PARTIAL EFFICACY OF A BROADLY NEUTRALIZING ANTIBODY AGAINST CELL-ASSOCIATED SHIV INFECTION

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Background: Prophylactic vaccines are required to alleviate HIV-1 spread. Broadly neutralizing antibodies (BnAbs), capable of neutralizing arrays of viral isolates, are promising immunological prophylactics. Although BnAbs protect macaques from challenge with cell-free SHIV, their efficacy against cell-associated virus (CAV) challenges remains unclear. While some *in vitro* studies have raised concerns about BnAbs being less potent against CAV, several BnAbs equally capable of neutralizing cell-free and CAV *in vitro* have been identified. Amongst these antibodies is the PGT121 clone that recognizes an epitope including the third variable loop of the viral envelope and surrounding glycans. As HIV-1 immunological prophylactics will likely need to eliminate both cell-free virus and CAV, we assessed if passively transferred PGT121 could protect macaques from high-dose intravenous challenge with cell-associated SHIV.

Methods: Eleven macaques, six intravenously infused with PGT121 (1mg/kg) and five intravenously infused with human IgG_1 isotype control (1mg/kg) or receiving no antibody, were challenged intravenously, one hour following antibody infusion, with $24.5x10^6$ splenocytes obtained from an $SHIV_{SF162P3}$-infected animal. Animals were followed for onset of viremia.
Results: All five isotype control/no antibody animals developed viremia one week post-challenge. Three of six PGT121-infused animals were completely protected from $SHIV_{SF162P3}$ challenge. Two PGT121-infused animals developed peak viremia two weeks post-challenge. Interestingly, these two animals exhibited only low plasma PGT121 levels one week post-infusion. The remaining PGT121-infused animal exhibited a delay of seven weeks prior to developing viremia.

Conclusion: These data provide the first evidence that BnAbs can protect non-human primates from challenge with CAV. The partial nature of the observed protection appears to be related to early suboptimal plasma concentrations of PGT121 and/or the long-term persistence of cells harbouring virus until waning of therapeutic antibody to suboptimal concentrations.

Disclosure of Interest Statement:
Swiderek KM is an employee of Theraclone Sciences Inc. who produced the PGT121 monoclonal antibody.