PE51 LB

Early initiation rather than prolonged duration of antiretroviral therapy in HIV infection contributes to reducing CD8 T-cell elevation: Relevance for clinical outcome

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Background: HIV infection is featured by profound immune dysfunction and skewed T-cell homeostasis. Elevation of CD8 T-cells occurs during primary HIV infection (PHI) and persists after long-term antiretroviral therapy (ART), which has been associated with increased risk of non-AIDS-related morbidity and mortality independently of CD4 T-cell recovery. We examined factors associated with trajectories of CD8 T-cell counts in early treated or untreated PHI and assessed influence of early vs. chronic ART initiation on CD8 T-cell elevation over time.

Methods: From 1996 to 2012, a total of 280 individuals (95.5% male, 92.5% Caucasians) were enrolled in the Montreal PHI study. Plasma viral load (VL), CD4 and CD8 T-cells were measured at each study visit. We also assessed 266 age and gender-matched HIV-infected individuals from McGill University Health Centre, Montreal, who initiated ART during chronic infection and have maintained undetectable VLs for at least one year. Another 40 uninfected individuals were included as controls. Regression analyses were performed.

Results: 251 PHI individuals were longitudinally assessed, where 84 started ART before 6 months of infection (early ART), 49 between 6 and 24 months (delayed ART) and 118 remained untreated as per physician/patient decision. Baseline characteristics and stratified CD8 T-cell counts were summarized in Table 1. At first PHI visit, CD8 T-cell counts were significantly associated with duration of infection ($p=0.019$), VLs ($p< 0.001$) and CD4 T-cell counts ($p< 0.001$). Early ART group achieved a marked decrease in CD8 T-cell counts from 797 to 588 cells/µl over 2 years ($p< 0.001$), which remained elevated compared to uninfected controls (median 376 cells/µl, $p< 0.001$), but significantly lower than untreated (834 cells/µl, $p=0.004$) and chronic patients after a median of 8-year-ART (801 cells/µl, $p=0.004$). Early ART group displayed more CD4 T-cell recovery than the delayed group. However, overtime CD8 T-cell counts remained similar in the 2 groups.

Characteristics	Value	Stratification	No of participants	Median CD8 T-cell count, cells/μl	P value Univariate	P value Multivariate
Overall			266	800 (598-1265)		
Age, years	36.1±9.4	<50/≥50	247/19	826/710	0.771	0.991
Gender		Male/Female	254/12	824/715	0.641	0.308
Route of infection		MSM/Hetero/IDU	207/21/38	853/660/790	0.148	0.824
Time of infection, days	82(56-121)	Fiebig II-III/IV/V-VI	40/81/145	935/810/787	0.118	0.019
HIV RNA load, log copies/ml	4.59±1.07	<3/3-5/>5	19/152/95	650/782/1140	<0.001	<0.001
CD4 T-cell count, cells/μl	500(380-658)	<500/≥ 500	124/142	740/880	0.005	<0.001

[Tab1 Baseline characteristics of PHI participants]

Conclusions: ART initiated in early HIV infection was associated with better resolution of CD8 T-cell elevation, while long-term ART initiated in chronic phase showed limited benefit in CD8 T-cell decrease. In addition to CD4 T-cell recovery, early ART may further contribute to reducing risk of non-AIDS events by alleviating CD8 T-cell elevation.