Lack of Detectable HIV DNA in a PrEP Study Participant Treated During “Hyperacute” HIV Infection

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Background: The study of ART initiation during “hyperacute” HIV infection may provide insights into a functional cure. We report such a case from The PrEP Demo Project, a pre-exposure prophylaxis program in at-risk MSM. This individual was HIV-uninfected (by pooled RNA, 4th generation EIA, and rapid antibody) at 2 pre-enrollment visits (21 and 13 days prior to PrEP baseline) but was found to be in Fiebig stage I HIV infection (RNA 220 copies/mL, 4th generation EIA negative, rapid antibody negative) at the PrEP baseline visit (estimated ~10 days after infection). The individual received PrEP (tenofovir/emtricitabine) for 7 days, at which time PrEP baseline test results returned and conventional ART was initiated. The patient was asymptomatic during this time and remains on ART.

Methodology: Single genome sequencing was conducted from the PrEP baseline plasma sample. Colorectal biopsy (~1.9 months after infection) and leukapheresis (~2.1 months after infection) were conducted and a large-volume blood sample (240mL, ~5.8 months after infection) was analyzed for replication-competent virus.

Results: Plasma HIV RNA levels were 220 copies/mL (PrEP baseline), 120 copies/mL (7 days after PrEP initiation), and “detected <40 copies/mL” (~32 days after infection); all subsequent plasma RNA levels have remained negative. There was a single occurrence of low-level cell-associated HIV RNA (4.7 copies per million CD4+ T cells) ~32 days after infection. All other HIV RNA/DNA tests have been negative, including those performed in colorectal biopsy samples enriched for total CD4+ T cells. Total CD4+ T cells and CD4+ T cell subsets (Tn, Tcm, Tm, Tem) from the leukapheresis sample were also negative for HIV RNA and DNA (analyzed at 2 independent laboratories), including total DNA, integrated DNA, and 2-LTR circles. The viral outgrowth assay did not detect any replication-competent virus from 62 million purified resting CD4+ T cells. HIV western blot assays were repeatedly indeterminate (p55 only) but eventually became non-reactive. The individual was CCR5 wild-type and HLAB5701 negative. Analytic treatment interruption is planned after 12 months of ART.

Conclusions: We report a case of extremely early initiation of ART (immediately after the “eclipse phase,” at approximately 10 days of HIV infection) in a PrEP participant. Whether very early ART exposure through PrEP or conventional ART contributed to this unique outcome remains unknown and warrants further study. PrEP programs should consider testing participants for acute HIV prior to and during PrEP use, and consider immediate conversion from PrEP to conventional ART following a diagnosis of acute HIV. Although HIV may persist indefinitely in this individual, a continuum may exist across PrEP, PEP, and curative early ART strategies.