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Oral Communication **Session/Topic:** **Hepatitis: basic science and virology**

N. **Title:**

OC 29 **The impact of DAA-mediated HCV eradication on CD4+ and CD8+ T lymphocytes trajectories in HIV/HCV coinfected patients: data from the Icona Foundation Cohort**

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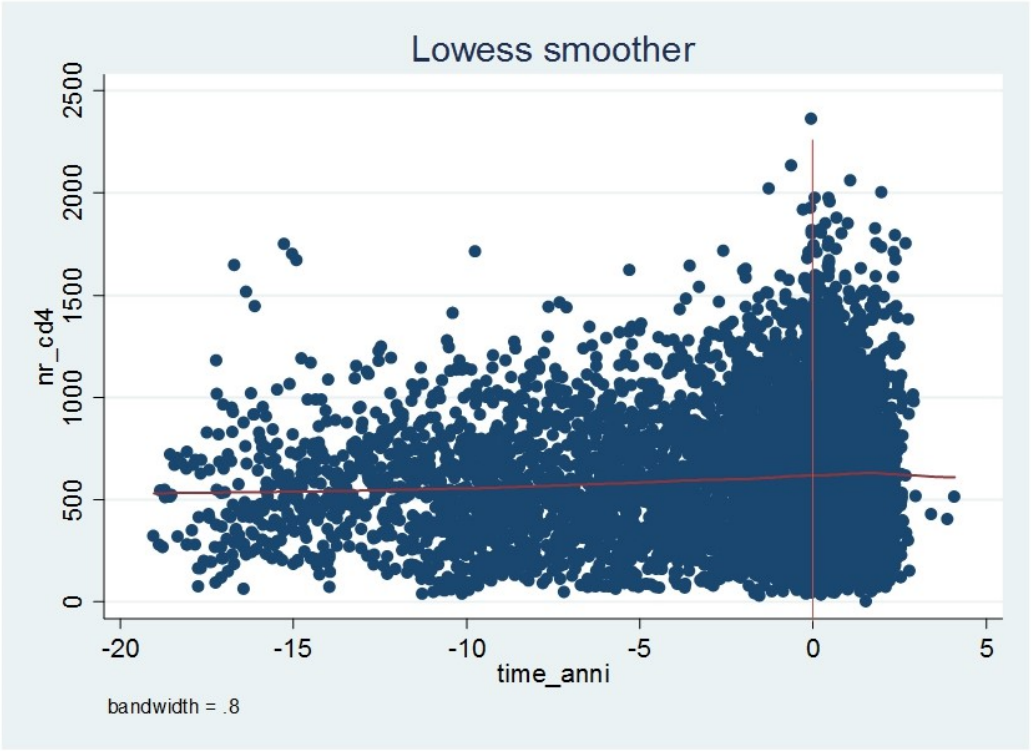
Abstract:

Background: HCV coinfection has been recognized as a possible contributor of poor CD4+ recovery under antiretrovirals (ART) and is known to promote systemic inflammation with accumulation of highly differentiated CD8+ T cells. We aimed to study immunological changes after direct-acting antiviral treatment (DAA) in HIV/HCV patients (pts) who achieved sustained virological response (SVR).

Methods: HIV/HCV pts in ICONA/Hepaicona cohort, treated with DAA since Apr 2013 who achieved SVR12, on ART for>12 months, with undetectable HIV-RNA at DAA start, and with available CD4+, CD8+ counts, HIV-RNA before and after DAA were included. Follow-up accrued from the first undetectable viremia before DAA to last visit or first value of HIV-RNA>200 cp/ml after DAA. Piecewise mixed effect linear regression with random slope and intercept was used to model CD4+ and CD8 trajectories before and after DAA. The following confounders were considered for an association with the intercept: age, sex, epidemiology, nationality, CD4 nadir, CD4 count at DAA start, previous AIDS diagnosis, HCV genotype, HCV-RNA at DAA start, type of DAA, change of ART pre-DAA, use of ribavirin, F4 at DAA start.

