Poster # 1069

CROI 2008

Hepatitis C Virus (HCV) Coinfection Does Not Influence the CD4 Cell Recovery in HIV-1 Infected Patients with Maximum Virologic Suppression within the EuroSIDA Cohort

L Peters[1], A Mocroft[2], V Soriano[3], J Rockstroh[4], P Aldins[5], M Losso[6], L Valerio[7], P Reiss[8], B Ledergerber[9], JD Lundgren[1], for the EuroSIDA study group

[1]Copenhagen HIV Programme, University of Copenhagen, Denmark, [2]Royal Free and University College Medical School, London, UK, [3]Hospital Carlos III, Madrid, Spain, [4]University of Bonn, Germany, [5]Infectology Center of Latvia, Riga, Latvia, [6]Hospital JM Ramos Mejia, Buenos Aires, Argentina, [7]CHU Nice Hopital de L'Archet 1, Nice, France, [8]Academisch Ziekenhuis bij de Universiteit van Amsterdam, The Netherlands, [9]Zurich University Hospital, Switzerland

Lars Peters, MD
Copenhagen HIV Programme
University of Copenhagen,
Faculty of Health Sciences
The Panum Institute/Build. 21.1
Blegdamsvej 3B
DK-2200 Copenhagen N
Tel: +45 35455764
Fax: +45 35455758
E-mail: lpe@cphiv.dk

INTRODUCTION

Conflicting data exist whether HCV coinfection affects the CD_4 T-cell recovery in HIV patients starting antiretroviral treatment. Of the major cohort studies some have found that coinfected patients had a blunted CD_4 increase compared to HIV-monoinfected patients (1;2), while others found no effect of HCV on CD_4 recovery (3;4). In addition, the influence of HCV genotype on the response to antiretroviral treatment is not well studied. Previous studies have been limited by using HCV seropositivity as a criterion for HCV infection, whereby patients with spontaneous HCV-RNA clearance are grouped with those with chronic infection. Furthermore, HIV-RNA viral load (VL) suppression was defined as HIV-RNA <400 copies/mL (1;4) or <500 copies/mL (2;3) which means that low level viral replication influencing the CD_4 cell recovery could not be ruled out.

OBJECTIVES

To investigate the influence of chronic HCV coinfection and HCV genotype on the CD_4 cell recovery in HIV-1 infected patients with maximum virologic suppression (HIV viral load <50 copies/mL) within the EuroSIDA cohort.

METHODS

Patients

3892 patients from the EuroSIDA observational cohort who fulfilled the following inclusion criteria

Inclusion criteria and definitions

- All patients tested for anti-HCV antibodies
- If anti-HCV positive, a quantitative HCV-RNA (limit of detection 615 IU/ml) should be available
- If HCV-RNA positive, patients were required to be HCV genotyped
- At least two consecutive HIV viral loads <50 copies/mL after starting combination antiretroviral therapy (cART)

cART was defined as a minimum of three drugs, of which at least two were nucleos(t)ides. For each pair of HIV VL <50 copies/mL the following criteria were required (**figure 1**):

- A CD_4 count measured within 28 days of each HIV VL measure
- The CD_4 count to be different for each of the viral loads in the viral load pair (VLP)
- No HIV treatment change between HIV VL measures in a VLP

Statistical methods

Change in CD_4 occurring between each pair of consecutive VL <50 copies/mL was calculated and standardized for the time between viral load measurements to give the rate of change in CD_4 (cells/µl per year). Each patient could contribute data for more than one viral load pair (VLP).

Generalised linear models, using a normal distribution and an identity link function, adjusted for repeated measures, were used to describe the rate in CD_4 count changes (5).

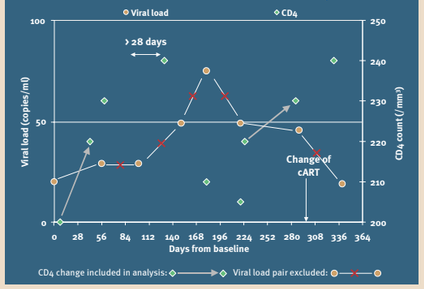
Three comparisons were performed:

- HCV-seronegative vs. HCV-seropositive patients
- Comparison between genotypes 1- 4 in HCV-RNA positive patients
- Among HCV-seropositive patients, comparison of those viremic vs. aviremic (HCV-RNA < 615 IU/mL)

Baseline was arbitrarily defined as the latest of the first of two consecutive VL <50 mL after starting cART and the date of first test for anti-HCV antibodies.

