TENOFOVIR ALAFENAMIDE REDUCES TRANSMISSION OF HUMAN T-LEUKAEMIA VIRUS 1 (HTLV-1) IN A HUMANISED MOUSE MODEL OF INFECTION

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Background: Pre-clinical animal models can be used to identify therapeutic intervention strategies against HTLV-1 infection. No anti-viral compounds have been developed specifically for HTLV-1. However, the HTLV-1 reverse transcriptase may be susceptible to some anti-retroviral compounds developed for HIV. A humanised mouse model of HTLV-1 subtype C infection was characterised that recapitulates aspects of human disease and was used to study the therapeutic potential of tenofovir alafenamide (TAF), an HIV nucleotide reverse transcriptase inhibitor.

Methods and results: Mice were generated by intra-facial injection of $CD34^+$ human stem cells into 1-2 day old NOD-*scid* $IL2Rg^{null}$ pups. Reconstitution of human immune cell populations in mice was confirmed at 16-weeks of age before infection by intraperitoneal injection of irradiated HTLV-1c-infected T cells. Mice develop persistent HTLV-1c pro-viral load ($>10^6$ copies/10^6 PBMC), lymphocytosis of mature CD4+ and CD8+ T cells ($>10^7$ T cells/ml blood), splenomegaly and lobed 'flower-like' nuclei of infected cells. Prophylactic administration TAF by daily oral gavage significantly reduced transmission of HTLV-1 in this model at clinically relevant doses of drug ($p=0.004$).

Conclusion and Impact: This work demonstrates in-vivo efficacy of tenofovir as a measure against HTLV-1 infection and aims to provide grounds to a conduct a clinical trial investigating the efficacy of TAF in preventing HTLV-1c transmission. Moreover, recent FDA approval of TAF for use in HIV significantly reduces the barriers to its implementation in the context of HTLV-1 disease.

Disclosure of interest: None to declared.