HCV Treatment and CD4 Cell Count Decline, in HIV/HCV Co-infected Patients: European Cohort Collaboration

Poster 965

Colette Smit[1], Antonella d'Arminio[2], Frank de Wolf[1,3], Massimo Puoti[2], Francois Dabis[4] on behalf of the HCV working group of COHERE*

[1] Stichting HIV Monitoring Amsterdam, The Netherlands; [2] Clinic of Infectious Diseases, University of Brescia, Italy ; [3] Imperial College, London, UK; [4] Université Victor Segalen Bordeaux, France

* cohorts participating in HCV working group:

AMACS, ANRS, ATHENA, CASCADE, CHIC, EUROSIDA, Gems-haemo, HSR, ICONA, PISCIS, SHCS, St Pierre, VACH

1. Background

Hepatitis C (HCV) treatment in HIV-HCV co-infected patients is important in reducing morbidity and mortality. HCV treatment includes pegylated interferon (PEG-IFN) or a combination of PEG IFN and ribavirin (RBV). This combination is associated with a drop in CD4 cell counts.

Aim: To study the impact of PEG-IFN+RBV on CD4 cell counts during treatment in HCV/HIV co-infected patients.

2. Methods

Population: - from 13 cohorts participating in COHERE European Network

- aged >16 years at HIV diagnosis

- enrolled after January 1996

- positive HCV antibody or RNA test result after enrolment.

Statistical methods:

- PEG-IFN+RBV treated patients were stratified according to CD4 cell count at treatment initiation: ≤250 vs >250 CD4 cells/ul.
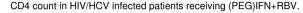
- CD4 cell trajectories during treatment were piecewise modeled within a random effects model, time was included in weeks from treatment initiation. slopes were allowed to change at treatment initiation, 12 and 24 weeks after treatment initiation.
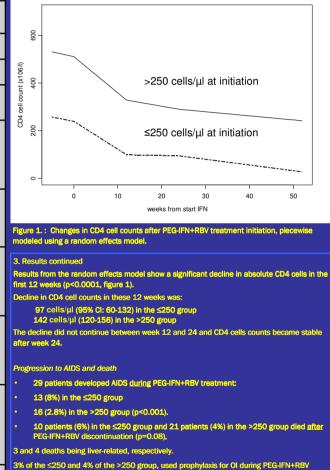
- Patients were censored after 52 weeks, death, loss to follow-up or 31 December 2009. Analyses were adjusted for nadir CD4, age, gender, risk group, region and combination antiretroviral therapy (cART) use.

- Differences in the number of AIDS cases and deaths were tested using Chi square

3. Results

HCV co-infection

• 7035 patients were included.

• 5068 (72%) tested positive for HCV antibodies

• 860 (12%) patients had a positive HCV RNA test result,

• 1107(16%) patients had a positive HCV test result without a specification of anti bodies or RNA.

• 780 patients initiated HCV treatment, 49 (6%) PEG-IFN monotherapy and 731 patients a combination of PEG-IFN+RBV (94%) .

Follow up and progression

• 7035 HCV-HIV co-infected patients contributed 511,154 person-months

• The median follow up was 72 months (IQR: 39-106).

• 2609 (37%) progressed to AIDS and 707 (10%) to death.

Median CD4 cell count at PEG-IFN+RBV treatment initiation:

• 189 CD4 cells/µl (IQR: 155-220) in the ≤250 group (n=161)

• 446 CD4 cells/µl (IQR: 350-582) in the >250 group (n=570).

Table 1: Demographic and clinical characteristics of HCV co-infected patients at baseline

	Overall (HCV+)	HCV untreated	HCV treatment
N	7035	6255 (89%)	780 (11%)
Total person-months	511154	438217	72937
Person months (median(IQR))	72 (39-106)	69 (36-102)	94 (67-125)
Age at baseline			
16-29	1414 (21%)	1300 (21%)	114 (15%)
30-39	3558 (51%)	3152 (50%)	406 (52%)
40-49	1642 (23%)	1430 (23%)	212 (27%)
>=50	421 (6%)	373 (6%)	48 (6%)
Sex			
Male	5207 (74%)	4587 (73%)	620 (79%)
Female	1808 (26%)	1649 (26%)	159 (20%)
Missing	20 (0.3%)	19 (0.3%)	1 (0.1%)
Transmission risk group			
MSM	881 (13%)	699 (11%)	182 (23%)
Heterosexuals	1226 (17%)	1079 (17%)	147 (19%)
IDU	4421 (63%)	4030 (64%)	391 (50%)
Other/unknown	507 (7%)	447 (7%)	60 (8%)
Region of origin			
Western	5310 (75%)	4867 (78%)	643 (82%)
African	213 (3%)	181 (3%)	32 (4%)
Other	200 (3%)	172 (3%)	28 (4%)
Unknown/missing	1112 (16%)	1035 (17%)	77 (10%)
Nadir CD4 cells/µl			
<50	1468 (21%)	1341 (21%)	127 (16%)
50-99	972 (14%)	893 (14%)	79 (10%)
100-199	1833 (26%)	1602 (26%)	231 (30%)
200-349	1989 (28%)	1708 (27%)	281 (36%)
>=350	773 (11%)	711 (11%)	62 (8%)
cART	4729 (67%)	4080(65%)	649(83%)
AIDS event	2609 (37%)	2397(38%)	212(27%)
Deaths	707 (10%)	676(11%)	31(4%)
Mortality rate (per 1000 person months)	1.38	1.54	0.42

CD4 count in HIV/HCV infected patients receiving (PEG)IFN+RBV.

>250 cells/µl at initiation

≤250 cells/µl at initiation

Figure 1. : Changes in CD4 cell counts after PEG-IFN+RBV treatment initiation, piecewise modeled using a random effects model.

3. Results continued

Results from the random effects model show a significant decline in absolute CD4 cells in the first 12 weeks (p<0.0001, figure 1).

Decline in CD4 cell counts in these 12 weeks was:

97 cells/µl (95% CI: 60-132) in the ≤250 group
142 cells/µl (120-156) in the >250 group

The decline did not continue between week 12 and 24 and CD4 cells counts became stable after week 24.

Progression to AIDS and death

• 29 patients developed AIDS during PEG-IFN+RBV treatment:

• 13 (8%) in the ≤250 group

• 16 (2.8%) in the >250 group (p<0.001).

• 10 patients (6%) in the ≤250 group and 21 patients (4%) in the >250 group died after PEG-IFN+RBV discontinuation (p=0.08),

3 and 4 deaths being liver-related, respectively.

3% of the ≤250 and 4% of the >250 group, used prophylaxis for OI during PEG-IFN+RBV treatment.

Conclusions:
Absolute CD4 cell counts sharply declined during the first 12 weeks of PEG-IFN+RBV treatment. This decline was stronger among patients who initiated treatment with low CD4 cell counts. The frequency of AIDS events during treatment and post treatment deaths was higher in this group compared to patients who initiated PEG-IFN+RBV with higher CD4 cell counts and only a small proportion of these patients received prophylaxis for OI.