Abstract: 2349

Selatogrel, a novel P2Y12 inhibitor for emergency use, achieves rapid, consistent and sustained platelet inhibition following single-dose subcutaneous administration in stable CAD patients

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Background: In the setting of AMI, rapid platelet inhibition is desirable but the onset of pharmacodynamic (PD) effect of oral platelet P2Y12 inhibitors is delayed, sometimes for hours. Subcutaneous (s.c) administration of a rapidly-acting P2Y12 inhibitor would overcome many of the limitations of available therapies. Patients with stable CAD were investigated initially.

Purpose: To characterise the inhibition of platelet aggregation and pharmacokinetics (PK) of a single dose of selatogrel, a novel s.c P2Y12 inhibitor, in patients with stable CAD.

Methods: Patients with stable CAD receiving oral antiplatelet therapy (aspirin and/or oral P2Y12 inhibitor) were randomized to 1 of 8 groups based on treatment (selatogrel or matching placebo), dose (8 mg or 16 mg) and s.c injection site (thigh or abdomen). Venous blood samples were collected into PPACK anticoagulant tubes. Platelet reactivity was assessed by VerifyNow PRU (P2Y12 reaction units) test before and 15 min, 30 min and 1, 2, 4, 8 and 24 h after injection. Light-transmittance aggregometry (LTA; ADP 20 uM) was also performed. PK samples were collected up to 24 h post-dose. Adverse events occurring within 30 days were recorded. Responders were defined as having PRU <100 at 30 min after injection and lasting ≥3 h.

Results: 345 patients (mean age 65 y; 20% female; 31% diabetes) received selatogrel 8 mg (n=114), selatogrel 16 mg (n=115) or placebo (n=116). 97% were on background therapy with aspirin (or its derivative carbasalate) and 35% with oral P2Y12 inhibitor (clopidogrel 23%, prasugrel 4%, ticagrelor 8%). 89% of subjects were responders to selatogrel 8 mg, 90% to selatogrel 16 mg and 16% to placebo (P<0.0001). At 15 min post-dose, PRU values (mean ±SD) were 10±25 with selatogrel 8 mg, 5±10 with selatogrel 16 mg and 163±73 with placebo (Figure). PRU levels were maintained at 2 and 4 h for both doses and gradually returned to pre-dose levels by 24 h post-dose (Figure). LTA results were consistent with the VerifyNow results. PD responses were similar for thigh and abdomen injection sites. Selatogrel was well tolerated: mild dyspnoea (or moderate dyspnoea, n=1, with 16 mg) occurred in 5% and 9% with selatogrel 8 mg and 16 mg, respectively, vs 0% with placebo; dizziness occurred in 4% and 4% vs 1%, respectively, without significant haemodynamic or ECG changes. Bleeding events occurred in 9.6% and 4.3% with selatogrel 8 mg and 16 mg, respectively, vs 6.9% with placebo. Pharmacokinetic data will be presented.
Conclusions: Selatogrel has a rapid PD effect following s.c injection in patients with stable CAD, within 15 min in most patients. The consistent and high levels of P2Y12 inhibition with a single 8 mg or 16 mg dose are sustained for over 4 hours, following which platelet reactivity progressively recovers over 24 h. Selatogrel was well tolerated, with mostly mild, transient dyspnoea observed in <10% patients. These data support further studies of selatogrel for emergency treatment of AMI patients.