Impact of alirocumab added to high-intensity statin therapy on platelet function in AMI patients: a pre-specified substudy of the randomized, placebo-controlled PACMAN-AMI trial

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Background: Previous small observational studies have suggested a potential association of proprotein convertase subtilisin kexin type 9 (PCSK9) and platelet reactivity. However, the role of the PCSK9 inhibitor alirocumab on platelet aggregation among patients with acute myocardial infarction (AMI) remains unknown.

Purpose: We investigated the effect of alirocumab on P2Y12 reaction unit (PRU) on top of high-intensity statin therapy among AMI patients receiving dual antiplatelet therapy (DAPT) with a potent P2Y12 inhibitor (ticagrelor or prasugrel).

Methods: This was a pre-specified, powered, pharmacodynamic substudy nested within the PACMAN (effects of the PSCK9 antibody AliroCuMab on coronary Atherosclerosis in patieNts with Acute Myocardial Infarction) trial, a randomized, double-blind trial comparing biweekly alirocumab (150mg) versus placebo in AMI patients undergoing percutaneous coronary intervention (PCI). Patients recruited at Bern University Hospital, receiving DAPT with either ticagrelor or prasugrel at 4 weeks and adherent to the study drug (alirocumab or placebo) were analyzed for the current study. The VerifyNow P2Y12 point-of-care assays were used to measure PRU at baseline (i.e. before first study drug administration), 4 weeks, and 52 weeks after study drug administration (higher PRU levels indicating greater platelet aggregation). The primary endpoint was PRU at 4 weeks.

Results: Among 139 randomized patients (mean age 58.2 years [SD, 9.5], 21 [15.0%] women, mean LDL-C level 150.6mg/dL [SD, 30.9]), baseline characteristics were well balanced between groups including baseline PRU (50.0 [IQR, 120.0] in the alirocumab group vs. 62.0 [IQR, 122.0] in the placebo group, P=0.75). At 4 weeks, mean LDL-C was significantly lower in the alirocumab group (23.5 [SD, 23.7] mg/dL vs. 74.4 [SD, 30.5] mg/dL, P<0.001). The majority of patients received ticagrelor DAPT at 4 weeks (57 [86.4%] vs. 69 [94.5%], P=0.14). There were no significant differences in PRU at 4 weeks (12.5 [IQR, 27.0] vs. 19.0 [IQR, 22.0], P=0.26) and at 52 weeks (25.0 [IQR, 37.0] vs. 34.0 [IQR, 59.0], P=0.07) (Figure). Consistent results were observed in 126 patients treated with ticagrelor (i.e. after excluding 13 patients treated with prasugrel) at 4 weeks (13.0 [IQR, 20.0] vs. 18.0 [IQR, 27.0], P=0.28).

Conclusion: Among AMI patients receiving DAPT with potent P2Y12 inhibitors, alirocumab had no significant effect on platelet function as assessed by PRU.

Figure 1. PRU over time and between groups

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