The CYP2C19*1/*2 Genotype Does Not Adequately Predict Clopidogrel Response in Healthy Malaysian Volunteers

Yanti Nasyuhana Sani,1,2 Lim Sheau Chin,1 Lim Luen Hui,1 Nur Elyana Yazmin Mohd Redhuan Shah Edwin,1 Goh Teck Hwa,3 Victor L. Serebruany,4 and Yuen Kah Hay1

1School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia
2Sarawak General Hospital, Clinical Research Centre, 93586 Kuching, Sarawak, Malaysia
3Loh Guan Lye Specialists Centre, Heart Unit, 10400 Penang, Malaysia
4Johns Hopkins University, Johns Hopkins Medicine, Towson, Baltimore, MD 21204, USA

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Background.

The CYP2C19*2 allele may be associated with a reduced antiplatelet effect for clopidogrel. Here, we assessed whether CYP2C19*2 alleles correlate with clopidogrel responsiveness following the administration of clopidogrel in healthy Malaysian volunteers. Methods. Ninety volunteers were genotyped for CYP2C19*2 and CYP2C19*3 alleles. Forty-five of 90 volunteers were included in the clopidogrel response studies and triaged into three genotypes, namely, CYP2C19*1/*1, CYP2C19*1/*2 and CYP2C19*2/*2. All subjects received 300 mg of clopidogrel, and platelet reactivity was assessed after a four-hour loading utilizing the VerifyNow-P2Y12 assay. Platelet activity was reported using P2Y12 reaction units (PRUs), and nonresponder status was prespecified at PRU ≥ 230. Results. Following clopidogrel intake, CYP2C19*2/*2 carriers had a significantly higher mean PRU compared to the CYP2C19*1/*2 and CYP2C19*1/*1 (291.0 ± 62.1 versus 232.5 ± 81.4 versus 147.4 ± 87.2 PRU, ) carriers. Almost half of the participants (46.7%) were found to be nonresponders (3 were CYP2C19*1/*1, 11 were CYP2C19*1/*2, and 7 were CYP2C19*2/*2). Conclusion. In healthy Malaysian volunteers, CYP2C19*2 allele was associated with a decrease in platelet responsiveness to clopidogrel. However, clopidogrel nonresponders can be found not only in the carriers of CYP2C19*2/*2, but also in the carriers of CYP2C19*1/*2 and CYP2C19*1/*1. The present paper demonstrated that genotype information does not correlate with clopidogrel response, and genotyping may represent a less robust approach compared to platelet activity testing in guiding clopidogrel therapy.