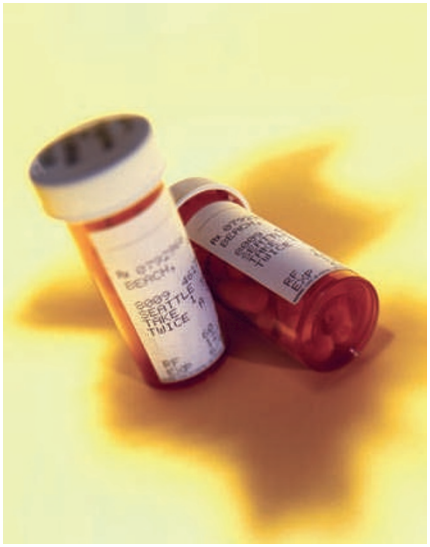
ANTIPLATELET THERAPY

Making the SWAP from clopidrogrel to prasugrel



The third-generation thienopyridine $P2Y_{12}$-receptor blocker, prasugrel, has been shown to have net clinical benefits over clopidrogrel in the treatment of patients with acute coronary syndromes (ACS). Switching from clopidrogrel to prasugrel is, therefore, an attractive option. However, the pharmacodynamic effects of such a strategy—including the potential for interaction between the two drugs—were unknown. Now, the SWAP investigators have reported that switching antiplatelet therapy from clopidrogrel to prasugrel in patients with ACS is well-tolerated and associated with increased platelet inhibition.

In the phase II, double-blind, randomized SWAP trial, patients aged 18–75 years were enrolled if they had been receiving dual antiplatelet therapy with clopidogrel and aspirin for 30–330 days following an acute coronary event.

After a 10–14 day run-in period, in which patients were given clopidogrel 75 mg per day, study participants were randomly assigned to receive one of the following regimens for 13–15 days: a loading dose (LD) of placebo followed by a maintenance dose (MD) of clopidogrel 75 mg per day ($n = 33$); an LD of placebo followed by an MD of prasugrel 10 mg per day ($n = 36$); or an LD of prasugrel (60 mg) followed by an MD of prasugrel 10 mg per day ($n = 31$).

Platelet function was evaluated at 2 h, 24 h, 7 days, and 14 days. The primary end point was maximum platelet aggregation at 7 days, as measured by light transmittance aggregometry. Maximum platelet aggregation was significantly lower in the placebo LD/prasugrel MD group (41.1%) and in the prasugrel LD/prasugrel MD group (41.0%) when compared with the placebo LD/clopidogrel MD group (55.0%; $P < 0.0001$ for both comparisons). Among the patients who received an LD of prasugrel, increased platelet inhibition was evident within 2 h of the dose being administered, and was still present at 24 h. These findings were confirmed by two other platelet-function assays (vasodilator-stimulated phosphoprotein phosphorylation and VerifyNow®-$P2Y_{12}$ [Accumetrics, Inc., San Diego, CA, USA]). "The practical implications [of these findings] are based on how quickly physicians want to achieve greater levels of platelet inhibition when switching to prasugrel therapy," explains SWAP investigator Dominick Angiolillo. "If needed quickly (e. g. for a patient presenting with ACS while on clopidogrel therapy who needs to undergo percutaneous coronary intervention), give an LD. If not needed immediately, then switch to maintenance dosing without a load."

Switching from clopidogrel to prasugrel also seemed to be safe; the incidence of adverse events was, in fact, lower among those who received prasugrel (36.2% and 25.0% for placebo LD/prasugrel MD and prasugrel LD + MD, respectively) when compared with that in the clopidogrel group (52.0%).

Dr Angiolillo acknowledges that the SWAP trial had a pharmacodynamic measure as a primary end point; the efficacy of switching from clopidrogrel to prasugrel will need to be assessed in randomized trials using hard clinical end points.

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