## PE16

## HIV-1 transcription is stable during frequent longitudinal sampling in aviremic patients on ART: implications for HIV cure research

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**Background:** Reversal of latency is currently being investigated in studies aiming to reduce the HIV-1 reservoir. To best evaluate the effect of such clinical interventions in HIV-1 eradication trials, it is essential that the longitudinal dynamics of HIV-1 transcriptional activity, as well as the HIV-1 reservoir size, be fully characterized. To address this need, we conducted a longitudinal, observational cohort study that enrolled aviremic, HIV-1 patients at Aarhus University Hospital, Denmark.

**Methods:** Inclusion criteria were CD4+ T-cell count >200/μL, 2 most recent viral load measurements < 19 HIV-1 copies/mL and at least 2 year on ART. For all participants, monthly blood samples were collected over six consecutive months. HIV-1 transcription as measured by cell-associated unspliced HIV-1 RNA (CA-US HIV-RNA) and the size of the viral reservoir as measured by total HIV-1 DNA (tHIV-DNA) were quantified in unfractionated CD4+ T cells using digital droplet PCR.

To calculate the longitudinal variation in these outcome measures, we first determined the absolute mean values of CA-US HIV-RNA and tHIV-DNA for each individual over the six visits. Then, we determined the fold-change of the absolute values from each of the six visits relative to that mean. Finally, we determined the maximum fold-change from the absolute mean value for each patient and calculated a maximum fold-change with 95% CI for the study population.

**Results:** During the study period (November-2013 to August-2014) we enrolled 25 patients, including 8 females and 17 males (Table-1). Each participant completed the 6-month study. The mean maximum fold change in CA-US HIV-RNA was 1.49 (95% CI: 1.32-1.65; max. 2.30). The mean maximum fold change in tHIV-DNA was of 1.30 (95%CI: 1.16-1.44; max. 2.50).

| Baseline characteristics n=25 | |
|---|---|
| Gender | |
| Male, n (%) | 17 (68%) |
| Female, n (%) | 8 (32%) |
| Age (years), median (range) | 49 (31-79) |
| Ethnicity | |
| Caucasian, n (%) | 23 (92%) |
| African Danish, n (%) | 2 (8%) |
| Months since HIV-1 diagnosis, median (range) | 90 (26-321) |
| Months from HIV-1 diagnosis to ART initiation, median (range) | 7,0 (0-138) |
| Months on ART, median (range) | 78 (25-206) |
| Months with HIV RNA <50 copies per mL, median (range) | 71 (15-172) |
| Nadir CD4+ count (10e6 cells/L), median (range) | 240 (0-710) |
| Baseline CD4+ count (10e6 cells/L), median (range) | 650 (240-1750) |
| Pre ART viral load (copies/ml) log10, median (range) | 4,74 (2,76-6,23) |
| ART regimen | |
| 2xNRTI +NNRTI, n (%) | 9 (36%) |
| 2xNRTI + protease inhibitor, n (%) | 11 (44%) |
| 1xNRTI + protease inhibitor, n (%) | 1 (4%) |
| 2xNRTI +1xNNRTI + protease inhibitor, n (%) | 1 (4%) |
| 2xNRTI + integrase inhibitor, n (%) | 2 (8%) |
| 1xNRTI + 1xNNRTI + integrase inhibitor, n (%) | 1 (4%) |

[Table 1]

**Conclusions:** HIV-1 transcription and reservoir size, as measured by CA-US HIV-RNA and tHIV-DNA, exhibited only minor fluctuations during the study period in aviremic HIV-1 patients. These data provide the first insights into the natural variation over time of CA-US HIV-RNA, a primary outcome measure in HIV-1 latency reversal trails. Furthermore, these data confirm the significance of previously observed increases in transcriptional activity during treatment with latency reversing agents and provide a solid foundation for both design and interpretation of future latency reversal trials.

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