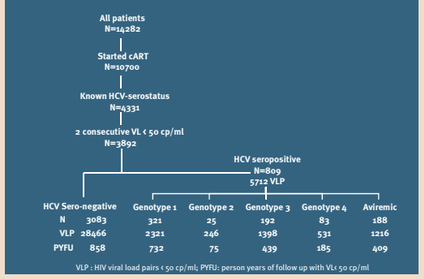
Figur 1

The treatment course in an individual patient



Figur 2

Inclusion of patients



VLP : HIV viral load pairs < 50 cp/ml; PYFU: person years of follow up with VL< 50 cp/ml

Table 1

Baseline characteristics of 3892 patients

		%
Gender	Male / Female	77.6 / 22.4
Exposure	Homo / Hetero / IDU	48.8 / 16.1 / 27.9
ARV naïve		45.1
Anti-HCV	- / +	79 / 21
HCV-RNA*	- / +	23 / 77
Prior AIDS		27.9
		Median (IQR)
Age		41.1 (35.3 – 48.2)
Baseline date		12/01 (9/99 – 03/04)
CD_4 at starting cART		214 (100 – 332)
CD_4 at baseline		429 (251 – 580)

*Among anti-HCV+ pts; IDU: intravenous drug users

RESULTS

Out of 14,282 patients in the EuroSIDA cohort 3,892 were included representing 34,178 pairs of HIV VL measurements with VL <50 copies/mL and 10,422 person years of follow up (**figure 2**).

Table 1 describes the baseline characteristics of the patients. 809 (21%) patients were HCV-seropositive and among them 621 (77%) had detectable HCV-RNA.

Median time between HIV VL pairs was 94 days (IQR 84 –124) and median number of pairs per person seven (IQR 4-12) .

Figure 3 shows the crude, unadjusted, annual change in CD_4 count with maximum virologic suppression. For HCV-seropositive and seronegative patients it was 42.1 cells/µL (95% confidence interval [CI] 33.2 – 51.0) and 40.8 cells/µL (95% CI 36.8 – 44.7), respectively, (p=0.86) Similarly, no significant difference in annual CD_4 change was found when comparing between HCV genotypes (p=0.50) or HCV viremic vs. aviremic in HCV seropositive patients (p=0.99).

After adjustment for nucleoside pair, third drug, age, treatment naïve at starting cART, change in CD_4 since starting cART, time since starting cART, time to initial virologic suppression < 500 cp/ml there was no difference in annual CD_4 change when comparing according to HCV serostatus (p=0.48), between genotypes (p=0.51) or when comparing HCV viremic vs. aviremic (p=0.78) (**figure 4**).

Adjusting additionally for HCV treatment and HCV-RNA VL did not change the findings.

CONCLUSIONS

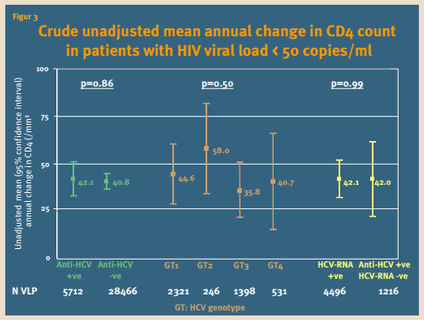
In this prospective EuroSIDA cohort study we have shown compelling evidence that HCV coinfection does not impair the CD_4 recovery in HIV-1 infected patients who are maximally HIV suppressed (VL <50 copies/mL) compared to HIV-monoinfected patients. Similarly, no difference in CD_4 increase was found when comparing HCV seropositive vs. seronegative patients or when comparing distinct HCV genotypes, although the power of this latter analysis is limited due to the small number of VLP for genotype 2 and 4. Adjusting for HCV-RNA viral load did not change the findings.

By restricting our analysis to calculate the CD_4 T-cell increase only when the patients are maximally HIV suppressed we have been able to overcome some potential confounders of previous cohort studies, most importantly differences in adherence between the individual patient groups and differences in potency of the used cART regimes. Furthermore, we included only patients with well-characterized hepatitis C status.

Although we have shown that hepatitis C coinfection did not impair the CD_4 response to cART, still HCV eradication will lower the risk of hepatotoxicity induced by antiretroviral drugs and progression of liver disease.

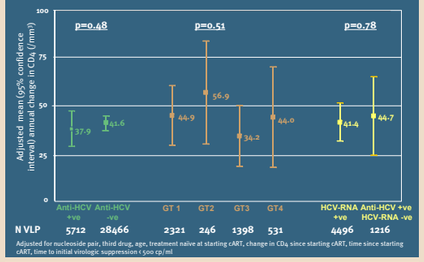
Figur 3

Crude unadjusted mean annual change in CD_4 count in patients with HIV viral load < 50 copies/mL



Figur 4

Adjusted mean annual change in CD_4 count in patients with HIV viral load < 50 copies/mL



Adjusted for nucleoside pair, third drug, age, treatment naïve at starting cART, change in CD_4 since starting cART, time since starting cART, time to initial virologic suppression < 500 cp/ml

References:

