Aspirin has little additional ex vivo anti-platelet effects in healthy volunteers receiving prasugrel

Philip D. M. Leadbeater¹, Nicholas S. Kirkby¹,², Al-Rehan Dhanji², Melissa V. Chan², Arthur T. Tucker², Jane A. Mitchell¹, Timothy D. Warner²

¹National Heart & Lung Institute, Imperial College, London SW3 6LY, United Kingdom, ²William Harvey Research Institute, Barts & the London School of Medicine, London EC1M 6BQ, United Kingdom

Although aspirin and ADP P2Y₁₂ receptor inhibitors are commonly co-prescribed as dual anti-platelet therapy, it is unclear if aspirin furthers the anti-aggregatory effect of strong standalone P2Y₁₂ inhibition. For example, in vitro, the active metabolite of prasugrel inhibits thromboxane A₂-dependent pathways of platelet aggregation. Here we have investigated the hypothesis that aspirin provides little additional anti-aggregatory effect in a group of healthy volunteers taking standard doses of prasugrel.

9 healthy males, aged 18-40, enrolled into the 21 day study. Prasugrel was loaded at 60mg on day 1 and maintained at 10 mg once daily until day 21. At day 8 aspirin 75 mg once daily was introduced in addition to prasugrel and the dose increased to 300 mg once daily on day 15. On days 0, 7, 14 and 21 platelet function was assessed by 96-well light transmission aggregometry (to arachidonic acid, ADP, collagen, epinephrine, TRAP-6 and U46619) and response to treatments by VerifyNow™.

All subjects had normal platelet function on day 0. After 7 days of prasugrel administration aggregation to arachidonic acid, ADP and the thromboxane mimetic U46619 was reduced by 75-95%; no further inhibition was seen on days 14 or 21 after the addition of 75 or 300 mg aspirin. Aggregation to collagen was reduced by prasugrel, with the largest reduction seen at lower concentrations. There was a small additional, dose-independent, inhibition with aspirin. VerifyNow™ P2Y₁₂ cartridge assay confirmed >80% inhibition with prasugrel, and that none of the subjects were aspirin resistant.

These data show that standard dosing of prasugrel in healthy volunteers produces a strong anti-aggregatory effect against a range of platelet agonists, which is little enhanced by the addition of aspirin. In conclusion, bearing in mind its potential to cause gastric and other bleeds, the addition of aspirin as a dual-therapy with potent P2Y₁₂ receptor inhibitors warrants further investigation.