Results: A total of 726 HCV/HIV pts were included and contributed for 7,513 values (mean 10/pt). Median follow-up was 2 years (IQR 0.6-10) and 1.6 years (IQR 1-2) before and after DAA. Median age was 53 (IQR: 50-55) years, 22% females, 76% acquired HIV trough IVDU. Nadir CD4+ T cell count was <200/mmc in 19% of pts, while CD4+ T cell count at DAA start was >500/mmc in 59%, 350-500/mmc in 19% and <350/mmc in 22% of pts. Median time of ART use at DAA start was 6.4 years (IQR: 2.6-10.9). At DAA start, NRTI + INSTI was the most represented ART (33.8%), followed by NRTI+NNRTI (18.3%) and NRTI+PI (18.4%). Fifty-eight percent of pts had g1, 23% g3 and 17% g4. A stiffness >12.5 kPa was reported in 42% of pts and median HCV-RNA at DAA start was 6 log10 UI/mL (IQR:5.3-6.4). More frequent DAA combinations included sofosbuvir+ledipasvir (36%), sofosbuvir+daclatasvir (24.3%) and sofosbuvir +velpatasvir (2.7%). Globally, ribavirin was used in 57.3% of pts. Duration of DAA was 8 weeks in 2.1%, 12 weeks in 58.7% and 24 weeks in 39.3% of pts. After treatment with DAA, CD4+ continued to increase, but at a significantly slower rate (on average, CD4 increased by 19.1 cells/year less than the rate observed before treatment with DAA, p<0.01 after adjustement for confounders). Conversely, after DAA treatment, a significant steeper decline of CD8+ T cells was observed (on average, CD8 decreased by 66.9 cells/year more than the rate observed before DAA, p<0.01 after adjustement for confounders) (Figure 1).

Conclusions: DAA treatment in HCV/HIV patients does not show a beneficial effect on CD4+ T cells recovery. However, a more rapid CD8+ T cell reduction was found after HCV eradication, possibly justified by removal of antigenic trigger and reflecting amelioration of systemic inflammation.



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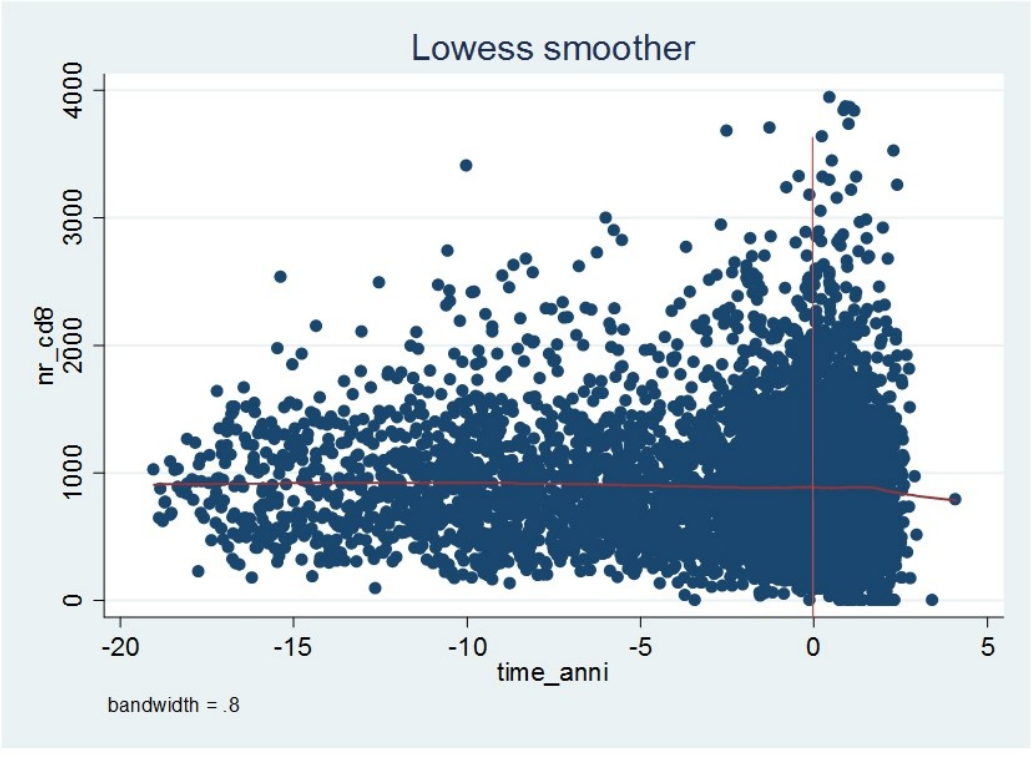

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Figure 1. Slope of CD4+ T cell count (A) and CD8+ T cell count (B) before and after DAA treatment.