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PLATELET REACTIVITY AFTER CLOPIDOGREL IN JAPANESE PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING PERCUTANEOUS CORONARY INTERVENTION ACCORDING TO CYP2C19 GENOTYPES

ACC Poster Contributions
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Session Title: CYP2C19 Variants, Clopidogrel, and Outcomes
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Background: Clopidogrel is an important antiplatelet drug for the prevention of stent thrombosis after percutaneous coronary intervention (PCI). This drug requires transformation into an active metabolite by CYP2C19 for antiplatelet effect. However, CYP2C19 *2 and *3 polymorphisms known to lack enzymatic activity are considered to reduce antiplatelet effect of clopidogrel.

Methods: We assessed the association between polymorphisms of CYP2C19 *2 and *3, and platelet reactivity after clopidogrel measured by the VerifyNow-P2Y12 assay in 29 consecutive patients with coronary artery disease undergoing PCI. All patients received dual antiplatelet therapy under 100mg aspirin therapy, 300mg clopidogrel was loaded on the 1st day and a daily 75mg dose was administered on the following days. Blood samples for the VerifyNow-P2Y12 assay were obtained beyond 24 hours after dual antiplatelet therapy administration.

Results: On the basis of CYP2C19 genotype, 13 patients (44%) were classified as extensive metabolizers (EMs), 9 patients (31%) as intermediate metabolizers [IMs; 7 (24%) patients were CYP2C19*2 heterozygotes (*1/*2), and 2 (6.9%) CYP2C19*3 heterozygotes (*1/*3)], and 7 patients (24%) as poor metabolizers [PMs; 3 (10%) patients were CYP2C19*2 homozygotes (*2/*2), 2 (6.9%) CYP2C19*3 homozygotes (*3/*3), and 2 (6.9%) both CYP2C19*2 and CYP2C19*3 mutant alleles (*2/*3)]. Twelve (41%) patients carried the CYP2C19*2 allele, and 6 (21%) the CYP2C19*3 allele. Platelet reactivity in PMs was significantly higher than that in EMs [349.0 ± 43.6 VS 238.1 ± 93.9 P2Y12 reaction units (PRU), p=0.009], and was also significantly higher than that in IMs (349.0 ± 43.6 VS 253.9 ± 78.7 PRU, p=0.01)

Conclusions: CYP2C19 polymorphisms are frequent in Japanese patients and the rates of carriers of the CYP2C19*2 and *3 allele were 41% and 21%. Platelet reactivity after clopidogrel is reduced by CYP2C19 polymorphisms.