI;
- prevalence of periprocedural myocardial biomarker leak;
- cardiac death, MI, definite or probable stent thrombosis, or urgent repeat revascularisation occurring within 30 days.

The secondary end-points will be assessed as a comparison between all three groups as well as between the controls and the bedside tested cohort (genotyping plus the phenotyping groups).

Safety outcomes

Among safety outcomes bleeding will be assessed according to the Bleeding Academic Research Consortium (BARC) definition [27]. Any clinical, laboratory, and/or imaging evidence of bleeding that triggers healthcare provider response (type 3) as well as any fatal bleeding (type 5) will be reported within seven days and 30 days after index procedure. All primary and secondary outcome measures are presented in Table 1.

Clinical follow-up

All patients will be followed-up until 30 days and six months after PCI either by phone or during clinical visits.

Statistical considerations

The sample size analysis was performed based on the published data on the prevalence of periprocedural MI in the stable CAD population undergoing elective stent implantation [11, 28]. The potential degree of reduction of this end-point using a more potent antiplatelet agent was based on the data from a randomised trial in which the impact of prasugrel in periprocedural MI in stable CAD was assessed [29]. Using the Fleiss method with continuity correction we estimated the sample size at 362 patients assuming the prevalence of periprocedural MI in the control group at 33% with 80% power to detect a clinically meaningful reduction to 25% of the event rates in the study group with a type I error of 5% (two-sided).

Statistical analysis

All analyses will be performed on end points verified by the independent cardiology clinical events committee. Efficacy analyses will be based on an intention-to-treat population, which will include all eligible patients enrolled in the study, and safety analyses will be done using the treated data set. Categorical variables expressed as counts and percentages will be compared using χ^2 or Fisher exact test, whereas continuous

Table 1. Outcome measures

Primary outcome measures
<ul style="list-style-type: none"> • The maximum level of CK-MB elevation within 24 h of elective PCI
Secondary outcome measures
<ul style="list-style-type: none"> • Periprocedural myocardial injury is defined as a troponin elevation greater than 5× of the ULN within 24 h of elective PCI
Other outcome measures
<ul style="list-style-type: none"> • The level of peak troponin-I elevation during 24 h of elective PCI • The rate of periprocedural MI defined as a peak troponin-I value greater than 5× the ULN and one of the following: 1) chest pain above 20 min, 2) ischaemic ST changes or new pathological Q waves, 3) angiographic evidence of a flow limiting complication, or 4) imaging evidence of myocardial ischaemia within 24 h • Periprocedural myocardial biomarker leak is defined as a troponin or CK-MB elevation greater than 1× of the ULN within 24 h of elective PCI • BARC-defined type 3 (clinical, laboratory, and/or imaging evidence of bleeding, with healthcare provider responses) and type 5 (fatal) bleeds happening within seven days of PCI • The rate of cardiac death, MI, definite or probable stent thrombosis or urgent repeat revascularisation within 30 days of elective PCI

CK-MB — creatine kinase muscle brain; PCI — percutaneous coronary intervention; ULN — upper limit of norm; MI — myocardial infarction; BARC — bleeding definition by the Bleeding Academic Research Consortium [27]

variables expressed as mean \pm standard deviation (SD) will be compared using the Wilcoxon rank-sum test. Data collected during follow-up will be analysed using appropriate univariate and multivariate techniques. Patients lost to follow-up will be censored on the date of last follow-up. Freedom from any major adverse cardiac event and overall survival will be assessed according to Kaplan-Meier, providing medians with 95% confidence intervals. The respective outcome measure comparisons between the aggregometry, genotyping, and control arms and between on-prasugrel and on-clopidogrel groups will be performed using the log-rank test. The potential influence of baseline risk factors on observed results will be assessed with the use of the Cox proportional hazards regression model. When hypotheses regarding risks cannot be suitably analysed with the Cox model, alternative statistical models will be used. In addition, multivariate models will be carried out for key bleeding variables (BARC defined type 3 and type 5 bleedings). All hypothesis tests will be two-sided, and a p value of < 0.05 will be considered statistically significant. The three arms will be compared between each other, and additionally the combined genotyping and phenotyping group will be compared with the control arm. Statistical analyses will be performed with SAS (version 9.2 or newer, SAS Institute Inc., Cary, North Carolina).

DISCUSSION

Many previous studies failed to identify the proper strategy to optimise antiplatelet therapy in patients undergoing PCI. Close scrutiny of methodologies revealed important aspects that influenced their results. Firstly, increased dosages of clopidogrel are not sufficient to decrease platelet reactivity in HPR patients. This was shown in the ARCTIC trial (Assessment by a Double Randomisation of a Conventional Antiplatelet Strategy vs. a Monitoring-guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption vs. Continuation One Year after Stenting). The study assessed if the adjustment of antiplatelet therapy in the study group based on platelet monitoring (monitoring arm) was superior to standard dose of clopidogrel. Although among the HPR patients the protocol allowed the increase of clopidogrel to 150 mg or switch to 10 mg of prasugrel, the later approach was very low (3.3%). The study showed no benefit of increased dose of clopidogrel in HPR in relation to the primary endpoint of death, MI, stent thrombosis, stroke, or urgent revascularisation after one year (HR 1.13, 95% CI 0.98–1.29) [30]. Similarly, a high dose of clopidogrel was also tested in the GRAVITAS trial, which showed no advantage in primary end point (cardiovascular death, non-fatal MI, or stent thrombosis) [12]. Secondly, the incidence of hard endpoints (cardiovascular death, MI) is very low among stable patients treated with current PCI techniques, making it very difficult to design and conduct an adequately powered trial. This was well exemplified by the TRIGGER-PCI study, which aimed to assess whether the risk of cardiovascular mortality or MI in low-risk CAD patients with high on-clopidogrel platelet reactivity after elective PCI with drug-eluting stents can be reduced by switching from clopidogrel to prasugrel [8]. The interim analysis revealed very low numbers of events in both arms (0% in prasugrel arm vs. 0.5% in clopidogrel arm, $p = \text{NS}$) and led to early termination due to futility.

