# The Control of HIV after Antiretroviral Medication Pause (CHAMP) study: post-treatment controllers identified from 14 clinical studies

## Supplemental Figures and Methods

| | Definition of early-treated participants |
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| A371<br>Acute infection: | Detectable plasma HIV RNA ≥2000 copies/mL by RT-PCR within 14 days prior to study entry and one of the following:<br>Negative ELISA within 14 days of study entry<br>OR<br>Positive ELISA but negative or indeterminate Western blot within 14 days of study entry<br>OR<br>Positive ELISA and Western blot within 14 days of study entry but with documented negative ELISA or plasma RT-PCR <2000 copies/mL within 30 days prior to study entry. |
| Recent infection: | Positive ELISA and Western blot within 14 days of study entry but with documented negative ELISA or plasma RT-PCR <2000 copies/mL within 31-90 days prior to study entry.<br>OR<br>Positive ELISA and Western blot plus a nonreactive, less sensitive ("detuned") ELISA in subjects with a CD4+ cell count >200/$mm^3$ all documented within 21 days (≤14 days preferred) prior to study entry. |
| A5187<br>Acute infection: | Participants with acute retroviral syndrome and who were diagnosed by a positive HIV-1 viral load and a negative or indeterminate Western blot. |
| Early infection: | Positive ELISA<br>OR<br>Positive Western blot with a non-reactive detuned ELISA (OD,0.75), provided the interval between the presumed acute retroviral syndrome and initiating antiretroviral therapy was 6 months or less. |
| Montreal PIC | Negative HIV p24 antibody testing by ELISA in the presence of detectable HIV-1 RNA<br>OR<br>Positive HIV p24 antibody testing by ELISA and an evolving (≤3 bands positive) HIV Western blot.<br>OR<br>Documented HIV-1 acquisition within the previous six months |
| SeaPIP | Detectable plasma HIV-1 RNA >2000 copies/ml and Negative HIV-1 EIA (acute HIV-1)<br>OR<br>Recent (within the last month) negative HIV-1 EIA, an indeterminate Western Blot and detectable HIV-1 RNA (>2,000 copies/ml on 2 consecutive specimens); subjects are excluded retrospectively if they do not evolve to have a positive Western Blot)<br>OR |

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| | Negative HIV-1 EIA within the previous 4 months, a credible history for exposure to HIV-1 and acute onset of symptoms within 30 days prior to screening and specimen acquisition, and a HIV RNA-1 greater than 400,000 copies/ml at screening<br>OR<br>Participants who enrolled within one month of their estimated date of HIV-1 infection (defined as the date of onset of seroconversion symptoms or, for asymptomatic individuals, the midpoint between dates of the last negative and first positive HIV-1 tests) |
| Ragon | Participants who were diagnosed by a positive HIV-1 viral load and a negative or indeterminate Western blot. |
| UCSF OPTIONS | Participants who were diagnosed by a positive HIV-1 viral load and a negative or indeterminate Western blot<br>OR<br>A positive Western blot with either a documented negative HIV test within 6 months or a non-reactive detuned ELISA. |
| NIH | Acute infection was defined as a plasma HIV RNA load of >2000 copies/ml with a negative HIV-1 enzyme immunoassay (EIA; criterion 1), a positive result from an HIV-1 EIA with a negative or indeterminate HIV- 1Western blot that subsequently evolves to a confirmed positive result (criterion 2), or negative result from an HIV-1 EIA within the past 4 months and HIV-1 RNA loads of >400,000 copies/ml in the setting of a potential exposure to HIV-1 (criterion 3). Early infection was defined as a negative result from an HIV-1 EIA within 6months before a positive result from an HIV-1 EIA and confirmatory HIV-1 Western blot (criterion 4), a negative result from a rapid HIV-1 test within 1 month before a positive result from an HIV-1 EIA and Western blot (criterion 5), or the presence of low level of HIV antibodies as determined by having a positive EIA and Western blot with a nonreactive detuned EIA according to a multiassay testing algorithm for recent infection (criterion 6) |
| UCSD | If there is a first positive RNA† and negative enzyme immunoassay (EIA) within 7 days of the first positive RNA, and no prior positive/indeterminate western blot (WB), then EDI = first positive RNA date − 11 days. (~Fiebig Stages I-II)<br>OR<br>If there is an indeterminate WB within 7 days of the first positive RNA, then EDI = first positive RNA date − 20 days. (~Fiebig Stages III-IV)<br>OR |

