Inhibition of platelet aggregation after subcutaneous administration of a single-dose of selatogrel, a novel P2Y12 antagonist, in acute myocardial infarction: a randomised open-label phase 2 study

Authors:
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Topic(s):
Acute Coronary Syndromes: Pharmacotherapy

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Background: Oral P2Y12 receptor antagonists exhibit a delayed onset of platelet inhibition in patients experiencing acute myocardial infarction (AMI). Selatogrel is a potent, reversible, and highly selective P2Y12 receptor antagonist with a rapid onset and offset of action when administered subcutaneously.

Purpose: To assess inhibition of platelet aggregation (IPA) after subcutaneous (s.c.) single-dose administration of selatogrel in patients with AMI receiving standard concomitant therapy.

Methods: Male and postmenopausal female adults (≤85 years) presenting with type 1 AMI (ST-elevation MI [STEMI] or non-STEMI [NSTEMI]) and onset of AMI symptoms >30 min to <6 h were randomised (1:1) to receive a single s.c. dose of either 8 mg or 16 mg selatogrel. Blood samples were collected at baseline and at 15, 30, and 60 min post-dose and evaluated for ADP-induced platelet aggregation (expressed as P2Y12 reaction units [PRU]) using VerifyNow. The primary endpoint was the response to treatment (defined by PRU <100) at 30 min post-dose. Safety was assessed up to 48 h post-dose.

Results: Forty-seven patients (median age 69 y; 72% male; 62% STEMI; 94% Killip class 1) received 8 mg (N=24) or 16 mg (N=23) selatogrel. Study-treatment concomitant medications included acetylsalicylic acid (98%), P2Y12 inhibitors (96%), heparins (94%), statins (94%), nitrates (68%) and morphine (38%). Oral ticagrelor (92%) with corresponding loading doses was only administered after selatogrel. The proportion of patients meeting the primary endpoint (responders) 30 min post-dose was 91% (95% CI: 72, 99) and 95% (95% CI: 77, 100) with 8 and 16 mg, respectively (p<0.001 for both doses). Response rates were independent from STEMI/NSTEMI diagnosis, age and sex. A response was observed as early as 15 min (8 mg: 75% of patients [95% CI: 53, 90]; 16 mg: 91% of patients [95% CI: 72, 99]), and sustained up to 60 min post-dose (8 mg: 75% of patients [95% CI: 53, 90]; 16 mg: 96% of patients [95% CI: 78, 100]). Platelet reactivity was decreased following selatogrel administration (Figure; interquartile range [box], min and max [whiskers], median and mean [horizontal line and symbol, respectively, within the box]). Overall, 43% of patients had ≥1 treatment-emergent adverse event (TEAE), which were mainly of mild/moderate intensity. Ventricular tachycardia (VT) 8 mg: 5/24; 16 mg: 3/23) was the most frequent TEAE. Treatment-emergent serious AEs of VT were reported in two patients receiving 8 mg (one patient also experienced ventricular fibrillation) and one patient receiving 16 mg selatogrel. Post-procedural haemorrhage (mild) occurred in one patient: bleeding at radial access after percutaneous coronary intervention (~1 h after selatogrel 8 mg).

Conclusion: Single-dose administration of s.c. selatogrel (8 mg and 16 mg) induced a rapid IPA response in patients with AMI at 30 min (as early as 15 min and maintained at 60 min post-dose) and was well-tolerated with no major bleeding events.
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