Pegylated IFN-α2b decreases latent HIV subjects in ART-suppressed HIV subjects.

Livio Azzoni1, Emmanouil Papasavvas2, Nicolas Chomont3, Qingsheng Li4, Bonnie Howell2, Douglas Richman2, Pablo Telo5, Karam Mounzer6, Jay Kostman7, Luis J. Montaner1


Introduction

HIV eradication and/or functional cure approaches require strategies aimed at reducing or eliminating latent HIV reservoirs located in all body sites (1). To this end, a number of strategies have been tested (2-4), ranging from Latency Reversing Agents (LRAs) 5 to immunological approaches (6), stem cell transplantation (7) and genetic engineering (8), with very limited success. In addition, the issue of what exactly constitutes the “true size of the latent HIV reservoir remains open” (1). Data from our NCT00940889 clinical trial (11) support that administration of pegylated interferon (PEG-IFNα2b (PegIntron)) results in viral suppression and reduction in integrated proviral HIV DNA in ART-suppressed subjects undergoing analytical ART interruption (ATI). The present study, NCT01950589, was designed to test Peglntron in an expanded cohort of subjects, combined with a brief Antiretroviral treatment interruption (ATI) intended to induce HIV reduction, would decrease the levels of latent virus in ART-suppressed individuals with chronic HIV infection.

1. Study design and disposition

Individuals with HIV-1 infection (18-65 y; >100 HIV-1 RNA copies/ml, CD4 count ≥ 500 cells/μl), where psychiatric conditions that would contraindicate the administration of Peglntron were excluded (Table 1). Participants undergoing ART (ATI) used to be in a stable condition for at least 50% of the time during the past 12 weeks. All individuals were infected with subtype B HIV and no history of T-cell depletion had been observed. A minimum of 12 weeks was retained from the last ART intervention to the start of the treatment. Participants were included after no evidence of ART failure or virological rebound after ART treatment.

3. Change in HIV measures upon exposure to Peg-IFN-α2b

Induction of expression of IFNα-dependent genes (IFNα gene signature) was observed in 20% of participants. An IFNα gene signature was correlated with the reduction of viral RNA copies in PBMCs and decrease in HIV DNA copies in PBMCs and circulating CD4 T-cells (Table 1).

4. Observed patterns of change in HIV measures

The combination of Peglntron and ATI was found to be safe and well tolerated.

Conclusions

Our results indicate that treatment with peg-IFN-α2b:

• was safe and tolerable.

• resulted in the control of viral replication to ≤50 copies/ml during a 4-week ATI in 53% of the study subjects, similarly to peg-IFN-α2a (67%), and significantly different from historical studies in subjects undergoing ATI without type-1 IFNs.

• resulted in significant decrease or complete loss of RNA-positive cells in the GALT was the most clearly affected,

• found in a trend of reduced in integrated HIV DNA in circulating CD4+ T cells, consistent with our previous reports.

• significantly alter other viral measures.

High baseline levels were associated with greater change over time for three of the variables assessed. Further testing in larger cohorts with multiple time point assessments will be required to confirm this finding.

We did not observe significant correlations between independent HIV latency/replication measures in tissue or PBMC.

We conclude that eradication strategies are currently best monitored by assessing multiple HIV latency and replication measures.

Acknowledgments

This work was supported by NIH grants R01AI072893, R01AI105798 and R01AI122836; by the侵中 and the NIH HWaw Project (K08 AI101909); and by an unrestricted grant (F30 AI 40920) from the Wistar Institute.

References