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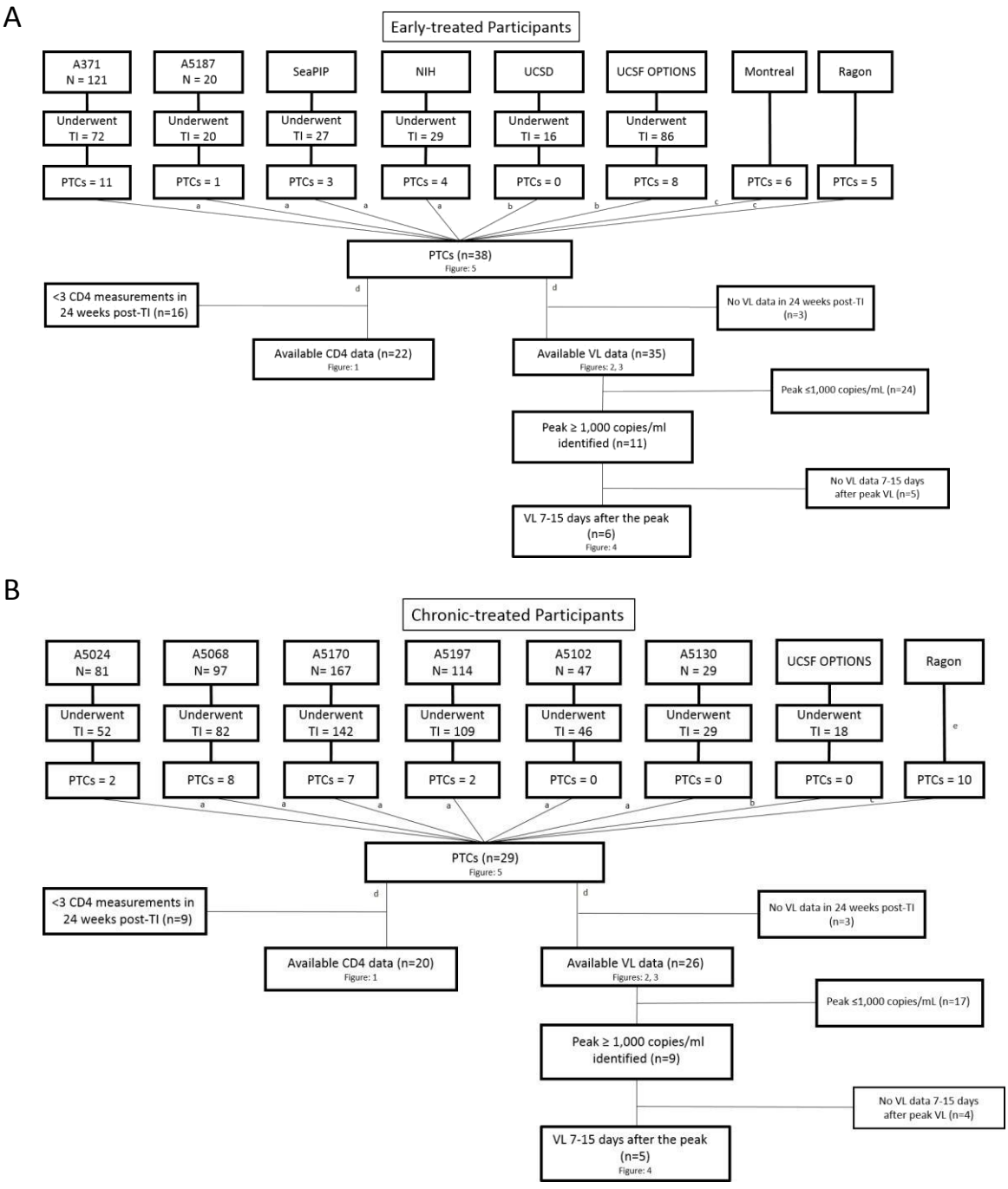
| | If the last negative EIA or negative/indeterminate WB occurred ≤ 30 days before the first positive WB (with associated positive RNA), then EDI = midpoint of the positive WB date and the negative EIA or negative/indeterminate WB date (earlier of two) − 19 days. (~Fiebig Stage IV)<br>OR<br>If the first positive WB p31/32 band is absent, then EDI = first positive WB date − 89 days. (~Fiebig Stage V)<br>OR<br>If there is a detuned EIA (dtEIA) consistent with infection of ~3 mo within 30 days of the first positive WB and CD4 count > 200 or CD4% >14 within 30 days of the first positive WB, then EDI = first dtEIA date −70 days. (Fiebig VI)<br>OR<br>If there is a dtEIA consistent with infection of ~3-6 mo within 30 days of the first positive WB and CD4 count > 200 or CD4% > 14), then EDI = first dtEIA date − 133 days. (Fiebig VI)<br>OR<br>If there is a dtEIA consistent with infection of ~6-12 mo within 30 days of the first positive WB and CD4 count > 200 or CD4% > 14, then EDI = first dtEIA date − 170 days. (Fiebig VI)<br>OR<br>If there is a first positive WB and a negative EIA within 365 days participant enrollment (Day 0), then EDI = midpoint between the last negative EIA and Day 0. (Fiebig VI) |

