

[#76] *Ex vivo, BIT225 Inhibits the Spread & Transfer of HIV-1 from the Infected Monocytes of Seropositive Individuals*

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Background: Specific viral proteins have ion channel activity (viroporins) led Biotron to develop a library of compounds targeting Vpu.

(Khoury et al., Antimicrobial Agents and Chemotherapy. 2009)

BIT225 has completed both preclinical safety and toxicity studies and a phase I dose escalation study. A phase Ib/IIa has recently been completed in HCV⁺ patients.

Aims: Prior to the commencement of a similar trial in HIV-1 patients, we examined the effect of BIT225 on virus replication within *ex vivo* monocytes isolated from a cohort of HIV-1 seropositive individuals with a range in viral load and variety of treatment regimens.

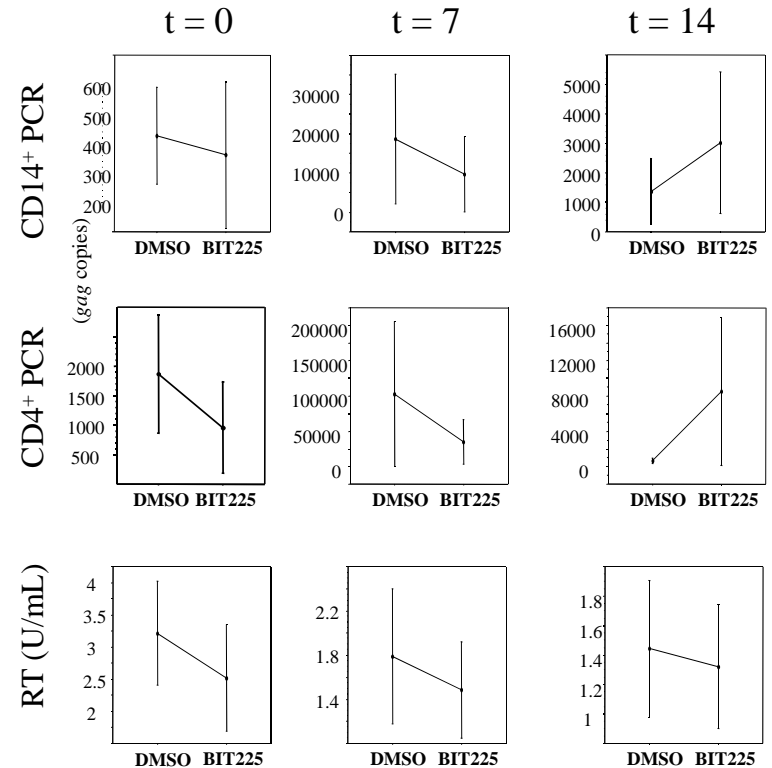
Methods: CD14⁺ monocytes were isolated using MACS beads and co-cultured with HIV-1⁻ CD4⁺ T cells. HIV-1 replication (adherent monocytes/MDM) and transfer (non- adherent T cells) was measured by RT or RT-PCR.

Results from HIV-1⁺ Individuals (n=18)

Of the 9 patients with detectable virus in culture:

- 6/9 demonstrated high viral loads (>5,000 copies/mL)
- 4/9 demonstrated low CD4⁺ counts (<200 cells/uL)
- 6/9 were not on therapy at the time of monocyte isolation but only 1 pt was naive wrt therapy
- HIV-1 could be cultured from 1/9 individuals with undetectable viral loads (<40 copies/mL)

Monocytes & MDM treated with BIT225 resulted in reduced spread & transfer to CD4⁺ T cells



“BIT225 has the potential to reduce the virus burden and prevent HIV-1 transfer that is associated with monocyte reservoirs in HIV-1⁺ individuals”