1) Greub G, Ledergerber B, Battegay M et al. Clinical progression, survival, and immune recovery during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV Cohort Study. Lancet 2000; 356(9244):1800-1805.
2) Weis N, Lindhardt BO, Kronborg G et al. Impact of hepatitis C virus coinfection on response to highly active antiretroviral therapy and outcome in HIV-infected individuals: a nationwide cohort study. Clin Infect Dis 2006; 42(10):1481-1487
3) Rockstroh JK, Mocroft A, Soriano V et al. Influence of hepatitis C virus infection on HIV-1 disease progression and response to highly active antiretroviral therapy. J Infect Dis 2005; 192(6):992-1002.
4) Sulkowski MS, Moore RD, Mehta SH, Chaisson RE, Thomas DL. Hepatitis C and progression of HIV disease. JAMA 2002; 288(2):199-206.
5) Mocroft A, Phillips A, Gatell J et al. Normalisation of CD_4 counts in patients with HIV-1 infection and maximum virological suppression who are taking combination antiretroviral therapy: an observational cohort study. Lancet 2007; 370(9585):407-413.

The EuroSIDA Study Group

Argentina: (M Losso), A Duran **Austria:** (N Vetter). **Belarus:** (I Karpov), A Vassilenko, VM Mitsura; O Suetnov **Belgium:** (N Clumeck) S De Wit, B Poll, R Colebunders. **Bulgaria:** (K Kostov) **Croatia:** (J Begovac) **Czech Republic:** (L Machala) H Rozsypal, D Sedlacek, Plzen. **Denmark:** (J Nielsen) J Lundgren, T Benfield, O Kirk, J Gerstoft, T Katzenstein, A-B E Hansen, P Skinhøj, Pedersen, L Oestergaard. **Estonia:** (K Zilmer) Jelena Smidt, Kohtla-järve **Finland:** (M Ristola). **France:** (C Katlama), J-P Viard, M Girard, JM Livozet, P Vanhems, C Pradier, F Dabis **Germany:** (J Rockstroh) R Shmidt, J van Lunzen, O Degen, H Stellbrink S Staszewski, J Bogner, G. Fätkenheuer, **Greece** (J Kosmidis) P Gargalianos, G Xylomenos, I Perdios, G Panos, A Filandras Karabatsaki, H Sambattakou **Hungary** (D Banhegyi). **Ireland:** (F Mulcahy). **Israel:** (I Yust) D Turner, M Burke, S Pollack, G Hassoun, S Maayan **Italy** (A Chiesi), I Mazeu, C Mussini, C Arici, R Pristera, F Mazzotta, A Gabbuti, V Vullo, M Lichtner, A Chirianni, E Montesarchio, M Gargiulo, G Antonucci, F Iaconi, P Narciso, C Vlassi, M Zaccarelli, A Lazzarin, R Finazzi, M Galli A Ridolfo, A d'Arminio Monforte **Latvia** (B Rozentale) P Aldins **Lithuania** (S Chaplinskas). **Luxembourg** (R Hemmer), T Staub. **Netherlands** (P Reiss). **Norway** (J Bruun) A Maeland, V Ormaasen, **Poland:** (B Knysz) J Gasiorowski, A Horban, D Prokopowicz, A Wiercinska-Drapalo, A Boron-Kaczmarska, M Pynka, M Beniowski, E Mularska, H Trocha **Portugal** Antunes) E Valadas, K Mansinho, F Maltez, **Romania** (D Duiculescu), V Babes **Russia** (A Rakhmanova), E Vinogradova, S Buzunova, **Serbia** (D Jevtovic) **Slovakia** (M Mokráš) D Staneková, **Spain** (J González-Lahoz) V Soriano, L Martin-Carbonero P Labarga, B Cloteť, A Jou, J Conejero, C Tural, JM Gatell, JM Miró, P Domingo, M Gutierrez, G Mateo, MA Sambeat **Sweden** (A Karlsson), A Persson, L Flamholc **Switzerland** (B Ledergerber) R Weber, P Francioli, M Cavassini, B Hirschel, E Boffi, Furrer, M Battegay, J Elzi **Ukraine** E Kravchenko) N Chentsova **United Kingdom** (S Barton), AM Johnson, D Mercey, A Phillips, MA Johnson, A Mocroft, M Murphy, J Weber, G Scullard, M Fisher, R Brettle

Virology group: B Cloteť (Central Coordinators) plus ad hoc virologists from participating sites in the EuroSIDA Study.

Steering Committee F Antunes, B Cloteť, D Duiculescu, J Gatell, B Gazzard, A Horban, A Karlsson, C Katlama, B Ledergerber (Chair), A D'Arminio Monforte, A Phillips, A Rakhmanova, P Reiss (Vice-Chair), J Rockstroh

Coordinating Centre Staff: J Lundgren (project leader), O Kirk, A Mocroft, N Friis-Møller, A Cozzi-Lepri, W Bannister, M Ellefson, A Borch, D Podlekareva, J Kjær, L Peters, J Reekie

Download poster at: www.cphiv.dk

FACULTY OF HEALTH SCIENCES UNIVERSITY OF COPENHAGEN

EuroSIDA

CHIP COPENHAGEN HIV PROGRAMME