**Supplemental Table 1: Definition of early-treated participants by study.**




**Supplemental Figure 1: Post-treatment controller (PTC) Flow Diagram**. Depiction of which PTCs are used in figures for **(A)** PTCs treated during early infection or **(B)** PTCs treated during chronic infection. VL, viral load; TI, treatment interruption.

[a]Used in the primary frequency calculations; [b]Used only in the secondary analysis as 1 UCSD and 8 UCSF participants met PTC criteria, but were lost-to-follow up or resumed ART without viral rebound prior to 24 weeks of treatment interruption. 1 of the 8 UCSF participants was treated during chronic infection; [c]Not used in frequency calculations; [d]These represent independent VL and CD4 analysis from the same PTC population; [e]Four Ragon PTCs were categorized as having ambiguous timing of ART start and are excluded from analyses that categorize PTCs by early vs. chronic-ART initiation.

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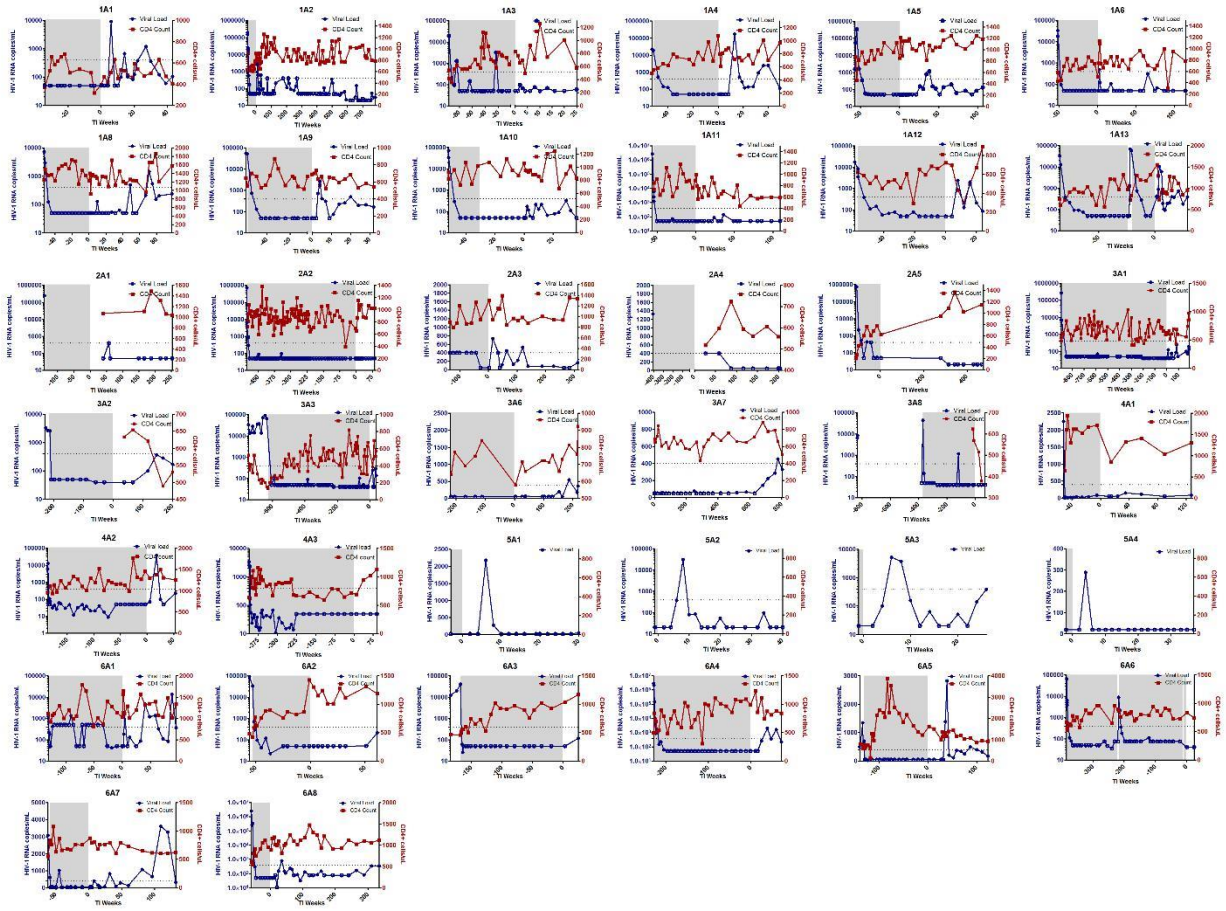
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Viral Load
CD4 Count
TI Weeks

