Background: The cytochrome P450 (CYP) 2C19 enzyme plays an important role in clopidogrel metabolism. The CYP2C19*2 variant is associated with high on-treatment platelet reactivity (HPR) and increase in stent thrombosis for homozygous patients. Homozygosity for CYP2C19*17 allele has been linked to increased active metabolite and bleeding risk. The impact of carrier status for these two common alleles is largely unknown.

Methods: We prospectively identified 184 patients with a history of percutaneous coronary intervention (PCI) on chronic clopidogrel therapy and tested for HPR using the VerifyNow P2Y12 assay and for *2 and *17 alleles of CYP2C19 using a TaqMan allelic discrimination assay. Using one way ANOVA with Bonferroni correction, we analyzed PRU values for patients within each genotype.

Results: A significant increase in PRU was detected in the *1*2 genotype when compared with wild type (240.4 vs. 168.06, p<0.001). *2*2 and *2*17 groups had similar PRU values to *1*2. PRU values for *1*17 were similar to wild type (P=1.0). There was a non-significant decrease in PRU within the*17*17 group compared to wild type (168.06 vs. 90.33, p=0.5).

Conclusions: Heterozygotes for the *2 allele had increased PRU, even in the presence of a *17 allele. Heterozygosity for the *17 allele (*1*17 or *2*17) had no impact on platelet reactivity. These data suggest that while *2 carrier status may be associated with clopidogrel resistance, carriers of a single *17 allele should not be at increased risk of bleeding events.