A higher number of endpoints was observed in the 3T/2R trial, in which periprocedural MI was chosen as the primary endpoint. This was a prospective, randomised, open-label, controlled trial that assessed the tailored treatment with an IIb/IIIa inhibitor, tirofiban, in patients with poor response to aspirin and/or clopidogrel, and elevation of troponin $3 \times > 99^{\text{th}}$ percentile ULN within 48 h after completion of the PCI was chosen as the primary end-point [7]. In this trial administration of IIb/IIIa significantly reduced the incidence of periprocedural MI in the study group; however, this was achieved at the cost of a higher rate of bleedings. A poor response to standard doses of clopidogrel is genetically conditioned as was shown by the RAPID GENE study. This proof-of-concept, prospective, randomised trial tested the genotype-based strategy to reduce the incidence of on-treatment HPR. So far there are no randomised trials designed to demonstrate superiority of the strategy of administration of a more potent P2Y₁₂ inhibitor, i.e. prasugrel, in suboptimal responders to clopidogrel,

as compared with conventional strategy with standard dose of oral antiplatelet medications.

SUMMARY

The ONSIDE TEST trial is an open-label, randomised, parallel-group, multicentre, international trial comparing bedside genetic and pharmacodynamic testing of resistance to clopidogrel in patients undergoing elective PCI.

This is the first study with a head-to-head comparison of the above bedside testing modalities in patients with stable CAD qualified for percutaneous revascularisation. The trial is expected to verify the impact of the tailored anti-platelet therapy, based on the point-of-care genetic or platelet function testing, on the periprocedural myocardial injury. Furthermore, the ONSIDE TEST trial will provide important information regarding the safety and efficacy of prasugrel and will show whether more potent P2Y₁₂ inhibition is superior to the current standard of care in patients with HPR, who are likely not to benefit fully from clopidogrel.

Trial status

The trial is currently undergoing with 50 patients being successfully randomised. The estimated final data collection date is March 2019 (for primary outcome measure), and the expected study completion date is May 2019.

Conflict of interest: *The trial is supported by the unrestricted scientific grant funded by the Club 30 of the Polish Cardiac Society. Daniel Aradi: Lecture fees: Roche Diagnostics, Accriva, AstraZeneca, Bayer AG, Pfizer, DSI/Lilly.*

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Protokół i metodologia oceny optymalizacji farmakoterapii przeciwplatek na podstawie przyłóżkowych testów genetycznych i agregometrycznych u pacjentów poddawanych planowym zabiegom angioplastyki wieńcowej: prospektywne, otwarte, wielośrodkowe badanie

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Streszczenie

Wstęp i cel: Wysoka reaktywność płytek i nosicielstwo mutacji genu CYP2C19 wiążą się z podwyższonym ryzykiem okołozabiegowego zawału serca u pacjentów poddawanych planowej angioplastyce wieńcowej. Mimo przesłanek teoretycznych brakuje dedykowanych badań klinicznych oceniających, czy zastosowanie spersonalizowanej farmakoterapii uwzględniającej wyniki przyłóżkowych testów funkcji płytek i genotypowania pozwoliłoby ograniczyć liczbę tych powikłań.

Metody: ONSIDE-TEST to wielośrodkowe, prospektywne, otwarte, kontrolowane badanie kliniczne z randomizacją, którego celem jest ocena, czy optymalizacja terapii przeciwplatekowej z uwzględnieniem wyników agregometrii i genotypowania przynosi dodatkowe korzyści kliniczne względem standardowego postępowania. Pacjenci będą randomizowani do trzech ramion badania: 1) agregometria, 2) genotypowanie, 3) grupa kontrolna. W grupie 1 agregometria będzie przeprowadzana za pomocą urządzenia VerifyNow P2Y₁₂ przed wykonaniem angioplastyki, chorzy z wynikiem reaktywności płytek > 208 otrzymają prasugrel. W grupie genotypowania nosiciele mutacji *2 zostaną poddani terapii prasugrelem. Pozostali chorzy, w tym osoby w grupie kontrolnej, będą stosować klopidogrel. Pierwszorzędnym punktem końcowym badania jest częstość okołozabiegowego zawału serca stwierdzonego w ciągu 24 h od angioplastyki. Do drugorzędowych punktów końcowych należą: wystąpienie zgonu sercowo-naczyniowego, zawału serca, pewnej lub prawdopodobnej zakrzepicy w stencie oraz ponowna rewaskularyzacja w ciągu 30 dni od implantacji stentu. W zakresie oceny bezpieczeństwa będzie oceniane ryzyko krwawień typu 3 i 5 wg skali *Bleeding Academic Research Consortium* (BARC) w ciągu 30 dni od zabiegu angioplastyki.

Podsumowanie: Badanie ONSIDE-TEST służy sprawdzeniu, czy strategia personalizacji farmakoterapii przeciwplatekowej przy zastosowaniu przyłóżkowych testów agregometrycznych i genotypowania pozwoli na redukcję liczby okołozabiegowych zawałów serca.

Rejestracja badania: ClinicalTrials.gov: NCT01930773.

Słowa kluczowe: personalizacja farmakoterapii, leczenie przeciwplatekowe, wysoka reaktywność płytek CYP2C19*2, klopidogrel, prasugrel, stabilna choroba wieńcowa, angioplastyka

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