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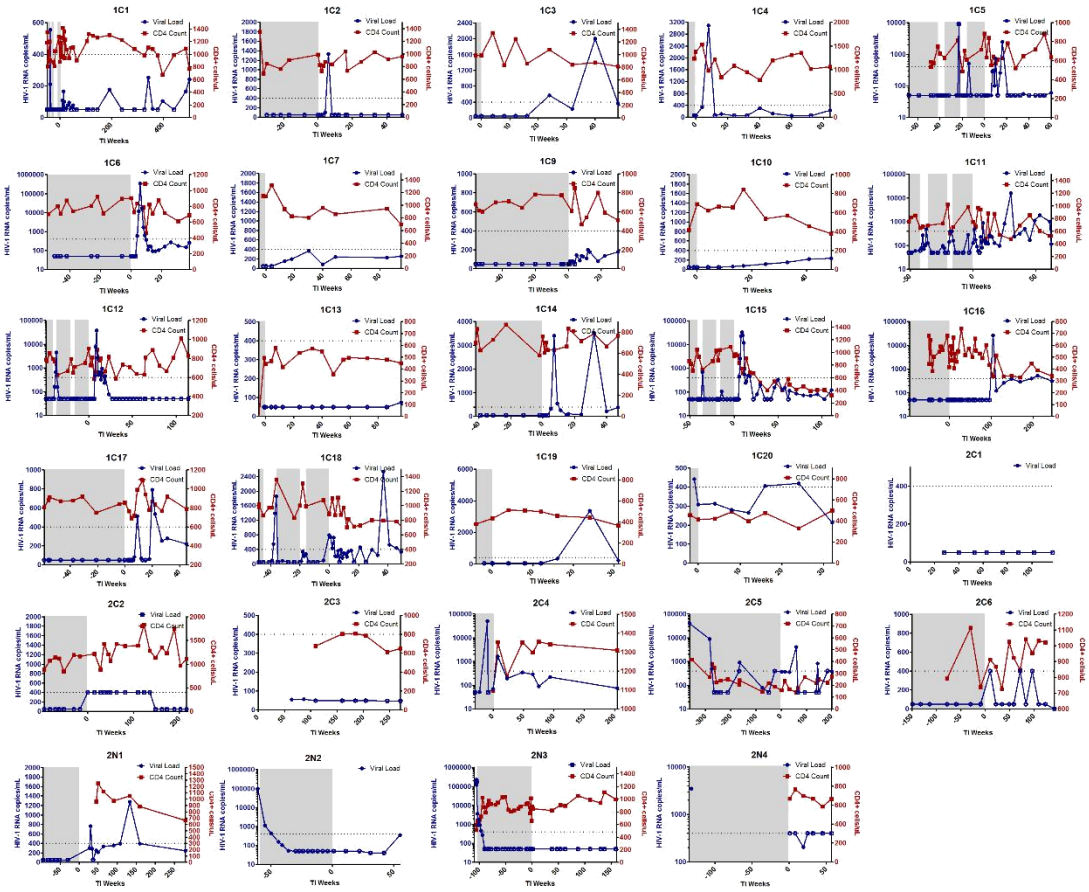
