Pegylated IFN-α2b decreases latent HIV-1 reservoirs in ART-suppressed subjects.

Livio Azzone1, Emmanouil Papasavvas1, Nicolas Chomont2, Qingsheng Li2, Bonnie Howell3, Douglas Richman4, Pablo Tebas5, Karam Mounzer5, Jay Kostman5, 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 (5,7), stem cell transplantation (8) and genetic engineering (9) with very limited success. In addition, the issue of what actually happens to the real size of the latent HIV reservoir remains open (10). Data from our NCT00135689 clinical trial (11) support that administration of pegylated interferon (Peg-IFN-α2b) (Pegylith) results in viral suppression and reduction in integrated proviral HIV DNA in ART-suppressed subjects undergoing analytical ART interruption (ATI). The present study, NCT01935689, was designed to test Peg-IFN-α2b, combined with a broad Analytical Treatment Interruption (ATI) intended to induce HIV reduction, would decrease the levels of viral latency in ART-suppressed individuals with chronic HIV infection.

1. Study design and disposition

Methods

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, similar to peg IFN-α2a (67%), and significantly different from historical studies in subjects undergoing ATI without type-1 R-1.
• resulted in significant decrease or complete loss of RNA-positive cells in the GALT was the most clearly affected.
• resulted in a trend in loss of integrated HIV DNA in circulating CD4+ T cells, consistent with our previous reports.
• was 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 studies are currently best monitored by assessing multiple HIV latency and replication measures.

References