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The CHAMP Cohort: Post-Treatment Controllers Identified from 9 Clinical Studies

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Background

- HIV post-treatment controllers (PTCs) are rare individuals who maintain HIV suppression after anti-retroviral treatment interruption (TI).
- Understanding the frequency of post-treatment control and post-TI viral dynamics has implications for the design and evaluation of HIV remission strategies.

Objectives

- Assess the frequency of post-treatment control after interruption of antiretroviral therapy (ART).
- Evaluate CD4+ count and viral load dynamics after treatment interruption.
- Determine the durability of post-treatment control.

Methods

- PTCs were identified from 9 clinical studies: 6 ACTG studies (ACTG 371, A5024, A5068, A5170, A5187, and A5197), the Montreal Primary HIV Infection Cohort (Montreal PIC), the Seattle Primary Infection Program (SeaPIP), and the Ragon HIV Controllers cohort (Ragon)
- PTCs were defined as individuals who underwent TI and maintained viral loads ≤400 copies/mL for ≥2/3 of the time points for at least 24 weeks.
- PTCs were compared to non-controllers (NCs) who did not meet the PTC criteria.
- PTCs with an early viral load peak of ≥1,000 HIV-1 RNA copies/mL and a subsequent viral load within 1-2 weeks were included in the viral decay analysis: (Ln [peak viral load] – Ln [subsequent viral load]) / days in between.
- PTC viral decay rates compared to: 1) NCs, 2) untreated acutely-infected participants and 3) phase 1 and 2 viral decay rates from participants of A5160s and A5166s initiating first-line ART.

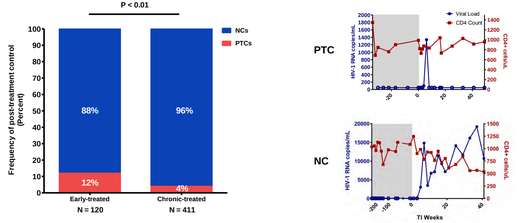
Results

Participant Demographics

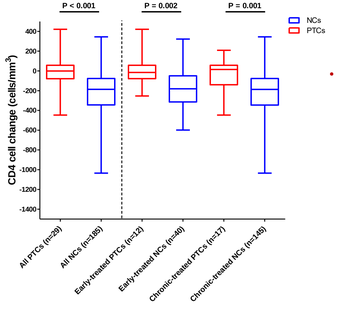
Characteristics	All (N=53)	Early treated (N=25)	Chronic treated (N=28)
Median age at treatment interruption (years)	41 [34,46]	34 [31,44]	42 [38,48]
Sex			
Male	74%	80%	73%
Female	26%	20%	27%
Race			
Black	32%	20%	39%
White	57%	68%	50%
Hispanic	9%	8%	11%
More than one race	2%	4%	0%
Median duration of ART (weeks)	167 [52,298]	52 [52,110]	255 [175,333]
Median duration of viral control (weeks)	98 [49,200]	106 [51,200]	96 [49,201]
Median pre-ART viral load (log_{10} HIV-1 RNA copies/mL)	4.7 [4.1,5.4]	4.8 [4.3,5.5]	4.6 [3.5,5]
Study			
AIDS Clinical Trials Group (ACTG)	53%	44%	61%
Montreal Primary HIV Infection Cohort	13%	28%	0%
Seattle Primary Infection Program (SeaPIP)	6%	12%	0%
Ragon HIV Controllers Cohort	28%	16%	39%

- There was no significant differences in CD4+ cell counts prior to treatment interruption between PTCs vs. NCs: 882 cells/mm^3 vs. 843 cells/mm^3, P=0.9.
- No significant differences in the pre-ART viral load of early-treated PTCs vs. NCs: 4.7 vs. 4.8 log_{10} HIV-1 RNA copies/mL, P=0.9.

Frequency of Post-Treatment Control

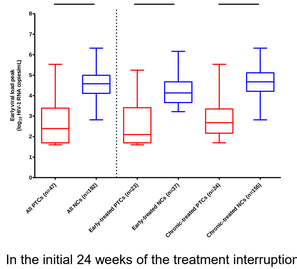


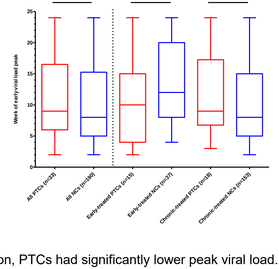
CD4+ Change Over Initial 24 Weeks of the Treatment Interruption



- CD4+ levels were generally preserved in the PTCs, but declined in the NCs.