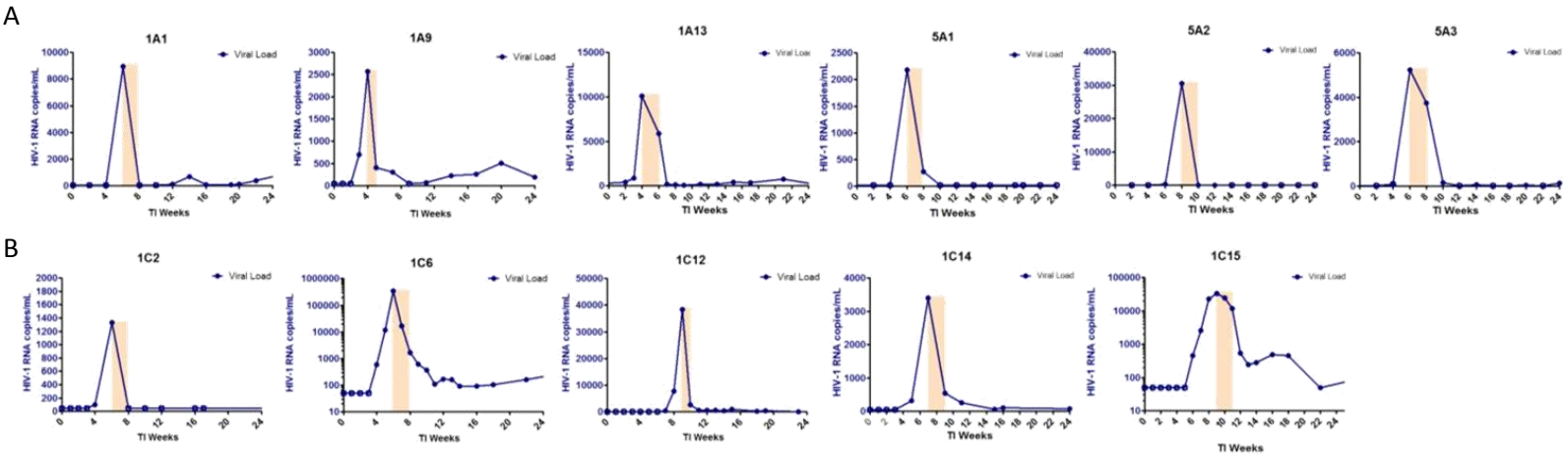
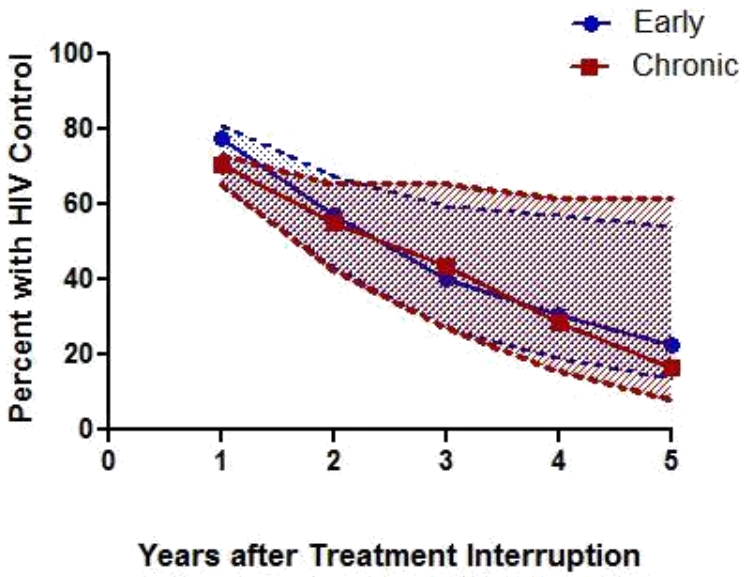


