Faster restoration of CD4:CD8 ratio during the first 12 weeks of ART initiated at early HIV infection compared with ART initiated at chronic infection in the same patients

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Background

Early initiation of antiretroviral therapy (ART) is believed to result in better immunological reconstitution than initiation of ART during chronic HIV infection (CHI). However, the degree and rate of immune restoration haven't been directly compared in the same patients between ART initiated during primary HIV infection (PHI) and CHI ART.

Study design

We studied 48 patients that received 24 or 60 weeks of temporary ART initiated at PHI and subsequently reinitiated ART during CHI after a median of 2.4 years without treatment. Clinical parameters were measured at ART initiation and every 12 weeks thereafter up to week 60 of both PHI and CHI ART.

Results

Median CD4+ counts were 505 (IQR: 303-713) and 310 (245-418) cells/mm3 at the PHI and CHI ART baselines, respectively ($p< 0.0001$, paired Wilcoxon test). No difference in the dynamics of CD4+ count reconstitution between the PHI and CHI ART was observed throughout the follow-up period. Median CD4+ count gains by 60 weeks ART were 210 cells/mm3 for both PHI and CHI ART. In contrast, although there was no significant difference in the CD4:CD8 ratio at the PHI and CHI ART baselines (0.48 (0.25-0.80) vs. 0.36 (0.25-0.41), respectively; $p>0.05$), by 12 weeks ART this ratio increased to 0.95 (0.74-1.29) on PHI ART and 0.52 (0.41-0.74) on CHI ART ($p< 0.0001$). Significant difference in CD4:CD8 ratio between PHI and CHI ART persisted throughout the follow-up period, but no further difference in the dynamics of CD4:CD8 ratio increase was observed after the first 12 weeks. By 48 weeks ART, 59% of patients treated during PHI and 24% of patients treated during CHI achieved the CD4:CD8 ratio of 1 ($p=0.0049$, Fisher´s test).

Conclusions

This is the first study to directly compare immune reconstitution between PHI and CHI ART in the same patients. Although no difference was observed in the dynamics of CD4+ count reconstitution, the CD4:CD8 ratio demonstrated faster restoration in the first 12 weeks of PHI ART compared to the CHI ART, which translated into a larger percentage of patients achieving the CD4:CD8 ratio of 1 by 48 weeks ART. Early initiation of ART conveys a significant immunological benefit to the patient.

Literature

1. Serrano-Villar S, et al. HIV-infected individuals with low CD4/CD8 ratio despite effective antiretroviral therapy exhibit altered T cell subsets, heightened CD8+ T cell activation, and increased risk of non-AIDS morbidity and mortality. PLOS Pathogens 2014; 10:e1004078.

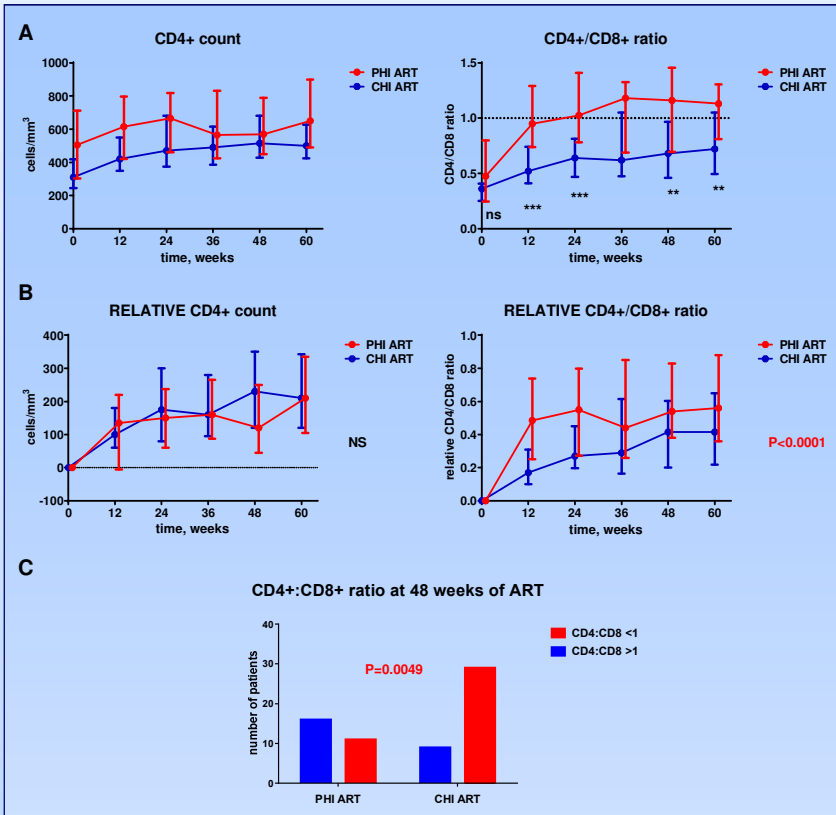

Figure 1. Longitudinal dynamics of absolute (A) and relative (B) CD4+ count and CD4:CD8 ratio during PHI ART and CHI ART. (C) Degree of the CD4/CD8 ratio normalization (<1 vs >1) by 48 weeks of PHI and CHI ART.

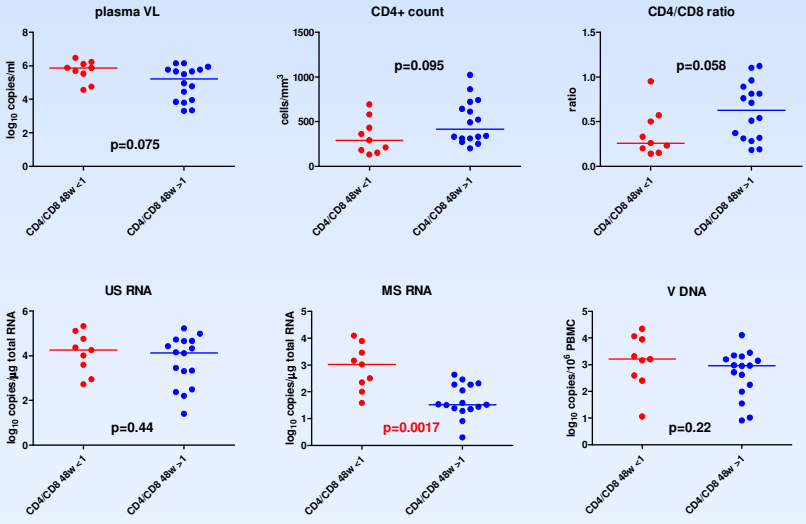

Figure 2. Predictors of CD4/CD8 ratio normalization (<1 vs >1) by 48 weeks of PHI ART. Variables were measured at PHI. Levels of statistical significance were calculated by Mann-Whitney tests. MS RNA was the only significant predictor of CD4:CD8 ratio normalization in the multivariate logistic regression adjusted for the above parameters ($p=0.015$).

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