

Background

Hepatitis C virus (HCV) infection is estimated to occur in around 45% of HIV-infected patients in southern Europe (EuroSIDA data). HIV-HCV coinfecting patients have higher levels of HCV RNA, an accelerated progression to liver disease with more rapid development of liver fibrosis and cirrhosis, and greater morbidity and mortality compared to those infected with HCV alone. Some studies have suggested that HIV-HCV coinfecting patients have a blunted immune response to HAART, compared with those with HIV infection alone, although others have found comparable degrees of immune restoration in persons with HIV-HCV coinfection.

In order to verify the impact of HCV on immune restoration in patients on a successful HAART regimen, we undertook this retrospective study on a large observational cohort of Italian HIV-positive patients (MASTER Database)

Methods

Patients enrolled in the MASTER Database Study were all considered eligible for this analysis. We searched the electronic database for patients with at least 12 months of viral suppression (pVL <50 cps/mL). Patients were included if the following were all available: CD4s and HIV pVL before starting the HAART regimen; composition of HAART; at least three CD4 and pVL values during treatment; HCV-RNA load and HCV genotype. Both naïve and experienced patients were included.

CD4+ cell increase was defined as change between values at baseline (before starting the HAART treatment that led to a pVL of <50 cps/mL) and after 12 months of undetectability.

Statistical analyses used univariate and multivariate linear regression analyses.

Results

885 HIV pos pts. (684 HCV neg and 201 HCV pos) were selected for this Study. Among coinfectd pts., 133 had a genotype 1 or 4 infection, 68 had genotype 2 or 3. Mean age was 36.8 yrs. [SD: 9] and males were 71.4%. HIV/HCV+ pts. were younger (35.4 yrs. [4.5] vs. 39.6 yrs. [10], $p<0.0001$) and more likely to be IVDUs (86.8% vs. 13.2 %, $p<0.0001$) –see tab 1-. Pts. were on first (44.6%), second (19.3%) or more advanced (36.1%) lines of therapy.

Mean time to reach undetectable pVL after starting the suppressive HAART regimen was 112.6 [112.5] days and mean CD4+ increase was 205 (194) cells/mm³ (HCV neg: 208 [189]; HCV pos genotypes 1 or 4: 205 [194]; HCV pos genotypes 2 or 3: 143 [187], $p=0.01$) –see graph 2-

The mean monthly CD4+ increase was 11.7 [11.8] cells/mm³ (11.8 [11.7]; 13 [12.4]; 8.2 [10.8] among the three groups cited above, respectively, $p=0.048$

At multivariate analysis, HCV genotypes 2 or 3 (vs. HCV neg) were associated with blunted CD4+ responses (regression coefficient: -70 cells/mm³, p=0.006), independently from age (-2 cells/mm³ for each year, p=0.001), occurrence of HIV pVL blips (-40 cells/mm³, p=0.03), baseline CD4+ cell count (p<0.001), high or low HIV pVL at baseline (+30 cells/mm³ for low pVL, p=0.003) and advanced treatment lines (+44 cells/mm³ in 1° line pts, p=0.03). Time to HIV pVL suppression, type of drugs (PI vs. NNRTI-based regimens; AZT-containing vs. non AZT-containing regimens), length and type of previous treatment exposure did not show significant associations with outcome –see graphs for results-

Caption to all graphs:

***Baseline:** last value before suppressing HAART*

***Baseline +1 and +2:** two intermediate determination between baseline and first undetectable HIV pVL. In our series baseline + 1 corresponds to a mean of 32 days, baseline +2 to a mean of 90 days*

