Platelet reactivity pattern in a patient with multiple pharmacogenetic factors of reduced clopidogrel efficiency

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INTRODUCTION: Single nucleotide polymorphism of genes involved in clopidogrel metabolism may modulate platelet reactivity (PR) on clopidogrel and clinical outcome. Certain multidrug resistance gene 1 (MDR1) and CYP2C19 gene variants have been shown to impact clopidogrel pharmacodynamic effect by changing its absorption and biotransformation, respectively. Herein, we report PR pattern during 12 months of clopidogrel treatment in a patient with acute coronary syndrome (ACS) and multiple pharmacogenetic variations contributing to reduced clopidogrel effect.¹⁻³

FIGURE 1. Platelet reactivity pattern during 12-month follow up.

PATIENTS AND METHODS: We performed post hoc pharmacogenetic analysis in our previously published randomized controlled trial which evaluated the effect of serial clopidogrel dose adjustment based on continuous platelet function testing (PFT) in ACS patients treated with PCI and with initially determined high on-treatment platelet reactivity on clopidogrel. Eighty-five patients were genotyped for G2677T/A and C3435T variants of MDR1 and CYP2C19. Only one patient was identified as homozygote for all three variants associated with decreased clopidogrel effect (CYP2C19*2, 3435T and 2677T). The patient was assigned to control group and received standard clopidogrel dose.

PATIENT PRESENTATION: Fifty-four year old male, ethnic Roma (BMI 34 kg/m²) with a past history of dyslipidemia and previous myocardial infarction was enrolled in the study with unstable angina as index event. Throughout 12 months follow up PR level was

above cut-off value for HTPR set at 46U (Figure 1). Mean PR was 84.2U (min-max; 69-99U).

CONCLUSION: Routine pharmacogenetic testing in patients undergoing PCI is currently not recommended. Higher prevalence of CYP2C19*2 and 3435T alleles has been reported in Roma population compared to European Caucasians.^{3,4} Use of pharmacogenetic testing, PFT and administration of newer P2Y₁₂ blockers such as ticagrelor and prasugrel should be considered to reduce ischemic risk in these patients.

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