BRENTUXIMAB VEDOTIN REDUCES CD30 EXPRESSION AND GUT HIV DNA LEVELS IN HUMANIZED MICE

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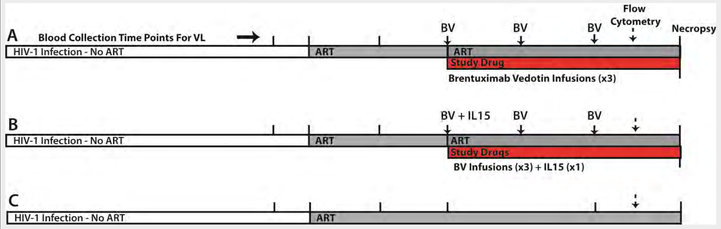
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BACKGROUND

- CD30 is preferentially expressed in HIV-infected and viral transcriptionally active CD4 T cells from viremic and ART suppressed individuals.
- CD30 is preferentially expressed on effector memory CD4+ T cells in HIV-infected individuals .
- Anti-CD30 antibody drug conjugate, brentuximab vedotin (BV), leads to reduced cell-associated HIV DNA in vitro and transient decreases in cell-associated HIV RNA in vivo.
- The impact of anti-CD30 therapy on tissue measures of HIV burden is unknown.

METHODS

- Humanized BLT mice were initiated on daily TDF, FTC, and DTG by oral gavage approximately 3 weeks following intraperitoneal infection with HIV-1 JR-CSF. After mice achieved viral suppression they were divided into three treatment cohorts:
  1] ART alone control (N=16)
  2] ART and 3 intraperitoneal (IP) weekly infusions of 20 mg/kg BV (N=18);
  3] ART, BV and a single 2.5/10 µg IP injection of IL15/IL15RaFC given with the first dose of BV (N=18).
- 3 weeks after the last BV infusion, mice were sacrificed and HIV DNA and RNA were isolated from blood, ileocecal junction, spleen, lymph nodes, and liver. Flow cytometric evaluation of CD30 expression and T cell phenotypes was performed on PBMC.
- Non-parametric tests were used to compare differences in flow cytometric and HIV-1 DNA and RNA measures in blood and tissues between treatment and control cohorts



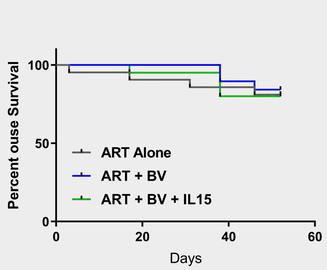
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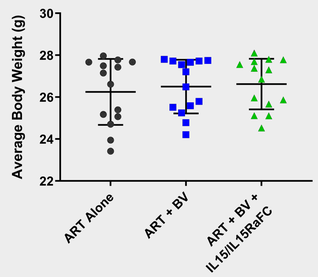
Brentuximab Vedotin (BV) with and without IL15/IL15RaFC led to a reduction in the frequency of peripheral blood human CD4+ T cells expressing CD30, HLA-DR, and those with an effector memory phenotype

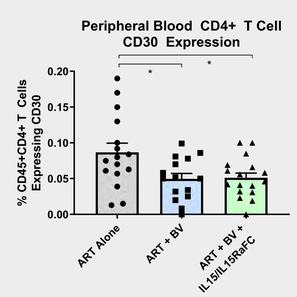
BV treated mice without concomitant IL15/IL15RaFC had significantly lower HIV DNA measured in gut tissue compared with ART-only controls

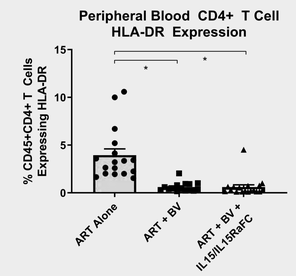
RESULTS

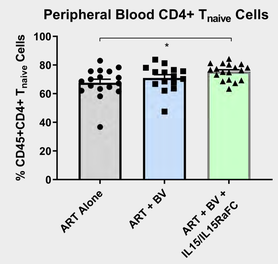
Impact of Brentuximab Vedotin (BV) ± IL15 on Mouse Survival and Peripheral Blood CD4+ T Cells

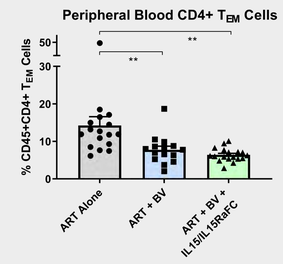




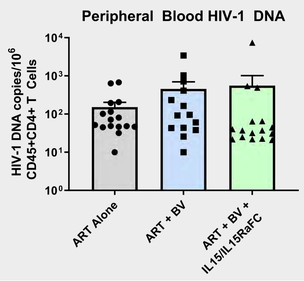


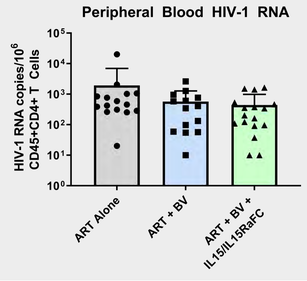






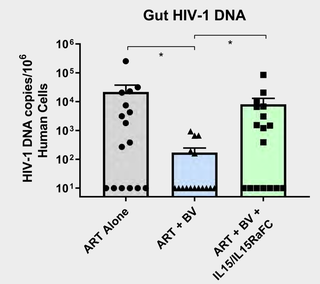
Impact of Brentuximab Vedotin (BV) ± IL15 on Peripheral Bood HIV-1 DNA and RNA Burden

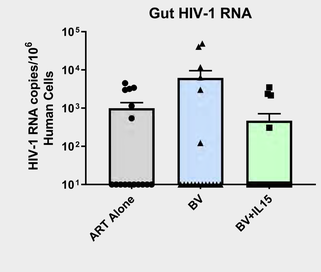


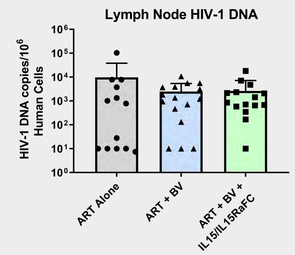


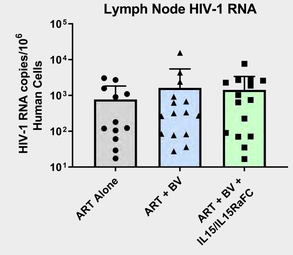
RESULTS, CONTINUED

Impact of Brentuximab Vedotin (BV) ± IL15 on Tissue HIV-1 DNA and RNA Burden









- No significant reductions in HIV-1 DNA or RNA were observed in spleen or liver

CONCLUSIONS

- Brentuximab vedotin reduces the frequency of circulating human CD4+ T cells expressing CD30, HLA-DR, and decreases the proportion of CD4+ T_{EM} cells.
- Brentuximab vedotin significantly reduces HIV-1 DNA burden in gut tissue in ART-suppressed humanized BLT mice; an effect that is mitigated by concomitant IL15/IL15RaFC.
- The high proportion of naïve T cells in the BLT mouse model may have abrogated the impact of brentuximab vedotin on blood and tissue HIV burden.

ACKNOWLEDGEMENTS

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