PA-066 VITAMIN D FOR TREATMENT AND PREVENTION OF TB-HIV

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Background Susceptibility to reactivate tuberculosis infection is influenced by immunosuppression. Amongst the greatest risk

factors for active TB are HIV-1 infection and vitamin D deficiency. These risks factors are not mutually exclusive and may exacerbate each other. However, the phenotype of immunodeficiency induced by each is different. Vitamin D deficiency not only associates with TB risks, but it is greater in HIV-co-infected patients. The effects of vitamin D on the immune system are pleiotropic, being both anti-inflammatory and antimicrobial. Evidence suggests that vitamin D may not only reduce risk of TB by increasing anti-mycobacterial immunity and reducing inflammation, but it may also reduce HIV replication and the associated effects on innate and adaptive immunity; thus concomitantly reducing the associated risk of HIV on TB.

Methods We investigated *in vitro* and *ex vivo* the effect of vitamin D supplementation on the response of monocyte-derived macrophages (MDM) and peripheral blood mononuclear cells (PBMC), respectively, to HIV-*M. tuberculosis* (*Mtb)* co-infection. The effects of pathogen growth and susceptibility to infection were correlated to cytokine, chemokine and antimicrobial peptide production, by expression, secretion and flow cytometry analysis.

Results MDM differentiated in the presence of vitamin D metabolites, significantly restricted HIV-1 replication, alone and during co-infection with *Mtb*. Type 2 MDM were considerably more susceptible to HIV-1 infection than type 1. This correlated with the level of CCL2 production, which was significantly inhibited by vitamin D metabolites. PBMC isolated from healthy individuals in summer and in winter after receiving vitamin D, significantly restricted HIV-1 infection, compared to PBMC collected in winter before supplementation. There was a significant difference in circulating cell populations and serum cytokines/chemokines in summer, compared to winter, and these were investigated for correlations with HIV replication.

Conclusions Vitamin D may prove a cheap, effective, tool for preventing TB-HIV disease progression and clinical trials are warranted in at-risk populations.