***Undetectable 1:** first undetectable HIV pVL (mean of 104 days from baseline)*

***Months 3, 6, 9 and 12:** time points in follow-up*

Conclusions

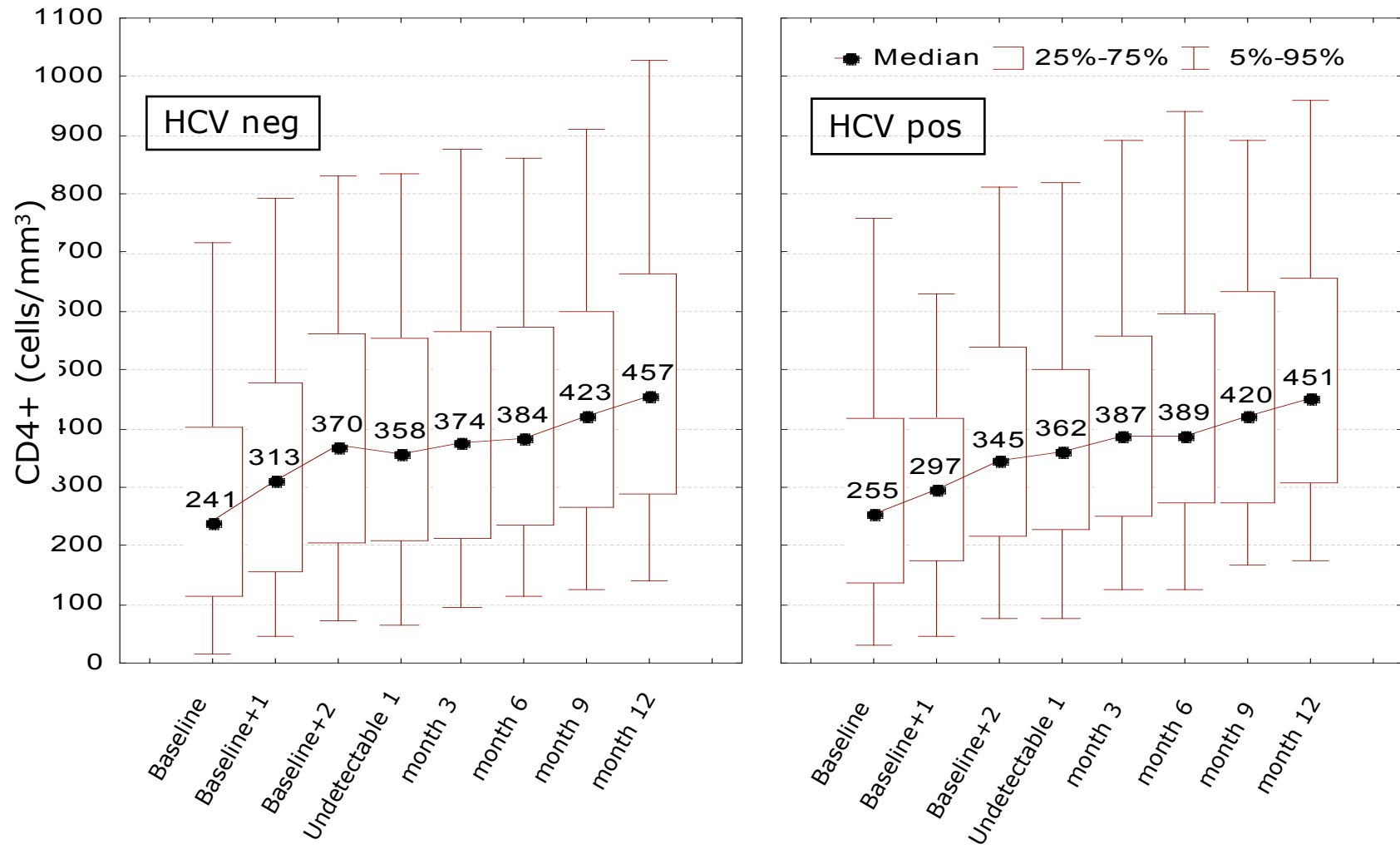
Patients with HIV/HCV+ co-infection did not show a blunted CD4+ cell response following 12 month complete viral suppression when compared to HIV+ individuals. However, having genotypes 2 or 3 HCV was significantly associated to worst CD4+ recovery in presence of undetectable pVL, when compared to either HCV neg or HCV pos pts. infected with genotypes 1 or 4.

In the whole cohort (independently from having or not a HCV infection) being younger, with a lower HIV pVL and a higher CD4 cell count at baseline and being on first HAART regimen, were all factors associated with a significantly better CD4 recovery during a suppressive HAART.

