

## Prasugrel versus adjusted high-dose clopidogrel in patients with high-on-clopidogrel platelet reactivity: the PECS-HPR randomised, multicentre study

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**Aims:** Repeated loading doses (LD) of clopidogrel were shown to effectively overcome high-on-clopidogrel platelet reactivity (HPR); however, comparison to potent P2Y<sub>12</sub>-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 (NCT01493999).

**Methods and results:** ACS patients receiving 600 mg clopidogrel pre-treatment were randomised to prasugrel or high-dose clopidogrel in a multicentre, controlled trial if platelet function testing revealed HPR (>46 U) 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 randomised to either standard (10 mg) or reduced (5 mg) maintenance doses (MD-s) up to 30 days. Patients randomised to high dose clopidogrel received repeated LDs of 600 mg clopidogrel based on controlled platelet function testing for three days, and then were randomised to 75 mg or 150 mg MDs for 30 days. ADP-induced platelet reactivity was measured with the Multiplate assay at day 0 (randomisation), 1, 2, 3 and 25. Between May 2011 and March 2013, 147 patients were randomised. 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 LDs of clopidogrel through all three days after randomisation (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).

**Conclusions:** 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.