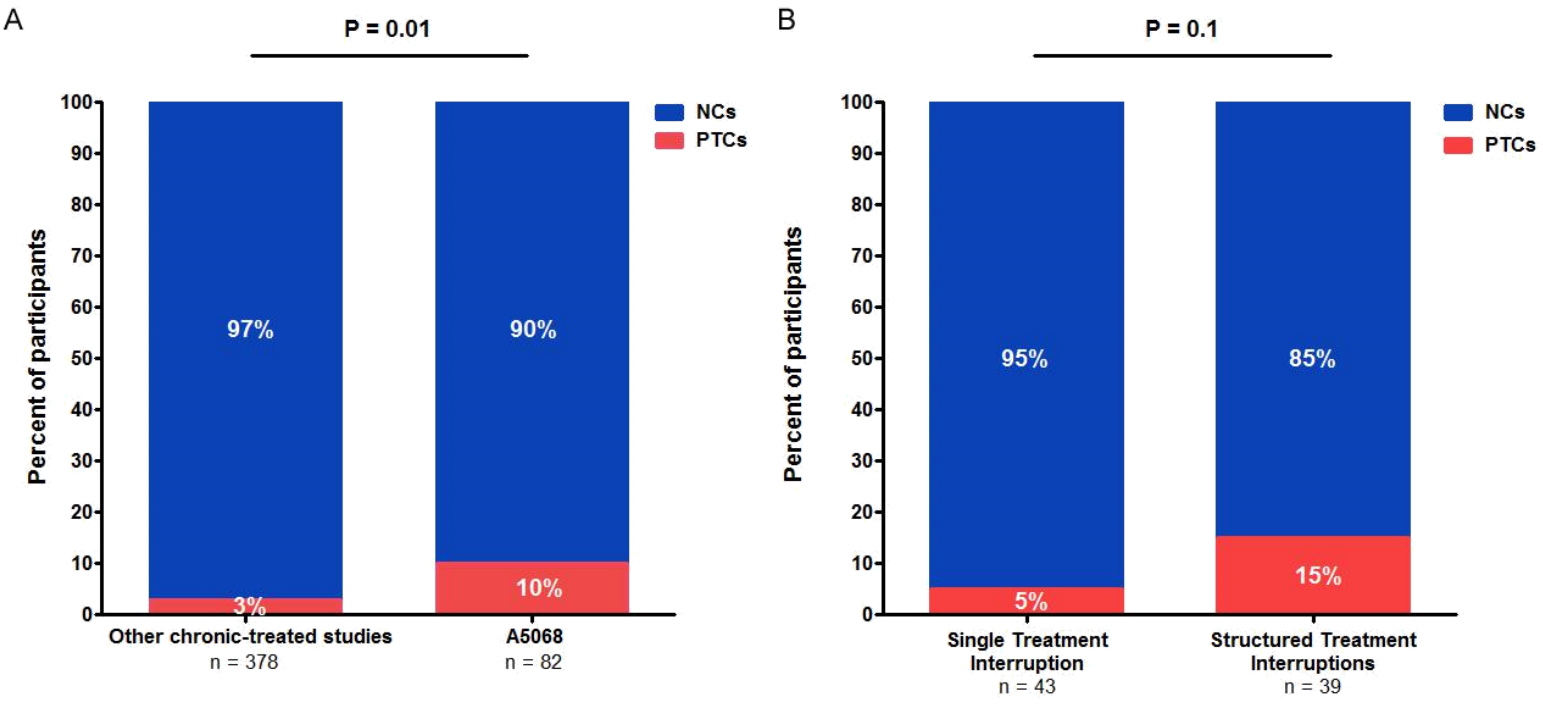

**Supplemental Figure 2: Viral load and CD4+ cells for the post-treatment controllers (PTCs)**. PTCs with ART initiation during early **(A)** or chronic **(B)** HIV infection. Blue line represents viral loads and red line shows CD4+ counts. Open circles represent a viral load that is below the limit of assay quantification. The gray boxes represent the period that PTCs were on ART. The dotted lines show the 400 HIV-1 RNA copies/mL viral load threshold. TI, treatment interruption.




**Supplemental Figure 3: Viral decay rate early (A) and chronic-treated (B) post-treatment controllers (PTCs)**. Participants were included with a peak viral load ≥1,000 HIV-1 RNA copies/mL in the initial 24 weeks post-treatment interruption and a subsequent viral load between 1-2 weeks. The orange boxes depict the time period over which viral decay was calculated.




**Supplemental Figure 4. Durability of viral control.** Durability of control when post-treatment controllers (PTCs) are grouped by timing of ART-initiation. For each time point, the upper bound is calculated by assuming that all participants who did not have virologic data maintained HIV control and the lower bound assumed that they had all lost viral control.




**Supplemental Figure 5. Frequency of post-treatment control in A5068. (A)** Frequency of post-treatment control in A5068 versus other ACTG studies enrolling chronic-treated participants. P-value represents Fishers exact comparison of post-treatment controllers (PTCs) identified in A5068 vs. other ACTG studies of chronic-treated participants. **(B)** Frequency of post-treatment control in A5068 based on number of treatment interruptions. Amongst the PTCs identified in A5068, the majority were randomized to the arm with three sequential structured treatment interruptions**.