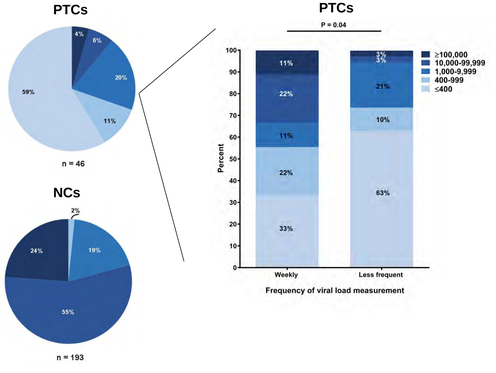
Magnitude and Timing of Early Viral Load Peak





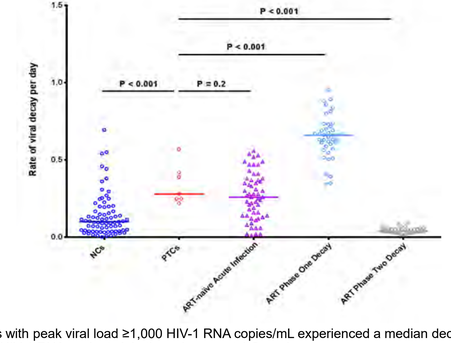
- In the initial 24 weeks of the treatment interruption, PTCs had significantly lower peak viral load.
- In participants with a viral load peak ≥1,000 HIV-1 RNA copies/mL, there was no difference in time to peak viremia between PTCs and NCs.

Early Viral Load Peak after Treatment Interruption



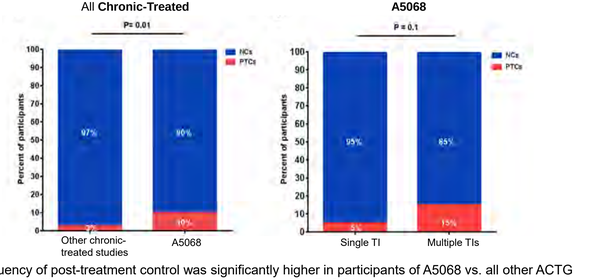
- Higher viral load peaks observed in those with more frequent (i.e., weekly) viral load monitoring.
- In PTCs with weekly viral load monitoring, 45% had a peak post-TI viral load of ≥1,000 copies/mL and 33% had a peak viral load ≥10,000 copies/mL.

Viral Load Decay Rate after Early Viral Load Peak



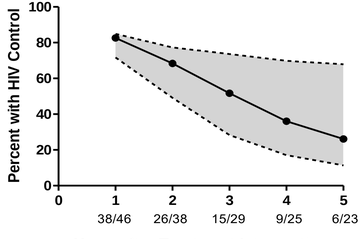
- PTCs with peak viral load ≥1,000 HIV-1 RNA copies/mL experienced a median decrease of 1.4 log_{10} HIV-1 RNA copies/mL in the subsequent 1-2 weeks.
- Viral decay in PTCs was 0.28 per day, which was significantly faster than the viral decay of NCs after treatment interruption, and similar to the viral decay seen during untreated acute infection.
- Viral decay in PTCs was slower than phase 1 decay after NNRTI-based ART initiation, but faster than phase 2 decay after ART initiation.

Effect of Multiple Treatment Interruptions



- Frequency of post-treatment control was significantly higher in participants of A5068 vs. all other ACTG studies enrolling chronic-treated participants (10% vs. 3%, P=0.01).
- The majority of PTCs in A5068 were randomized to receive multiple structured treatment interruptions.

Durability of Post-Treatment Control



- The proportion of PTCs who remained virologically suppressed in years 1-5 were 83%, 68%, 52%, 36%, and 26%, respectively.
- 2 PTCs maintained documented viral control for 10+ years.

Conclusions

- Early initiation of ART may lower the barrier to sustained HIV remission.
- Treatment interruption trials that restart ART at the 1,000 HIV-1 RNA copies/mL threshold will miss almost half of the PTCs, while trials that use a 10,000 copies/mL threshold will miss ~1/3 of PTCs.
- While a subset of PTCs had elevated post-treatment interruption viral loads, subsequent viral control was achieved relatively rapidly, with viral decay rates similar to that seen in untreated acute HIV infection.
- There was substantial variation in the durability of post-treatment control amongst the PTCs, with the median duration of viral control lasting for approximately 3 years post-treatment interruption.

Acknowledgements

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