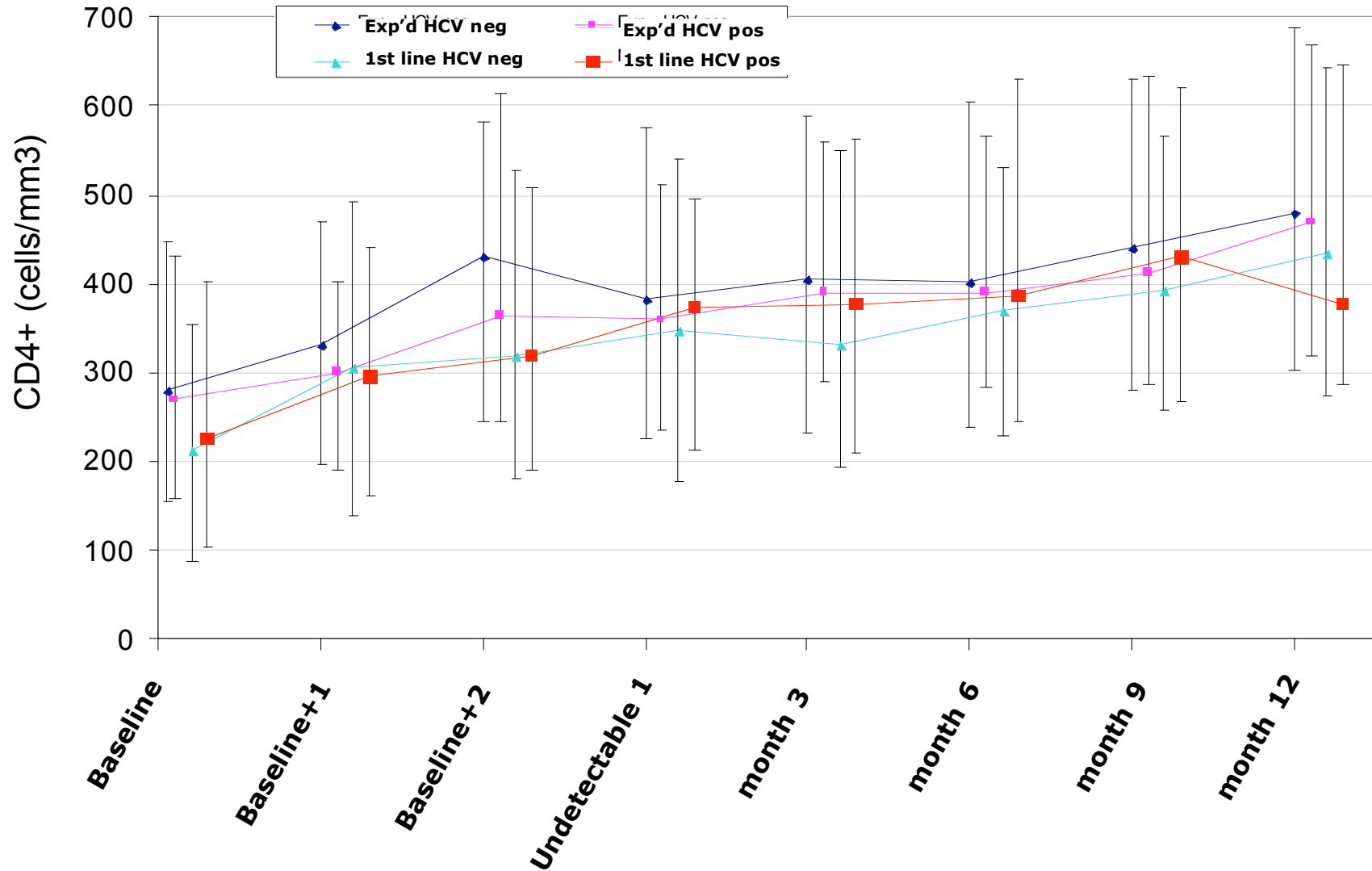
References

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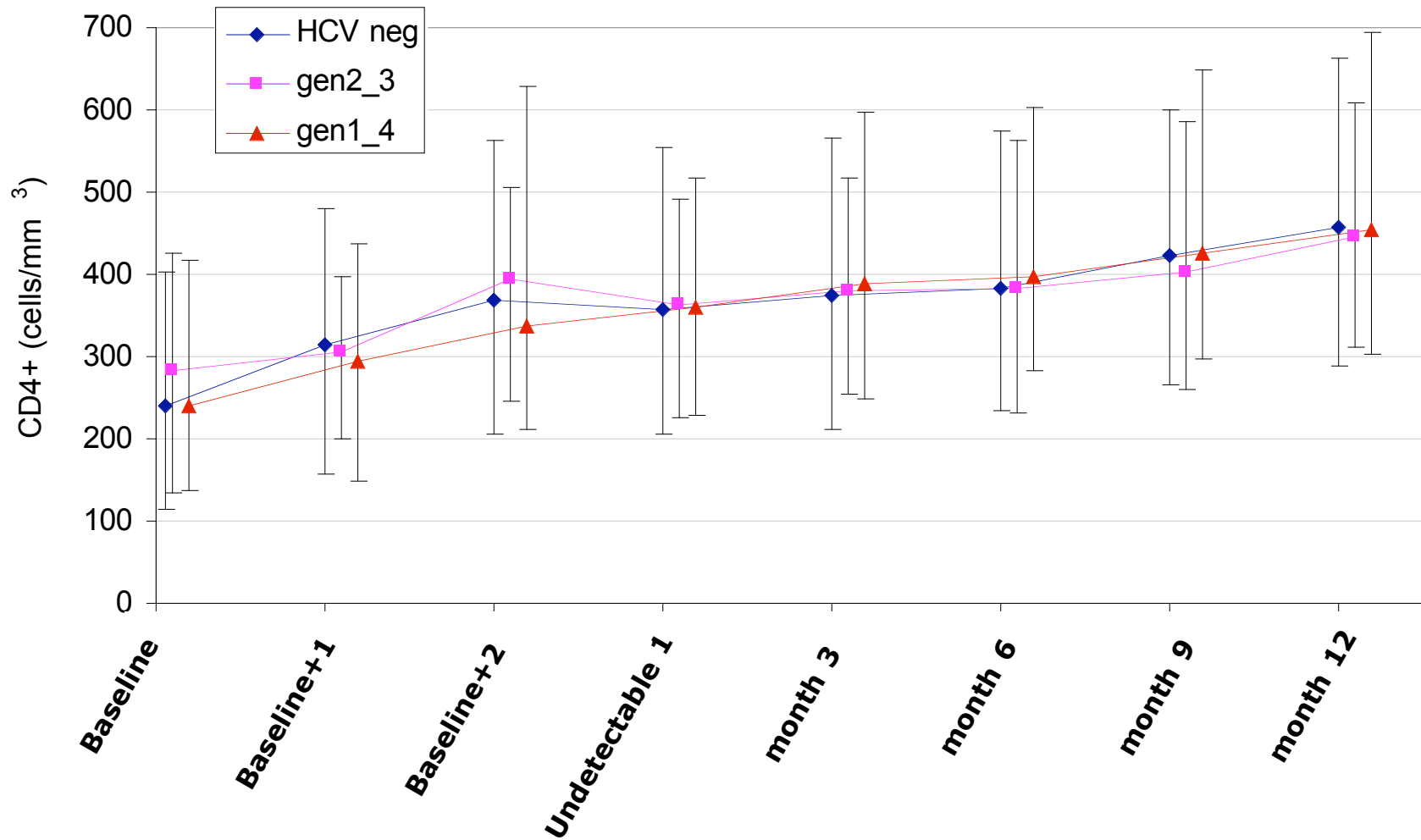
Graph 1. CD4+ cell count across time in HCV pos vs. HCV neg pts. Absolute values (cells/mm³) expressed as medians. Boxes: 25° and 75° percentiles; bars: 5° and 95° percentiles