**

## SUPPLEMENTARY METHODS

### Ragon Controller Participants

The Ragon HIV Controller cohort is comprised of both spontaneous and post-treatment controllers, only the latter of which is included in this analysis. A subset of the Ragon PTCs were also treated during early HIV infection as defined by a positive HIV-1 RNA and either a negative or indeterminate Western blot. Individuals who initiated ART shortly after diagnosis, but with incomplete laboratory records were categorized as having an “ambiguous” timing of ART initiation and were excluded from the subgroup analyses of early vs. chronic-treated participants. The remainder were presumed to have been treated during chronic infection.

### Calculation of PTC Frequency

In the UCSF OPTIONS and UCSD cohorts, there were several early-treated participants who maintained viral suppression, but had less than 24 weeks of follow-up after treatment interruption. Participants from these two cohorts were included in a secondary analysis to calculate potential upper and lower bounds for the PTC frequency estimates of early-treated individuals. The upper bound was calculated by assuming that all such participants became PTCs while the lower bound assumed that they had all lost viral control before 24 weeks of treatment interruption. Participants from the Ragon and Montreal PIC studies were not included in the calculation of PTC frequency as the numbers of total individuals undergoing treatment interruption were not available. All included studies were approved by institutional review boards of the participating centers and all participants provided written informed consent.