In this issue of Circulation: Cardiovascular Interventions, Wang et al1 publish on the real-world impact of platelet function testing where clinicians have direct access to point-of-care platelet function testing without protocol-mandated treatment strategies. Their hypothesis was that no-cost access to platelet function testing would increase treatment adjustment with P2Y12 receptor inhibitors and subsequently improve clinical outcomes of acute coronary syndrome (ACS) patients. Their conclusion is that access to no-cost platelet function testing had a modest impact on ADP receptor inhibitor selection and dosing and no impact on clinical outcome. Strikingly, switching from clopidogrel to more potent P2Y12 receptor inhibitor seemed to be independent of platelet function test results. The Treatment With Adenosine Diphosphate Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome Prospective Open Label Antiplatelet Therapy (TRANSLATE-POPS) is a relevant study as it brings into light how evidence-based medicine is translated into the real-life setting.1

The way trials are designed is critical to avoid lost in translation of personalized medicine. Although TRANSLATE-POPS and are demonstrated to be cost-effective is also a strong driver for such discrepancy.4 This is further reflected by the guidelines that have given a class IIb recommendation for platelet function testing or genotyping if the results of testing may alter management.5 In other words, this approach should be restricted to clinical research or unexpected situations but not be routinely used.

The second most striking finding of the TRANSLATE-POPS is that clopidogrel was the predominantly used P2Y12 inhibitor in an ACS population treated by percutaneous coronary intervention, a situation where more potent P2Y12 inhibitors have demonstrated a mortality benefit as compared with clopidogrel.6 The slow uptake of prasugrel and ticagrelor remains a concern for which the most likely explanation is the availability of generic clopidogrel which can be <10% of the cost of more potent P2Y12 inhibitors. Although clopidogrel remains the leading drug sold worldwide to avoid stent thrombosis, its nonselective administration remains counterintuitive in an ACS patient population when a measurable drug effect is mandated and when there is the possibility to identify patients at risk of developing adverse outcomes that can be prevented. In addition, despite clopidogrel carries a genomic label by the Food and Drug Administration, meaning that there is a recommendation for genotype assessment before the drug is used, there is rarely any pharmacogenomics assessment in clinical practice.7 The question arises why there are such gaps and where to go now?

We are living in a world where continuous tracking is now obtainable for most key physiological metrics. Refinements that are actively being pursued also include point-of-care platelet function test and genotyping to make this much more rapid and inexpensive. There is hope and room for improvement. In the Genotyping Infarct Patients to Adjust and Normalize Thienopyridine Treatment trial (GIANT, NCT01134380), genotype-guided antiplatelet therapy after primary percutaneous coronary intervention was evaluated and use of prasugrel was strongly recommended in carriers of the CYP2C19 clopidogrel loss of function allele leading to a similar 1-year composite risk of ischemic events as compared with noncarriers on clopidogrel. Although the use of genotyping was not randomized, it demonstrates that point-of-care genetic testing is feasible to refine treatment strategy in high-risk patients. The ongoing Cost-Effectiveness of CYP2C19 Genotype Guided Treatment With Antiplatelet Drugs in Patients With ST-Segment—Elevation Myocardial Infarction Undergoing Immediate PCI With Stent Implantation: Optimization of Treatment (POPular Genetics) trial is now testing this hypothesis in 2700 ST-segment—elevation myocardial infarction patients randomized to a CYP2C19-guided genotype therapy or a conventional therapy to improve net clinical benefit.8

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used a pragmatic cluster-randomized design, it was underpowered to detect differences in outcomes between strategies because of a lower than expected penetration of platelet function testing. In the TRIGGER-PCI trial, one-third of the enrolled patients declined randomization after being identified as having high platelet reactivity further outlining the limitation of a strategy of identification of deemed nonresponders instead of randomizing the use of platelet function testing and adjusting treatment.9 The low-risk population and the lack of strong pharmacological intervention were the major drawbacks of the Gauging Responsiveness With a VerifyNow Assay—Impact on Thrombosis and Safety (GRAVITAS) trial.10 This highlights the need for considering different study designs with more appropriate population risk level, cutoff value used to define platelet reactivity and outcome definitions.

The goal of personalized medicine is to focus on patients in whom the one size fits all approach does not apply easily but in whom the benefits derived from megatrails can be important and validated for the individual patient. This is the objective of the ongoing ANTARCTIC study (Assessment of a Normal Versus Tailored Dose of Prasugrel After Stenting in Patients Aged >75 Years to Reduce the Composite of Bleeding, Stent Thrombosis and Ischemic Complications; ClinicalTrials.gov number, NCT01538446) that is evaluating the superiority of a strategy of platelet function monitoring with dose and drug adjustment in patients initially treated with prasugrel 5 mg as compared with a conventional strategy using prasugrel 5 mg without monitoring and drug adjustment in ACS patients aged ≥75 years.11 For the first time the concept of a therapeutic window of P2Y12 inhibition is being tested and the outcome is powered to detect differences in outcomes between strategies of randomizing the use of platelet function testing and adjusting treatment.12


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Platelet Function Test–Guided Strategy: Lost in Translation?
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