HIV TRANSCRIPTS PERSIST DESPITE VIRAL SUPPRESSION WITH INTEGRASE INHIBITOR REGIMENS

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Background/Purpose:
Despite viral suppression using conventional assays, intracellular HIV transcripts are detectable using the double R assay in the majority of people living with HIV (PLWH). Such transcripts are significant, as they have been associated with more frequent viral blips, greater reservoir activity, and HIV-associated neurocognitive disorders (HAND). Using conventional assays, blips have been shown to occur less frequently on integrase inhibitor-based (II) regimens when compared to protease inhibitor-based (PI) regimens. We initially hypothesized that II-based regimens would be associated with lower transcript load using the double R assay.

Approach:
The double R assay was used for HIV-1 RNA and HIV-1 DNA measures. Patient records were collected utilising St Vincent's hospital electronic database. We defined 'Blips' as elevated routine patient monitoring pVL between 20 and 200 copies/mL. Patients were grouped into integrase inhibitor predominant combination therapy (II) or protease inhibitor predominant combination therapy (non-II). Statistical analyses were conducted using JMP version 24 (SAS Inc.) and figures were generated using Python software version 3.12.

Outcomes/Impact:
Intracellular HIV-1 RNA transcripts were identified and compared in all patients (n=89). There were significantly higher transcripts levels in 'Blip' samples (n=61) than 'Non-Blip' (n=28) (4.06±1.65 vs. 2.74±1.64 Log HIV-1 RNA copy/10e6 cells) p=0.0009*. One-way Anova showed no difference in HIV-1 RNA between II group (n=70) (3.794±0.207) and non-II group (n=19) (3.097±0.398), p=0.1239 (Fig 1A).

Innovation and Significance:
HIV-1 RNA transcripts persist in virally suppressive ART even with II-based regimens, with implications for reservoir activity and HAND. Importantly, we found that patients with history of Blip's exhibit higher levels of RNA transcripts than Non-Blip patients, regardless of ART regimen. Additional studies with the double R assay using lifetime cumulative exposure data to different ART regimens are required to determine the impact on the reservoir and HAND. These preliminary findings are important to support the clinical need for development of a novel class of ART directly targeting HIV transcription.

Figures:

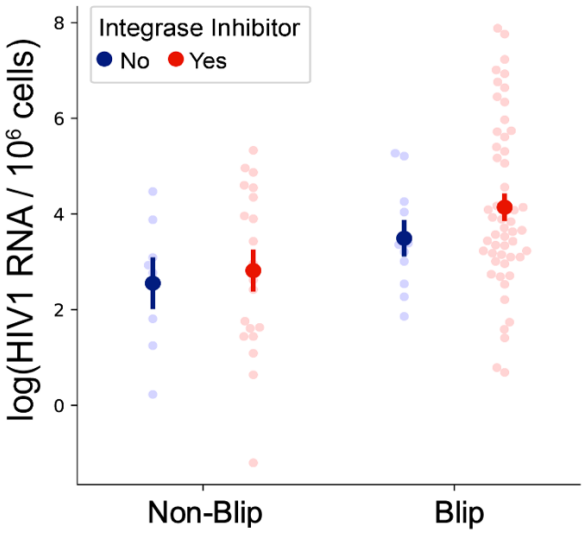

Figure 1A: Log transformed HIV-1 RNA transcript levels in patients with positive 'Blip' status, grouped by ART treatment regimen (integrase inhibitor vs non-integrase inhibitor regimen).

Disclosure of Interest Statement:
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