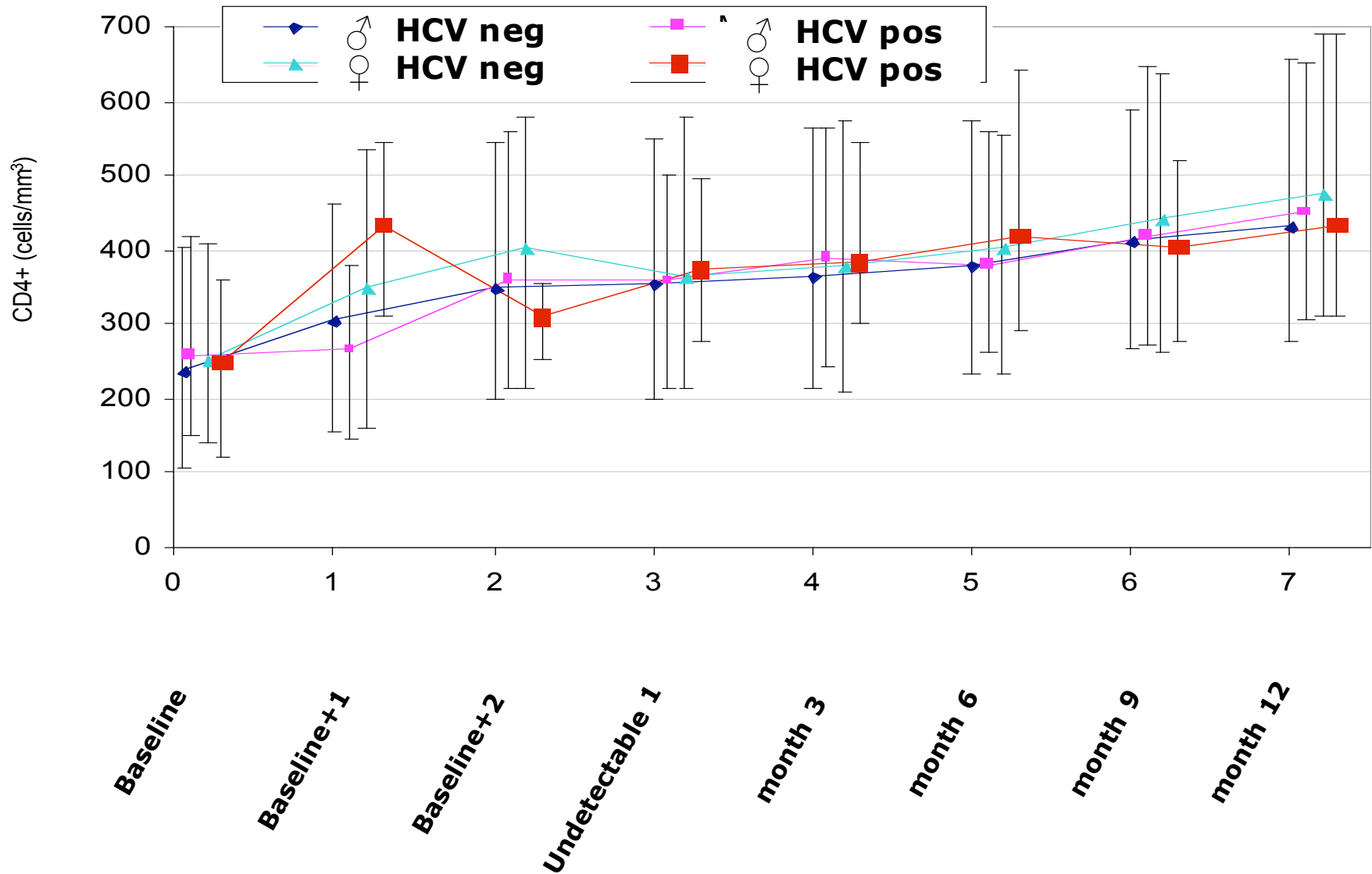
Graph 2. HCV neg vs. HCV pos subdivided between first line and experienced. CD4 cells/mm³ across time, expressed as medians. Bars represent 25° and 75° percentiles



