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PLATELET FUNCTION UPON SWITCHING TO TAF VS CONTINUING ABC: A RANDOMIZED SUBSTUDY

Clinical: (M) Cardiovascular Complications of HIV Infection and Antiretroviral Therapy

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Background: Abacavir (ABC) use has been associated with increased risk of myocardial infarction (MI), with altered endothelial and platelet function as proposed underlying mechanisms. We hypothesized that a switch from ABC to tenofovir alafenamide (TAF) would result in decreased platelet reactivity.

Methods: In a platelet function substudy of a randomized double-blind trial of virally suppressed, HIV1-positive individuals on ABC/lamivudine (3TC), randomized to switch to TAF/emtricitabine (FTC) or remain on ABC/3TC while continuing their 3rd agent, we measured platelet aggregation (PAg) at baseline (BL), week (W) 4, and 12 in response to increasing concentrations of five agonists: collagen (Col), thrombin receptor-activating peptide (TRAP), adenosine diphosphate (ADP), epinephrine (Epi) and arachidonic acid (AA). We compared population-derived agonist concentrations inducing 50% platelet aggregation (EC50) between-groups at BL, W4 and 12 by four parameter logistic regression. We measured platelet surface expression of the GPVI receptor, CD42b and P-selectin (P-sel) by flow cytometry and compared between-group differences at BL and W12 pre- and post-stimulation with collagen-related peptide (CRP) by Wilcoxon rank sum test.

Results: The 61 participants (29 in TAF/FTC and 32 in ABC/3TC group) were well matched at BL. Although baseline PAg in response to Col, TRAP and ADP was similar between groups, W4 PAg with Col, TRAP and ADP was significantly lower in the TAF/FTC arm (reflected by greater EC50) compared to the ABC/3TC arm (Table). Reduced PAg in response to Col persisted through W12, while differences in PAg with TRAP and ADP were no longer significant at W12. PAg with Epi and AA did not differ between groups at any time point. Expression of the collagen receptor GPVI, which mediates endothelial-platelet interactions, was higher at W12 in the TAF/FTC group (P=0.031) while W12 GP42b and P-sel were similar between groups (P=0.10, P=0.8). There were no between-group differences in GPVI shedding or induction of P-sel with CRP activation (all P>0.1).

Conclusion: Within a randomized trial, switching from ABC/3TC to TAF/FTC was associated with significantly lower platelet reactivity to TRAP and ADP at W4 and Col through W12. Together with higher surface GPVI expression, these observations suggest improvements in measures of platelet function involving endothelial-platelet pathways with a switch from ABC/3TC and point to a potential underlying mechanism for increased risk of MI with ABC.