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PRASUGREL VERSUS ADJUSTED HIGH-DOSE CLOPIDOGREL IN PATIENTS WITH HIGH ON-CLOPIDOGREL PLATELET REACTIVITY: THE PECS-HPR RANDOMIZED, MULTICENTER STUDY

Poster Contributions
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Background: Repeated loading doses (LD) of clopidogrel were shown to effectively overcome high on-clopidogrel platelet reactivity (HPR); however, comparison to potent $P2Y_{12}$-inhibitors is lacking. We sought to compare the antiplatelet effect of high-dose clopidogrel versus prasugrel at both short- and long-term in acute coronary syndrome patients (ACS) with HPR.

Methods: ACS patients receiving 600 mg clopidogrel pretreatment were randomized to prasugrel or high-dose clopidogrel in a multicenter, controlled trial if platelet function testing revealed HPR (>46U) after PCI. In the prasugrel group, patients received an immediate 60-mg LD followed by 10 mg for three days. After day 3, patients were randomized to either standard (10 mg) or reduced (5 mg) maintenance doses up to 30 days. Patients randomized to high-dose clopidogrel received repeated loading doses of 600 mg clopidogrel based on controlled platelet function testing for three days, then were randomized to 75 mg or 150 mg maintenance doses for 30 days. ADP-induced platelet reactivity was measured with the Multiplate assay at day 0 (randomization), 1, 2, 3 and 25.

Results: Between May 2011 and March 2013, 147 patients were randomized. Although baseline platelet reactivity did not differ between groups (p=0.22), prasugrel provided significantly more rapid and more potent platelet inhibition compared to repeated LD-s of clopidogrel through all three days after randomization (p<0.0001). During the maintenance phase, there was a dose-dependent increase in platelet reactivity from prasugrel 10 mg to clopidogrel 75 mg (p for trend <0.0001), demonstrating the superiority of both doses of prasugrel over 75 and 150 mg clopidogrel. No difference was observed between clopidogrel groups at day 25 (p=0.35), leading to a rebound in HPR and returning to the level of baseline platelet reactivity with both 75 and 150 mg clopidogrel (p=0.66 vs. day 0).

Conclusion: Prasugrel provides significantly more rapid and more potent platelet reactivity inhibition compared to repeated loading doses of clopidogrel. The observed differences persisted with maintenance dosing, leading to rebound in HPR with both standard and high-dose clopidogrel. (NCT01493999)