Conclusions: The VerifyNow™ P2Y12 platelet function assay can be used to predict periprocedural bleeding in patients exposed to clopidogrel undergoing CABG. A threshold of $\geq 230$ PRU is associated with less bleeding, and may assist clinicians in optimizing the timing of surgery.

TCT-723

Transferring from Clopidogrel Loading Dose to Prasugrel Loading Dose in Acute Coronary Syndrome Patients: High on-Treatment Platelet Reactivity

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Background: High on-treatment platelet reactivity (HPR) has been identified as an independent risk factor for ischemic events in acute coronary syndrome (ACS) patients (pts). In TRIPLET, ACS pts undergoing percutaneous coronary intervention (PCI) were given a prasugrel (pras) loading dose (LD) with or without a prior clopidogrel (clop) LD. An analysis of HPR was included.

Methods: TRIPLET was a randomized, double-blind study in ACS-PCI pts on aspirin using VerifyNow P2Y12 assay to evaluate Pras with or without prior Clop in 3 arms: (1) placebo (PBO) followed by Pras 60 mg LD (2) Clop 600 mg LD followed by Pras 30 mg LD (3) Clop 600 mg LD followed by Pras 60 mg LD. Pts undergoing PCI received Pras 10 mg once daily (qd) for 2-4 days. HPR (P2Y12 Reaction Units [PRU] $\geq 240$ were evaluated in the pharmacodynamic population within 24 hrs following the PBO/Clop LD, immediately prior to Pras LD and at 2, 6, 24, 72 hrs following Pras LDs.

Results: HPR following Clop was 58.5% in the combined Clop LD arms. No substantial difference was noted when stratified by time between the Clop and Pras LDs ($< 6$ hrs vs $\geq 6$ hrs). At $6$ hrs in the combined Pras LD arms, HPR was 7.1%, with 0% HPR by 72 hrs. Because a high number of HPR occurred in a single site, a statistical outlier analysis was performed. When outliers were excluded, HPR occurred in 1.9% at 6 hours and in 0% by 24 hrs.

Conclusions: In TRIPLET, pts with ACS intended for PCI showed a high prevalence of HPR after Clop 600-mg LD, even when measured after 6 hrs. When Pras LD was added, HPR decreased substantially by 6 hrs and was absent by 72 hrs.

Figure. Perioperative Blood Loss and Platelet Reactivity.

Data graphed as mean $\pm$ 95% confidence interval.

Conclusions: The VerifyNow™ P2Y12 platelet function assay can be used to predict periprocedural bleeding in patients exposed to clopidogrel undergoing CABG. A threshold of $\geq 230$ PRU is associated with less bleeding, and may assist clinicians in optimizing the timing of surgery.

TCT-724

Clopidogrel Loading doses result in Favorable Changes in Nitric Oxide (NO) Metabolism in Patients With Stable Angina Undergoing Percutaneous Coronary Intervention (PCI)

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Background: Clopidogrel loading dose of 600mg is used in patients undergoing PCI and those treated for acute coronary syndromes. 600mg of clopidogrel can significantly inhibit platelet inhibition within 2 hours but also improve endothelial dysfunction in stable CAD patients via a mechanism independent of platelet function. We sought to study the effect of both acute clopidogrel 600mg loading and chronic 75mg therapy on markers of NO metabolism, vasodilatory effect and antioxidant status in these patients.

Methods: 58 CAD patients were recruited. In the clopidogrel naïve group (36 subjects) blood was taken before and 2h after 600mg dose of clopidogrel and 75mg aspirin (ASA) who were attending for PCI for stable angina. We studied another cohort on chronic ASA and clopidogrel 75mg (22 subjects) after 2 months of therapy. All plasma samples were measured for NO metabolites (nitrite, nitrate and S-nitrosothiols), cGMP (a marker of vasodilatory effect) and antioxidant capacity of the plasma (ORAC index). Pearson correlation statistics were performed on all acute pre and post clopidogrel loading and chronic therapy to explore the relationships seen in NO metabolites.

Results: 2 hours after clopidogrel 600mg dose, plasma nitrite was increased from 157.1 to 194.2 to 87.64 nM (p = 0.012), cGMP from 214.2 to 214.4 to 231.5 to 107.8 pmol/ml (p = 0.037) and ORAC index from 60.6 to 86.5 to 64.15 to 10.61% (p = 0.037). Acute loading - the rise in cGMP was inversely related to the total antioxidant capacity of the plasma (ORAC index $r = -0.0001$) also the rise in nitrite with the increase in cGMP $p = 0.0043$. There was a weaker correlation in the rise in nitrate as a consequence of 600mg with the rise in ORAC $p = 0.0782$. After chronic clopidogrel, nitrite was increased from 157.1 to 244.2 to 139.6 to 139.6 nM (p = 0.0028), as well as cGMP from 214.2 to 124.4 to 276.9 to 72.15 pmol/ml (p = 0.05). In both acute and chronic groups RSNO (nitrosodioxide) was unchanged.

Conclusions: Patients receiving clopidogrel exhibit a time-proportional increase in NO bioavailability and effective vasodilation. Clopidogrel has beneficial effects on redox status 2 hours after 600mg. These results suggest non-platelet - pleiotropic effects of clopidogrel in CAD patients.

TCT-725

Point-of-Care Genetic Testing of Eleven CYP2C19 Single Nucleotide Polymorphisms Identifies Extensive and Reduced Metabolizers of Clopidogrel With High Accuracy in Patients With Coronary Artery Disease

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Background: The clinical use of genetic testing in ACS is limited by accessibility and turn-around-time. Nanosphere Verigene® System is a novel point-of-care (POC) genetic test analyzing 11 CYP2C19 variants within 3 hours. We evaluated the accuracy of the method to identify extensive (EM) and reduced clopidogrel (clop) metabolizers (RM) in