

Enhanced Immune Reconstitution with Early Antiretroviral Treatment (ART) Initiated at HIV-1 Seroconversion (PHI)

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INTRODUCTION

Early ART initiation has been shown recently to delay the time to AIDS, strengthening the idea for early intervention. It is unclear whether immune reconstitution in particular, CD4/CD8 ratio, is enhanced with intervention at Primary HIV Infection (PHI).

METHODOLOGY

Retrospective study of a PHI cohort (ART initiation ≤ 3 months from diagnosis of PHI) from a single center [Royal Free Hospital (RFH), London, UK] who had received ≥ 5 years (y) of continuous ART. The group was compared to a cohort of individuals who started ART at the same center during chronic infection (CI; ≥ 1 year after diagnosis) with a pre-ART CD4 count >350 cells/mm³ and who remained on ART for a minimum of 5 years. Levels of CD4, CD4%, CD4/CD8 ratio and optimal immune reconstitution (OIR) (defined by a CD4 ≥ 800 cells/mm³ or CD4% $\geq 40\%$ or CD4/CD8 ratio ≥ 1) were assessed and compared between the two cohorts at 1, 5 and 10 years post-ART initiation. Time to normalization of the CD4/CD8 ratio to >1 was also assessed using Kaplan-Meier methods.

RESULTS

Thirty-seven PHI and 115 CI individuals were included. The median age at time of HIV diagnosis was 34 vs 32 years, 35 (94.6%) vs 32 (87%) were male, 32 (86.5%) vs 84 (73%) were MSM. The median pre-ART nadir CD4, CD4% and CD4/CD8 ratios were: 417 vs 313 cells/mm³ 18% vs 16%, and 0.30 vs 0.29, respectively. The median maximum pre-ART VL were 511,000 (3,400 - $>1,000,000$) vs 278,022 (2593 - $>750,000$) copies/mL. Immunological outcomes at 1, 5 and 10 year after treatment initiation were shown in Table 1.

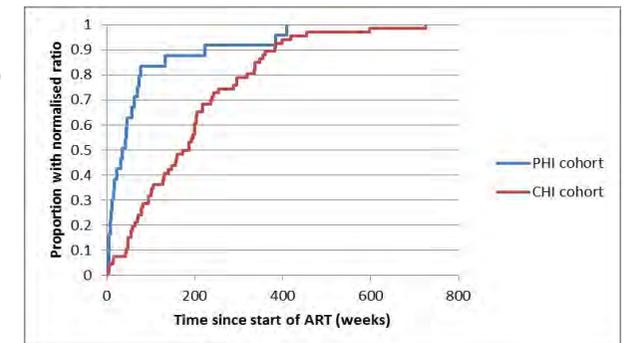
Kinetics of CD4/CD8 ratio showed that the median time to achieving CD4/CD8 ratio >1 for the first time was 36 (95% CI 16-63) weeks in the PHI cohort and 187 (127-204) weeks in the CI cohort ($p < 0.0001$; log rank test) (Figure 1).

Table 1. Comparison of Immunological Outcomes Between PHI and CI Patients at 1, 5 and 10 Years After Treatment Initiation

Time since start of ART	Median CD4 count (cells/mm ³)			Median CD4%			Median CD4:CD8 ratio			Presence of OIR*		
	PHI	CI	P-value	PHI	CI	P-value	PHI	CI	P-value	PHI	CI	P-value
1 Year	743	600	<0.0001	35	26	<0.0001	0.95	0.52	<0.0001	51%	25%	0.002
5 Years	850	779	0.005	39	33	<0.0001	1.05	0.78	<0.0001	73%	46%	0.003
10 Years	966	874	0.02	38	33	0.01	1.09	0.85	0.04	85% (23/27) [#]	53% (38/72) [#]	0.003

* OIR = Optimal Immune Reconstitution, defined by CD4 ≥ 800 cells/mm³ or CD4% $\geq 40\%$ or CD4:CD8 ratio ≥ 1.00
[#] 27 patients in PHI cohort and 72 in CI cohort had more than ten years of follow-up since treatment initiation

Figure 1. Kaplan-Meier Curve Showing the Time to CD4:CD8 ratio ≥ 1.00 for the First Time After Treatment Initiation



CONCLUSION

Early ART initiation within 3 months of HIV-1 seroconversion was associated with a better immunological recovery in terms of CD4 count, CD4% and CD4:CD8 ratio, as compared with treatment started in chronic phase of infection. Such differences persisted between the groups even after ten years of ART, suggesting damage to the immune system during early stages of HIV infection can result in long term consequences.