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PHARMACODYNAMIC EFFECTS OF PRASUGREL DOSING REGIMENS IN PATIENTS ON MAINTENANCE PRASUGREL THERAPY: RESULTS OF A PROSPECTIVE RANDOMIZED STUDY

i2 Poster Contributions

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Authors: *Antonio Tello-Montoliu, Salvatore Tomasello, Jose Luis Ferreiro, Masafumi Ueno, Naveen Seecheran, Bhaloo Desai, Murali Kodali, Fabiana Rollini, Lyndon Box, Martin Zenni, Luis Guzman, Theodore Bass, Dominick Angiolillo, University of Florida, Jacksonville, FL, USA*

Background: There are a growing number of patients on chronic prasugrel therapy, questioning the dosing regimen of prasugrel to administer if PCI is required. The pharmacodynamic (PD) effects of administering prasugrel in these patients are unknown. The aim of the present study is to assess the PD effects of different prasugrel dosing regimens in patients already on maintenance prasugrel therapy.

Methods: This is a prospective PD study in patients on maintenance prasugrel therapy (10mg/day) randomized to receive a 10 mg, 30 mg, or 60 mg dose of prasugrel. PD assessments were conducted at 3 time points: baseline, 1 hour and 4 hours post-dosing. The platelet reactivity index (PRI) values assessed by vasodilator-stimulated phosphoprotein (VASP) 4 hours after re-loading with prasugrel 60 mg was the primary endpoint. PD tests also included VerifyNow-P2Y12 assay and light transmission aggregometry (LTA).

Results: A total of 64 patients were studied: 10mg (n=22), 30mg (n=21), and 60mg (n=21). There were no differences in baseline PD parameters. Intra-group comparisons showed that a 60 mg dose reduced baseline PRI levels from $26.6 \pm 3.4\%$ to $11.5 \pm 3.2\%$ at 1 hour ($p=0.004$), and $2.8 \pm 2.7\%$ at 4 hours ($p<0.001$, primary endpoint; $p=0.002$ between 1 and 4 hours). A 30 mg dose also reduced baseline PRI levels from $29.5 \pm 3.5\%$ to $17.8 \pm 3.2\%$ at 1 hour ($p=0.006$) and $11.0 \pm 2.9\%$ ($p<0.001$, from baseline; $p=0.044$ between 1 and 4 hours). A 10 mg dose was associated with modest PD effects. Intra-group-comparisons showed similar findings with VerifyNow-P2Y12 testing and LTA. Inter-group comparisons showed that a 60 mg dose achieved lower PRI levels than 30 mg at 4 hours ($p=0.05$), and a numerical but non-significant trend towards better PD effects at 1 hour ($p=0.171$). Inter-group comparisons were similar with VerifyNow-P2Y12 testing, but not LTA.

Conclusions: In patients on maintenance prasugrel therapy, a 60 mg dosing strategy is associated with faster and higher platelet inhibition compared with lower doses as assessed by P2Y12 specific assays.