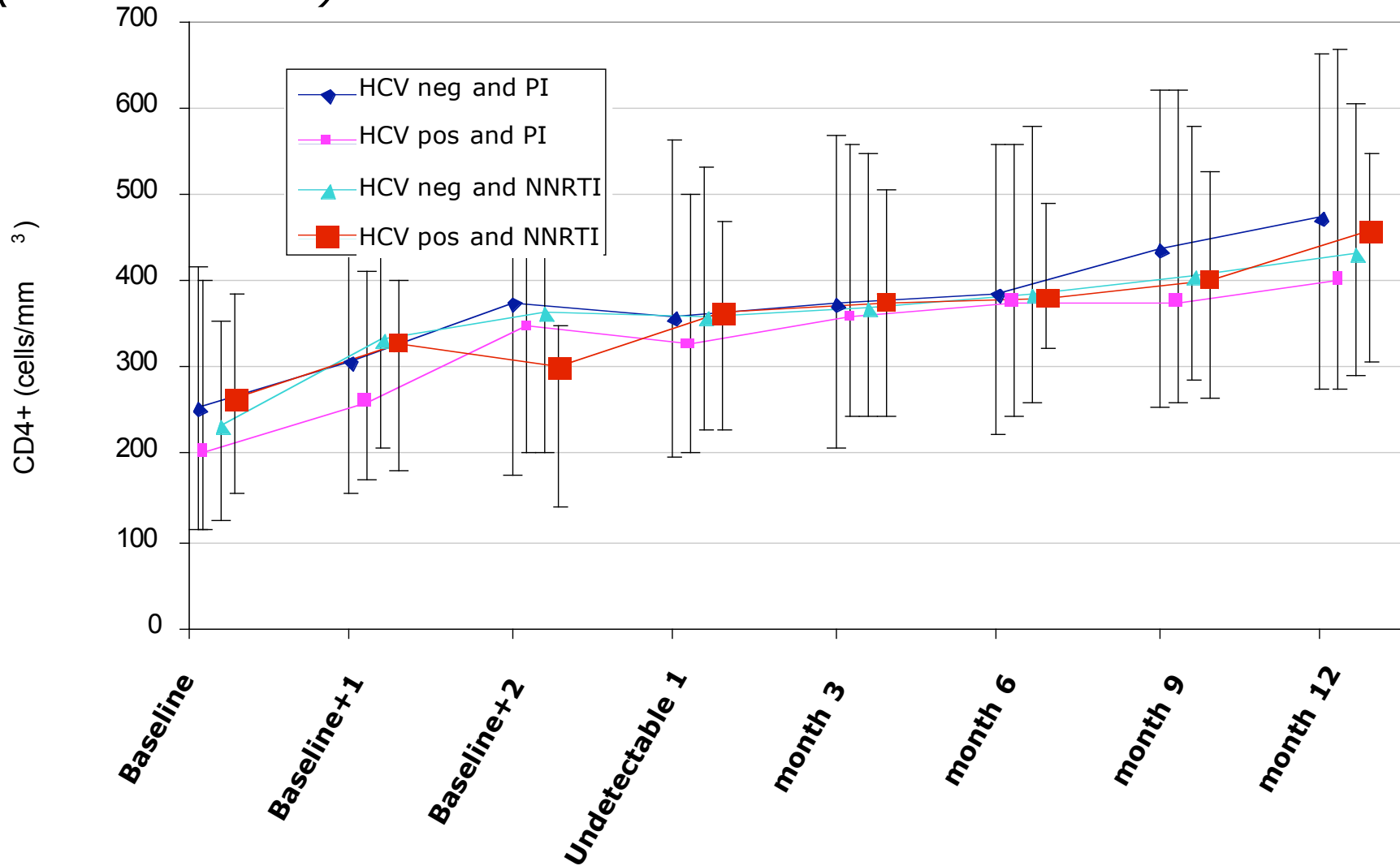
Graph 3. CD4 cell increase in HCV neg vs. HCV pos pts. subdivided according to HCV genotypes. Expressed as medians. Bars represent 25° and 75° percentiles



Graph 4. CD4 cell counts across time in HCV neg vs. HCV pos pts. with gender subsets. Expressed as medians. Bars represent 25^o and 75^o percentiles



Graph 5. CD4 cell count across time in HCV neg vs HCV pos pts. according to HAART composition. **PI** indicates a PI-based HAART; (PI+NRTIs); **NNRTI** indicates a NNRTI-based HAART (NNRTI+NRTIs)



Graph 6. CD4 cell counts in HCV neg vs. HCV pos pts. subdivided for AZT vs. non-AZT containing HAART. Expressed as medians, bars represent 25° and 75° percentiles

