Transient viral activation in HTLV-1-infected macaques treated with pomalidomide

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Background:
Human T-cell Leukemia Virus Type 1 (HTLV-1) persists in the host despite a vigorous immune response, that include cytotoxic T cells (CTL) and Natural Killer (NK) cells, suggesting that the virus has developed effective mechanisms to counteract host immune surveillance. We recently showed that in vitro treatment of HTLV-1 infected cells with the drug pomalidomide (POM) increases surface expression of MHC-I, ICAM-1, and B7-2, and increases the susceptibility of HTLV-1 infected cells to NK and CTL killing. Our main goal was to explore the in vivo effects of POM.

Methods:
We used the rhesus macaque model to determine if POM treatment would activate the immune system and allow recognition and clearance of HTLV-1 infected cells. We treated 4 HTLV-1 infected macaques over a 24 day period with POM (0.2mg/kg). Blood, urine, and bone marrow samples were collected throughout the course of the study.

Results:
In 3 of 4 animals, POM treatment resulted in increased antibodies to HTLV-1 antigens measured by western blot and p24Gag ELISA. Consistent with POM inducing HTLV-1 activation, elevated leukotriene (LTB4 and LTE4) levels in urine of all 4 animals were measured. In addition, HTLV-1-specific T-cell responses were detected. Immune system activation in POM treated animals is also detected by changes in cellular populations. We observed a marked increase in proliferating $CD4^+$, $CD8^+$, and NK cells as measured by $Ki67^+$ cells. We detected an increased frequency of B7-2 expressing $CD4^+$ and $CD8^+$ cells, peaking 18 days after beginning POM treatment. Activation markers HLA-DR, CD11b, and CD69, also increased during POM treatment. In all cases, two weeks after cessation of treatment, these populations decreased to baseline or lower levels as did leukotriene levels.

Conclusion:
These results indicated that POM treatment induces a transient HTLV-1 activation in infected individuals and may not be effective as a single-agent therapeutic.

Disclosure of Interest Statement:
The authors have declared that no competing interests exist.

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