Platelet inhibitory profiles of prasugrel versus ticagrelor in patients with CYP2C19 loss-of-function genotypes undergoing percutaneous coronary intervention: results of a randomized feasibility study

Authors:
F Franchi1, F Rollini1, J Rivas1, A Rivas1, M Agarwal1, M Briecno1, M Wali1, A Nawaz1, G Silva1, Z Shaikh1, A Pineda1, D Soffer1, MM Zenni1, TA Bass1, DJ Angiolillo1, 1University of Florida College of Medicine - Jacksonville - United States of America,

Topic(s):
Antiplatelet Drugs

Citation:

Background: Although clopidogrel is the most widely used P2Y12 inhibitor, loss-of-function (LOF) allelic variants located within the hepatic cytochrome P450 (CYP) 2C19 gene lead to attenuated bioactivation, increased rates of high platelet reactivity (HPR), and worse outcomes in patients undergoing percutaneous coronary intervention (PCI). Drug regulating authorities have suggested using alternative P2Y12 inhibitors (i.e., prasugrel or ticagrelor) in these patients. However, tailoring antiplatelet therapy in clinical practice according to results of genetic testing has been limited due to lack of access to promptly available results. Moreover, there are no head-to-head pharmacodynamic (PD) comparisons of prasugrel vs ticagrelor among patients with CYP2C19 LOF alleles.

Purpose: The aim of this study was to evaluate the feasibility of using rapid genetic testing in clinical practice and to compare the PD effects of prasugrel vs ticagrelor in patients undergoing PCI with CYP2C19 LOF alleles.

Methods: This was a prospective, randomized study conducted in patients with stable coronary artery disease and non-ST elevation acute coronary syndrome scheduled for left heart catheterization (LHC) with the intent to undergo PCI. Patients underwent rapid genetic testing using the Spartan RX assay, which defines CYP2C19 genetic status within 1 hour, allowing patients to be genotyped the same day of their LHC. Patients who were carriers of at least one LOF (*2 or *3) allele were randomized to receive either prasugrel [60mg loading dose (LD) - 10mg/day maintenance dose (MD)] or ticagrelor (180mg LD - 90mg b.i.d MD). Blood samples for PD analysis by VerifyNow were collected at 5 time points: baseline (prior to PCI), 30 minutes, 2 hours, 24 hours (or at hospital discharge whichever came first), and 1-4 weeks post-LD. All patients were treated with aspirin. The primary endpoint of our study was the non-inferiority in platelet reactivity, measured as PRU, at 24 hours of prasugrel vs ticagrelor in LOF allele carriers.

Results: A total of 781 consecutive patients scheduled for LHC were genotyped, of whom 223 (28.5%) were carriers of at least one LOF. Of these, 65 patients underwent PCI and randomized to prasugrel (n=32) vs ticagrelor (n=33). PRU levels at 24 hours were 33 vs 36 (prasugrel vs ticagrelor; mean difference = -3; 95%CI: -28 to 22; p=0.814) meeting the primary endpoint of non-inferiority. Both prasugrel and ticagrelor significantly reduced PRU to a similar extent with no differences between groups at all other time points (Figure). Accordingly, HPR rates were low and similar between groups.

Conclusion: Rapid genetic testing using the Spartan assay is feasible providing results in a timely fashion in a real-world clinical practice of patients undergoing PCI. Among patients with CYP2C19 LOF carrier status, prasugrel and ticagrelor are associated with similar levels of platelet inhibition.
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VerifyNow

- PRU
- 30 min: p=0.757
- 2 h: p=0.018
- 24 h: p=0.014
- 1-4 weeks: p=0.861