CD4 T Lymphocyte Recovery with Antiretroviral Therapy is Not Influenced by HCV Co-Infection Status

Curtis L Cooper*[1], Brian Hutton[1], Edward Mills[2], and Jonathan Angel[1]

The University of Ottawa Division of Infectious Diseases and Ottawa Health Research Institute Methods Centre, Ottawa, Canada[1]

and the British Columbia Centre of Excellence, Vancouver, Canada[2]

Corresponding Author: Curtis Cooper, MD, FRCPC
Ottawa Hospital - General Campus
501 Smyth Road
Ottawa, ON Canada K1H 8L6
E-mail: ccooper@ottawahospital.on.ca
Telephone: 613-737-8924
Fax: 613-737-8164

Introduction

❖It is unclear whether CD4 count recovery following combination antiretroviral therapy (cART) initiation is blunted in HIV-HCV co-infected patients compared to HIV mono-infected.
❖If so, it is unknown whether this is a direct consequence of HCV infection or a result of concurrent socioeconomic factors including substance abuse and/or other confounding variable.
❖We sought to use retrospectively collected data to pursue exploratory analyses to address these issues

Methods

Data Collection:
❖Data on CD4 cell counts of patients initiating a first course of combination antiretroviral therapy at The Ottawa Hospital Immunodeficiency Clinic between January 1996 and December 2007 was evaluated following collection in an SPSS 14.0 clinic database.

Outcomes:
❖Change in CD4 cell count from baseline at 3,6,9, & 12 months follow-up
❖Achievement of 50 and 100 cell/µL CD4 increase at follow-up visits

❖**Exposure of interest:**
❖Primary: HIV vs HIV/HCV co-infection status
❖Secondary: history of injection drug use (yes/no), history of alcohol use greater than 50 grams/day (yes/no), baseline CD4 cell count (<200, 200-349, 350+), composition of antiretroviral regimen (Nucleoside-only, NNRTI-based, protease inhibitor (PI)-containing, NNRTI and PI containing)

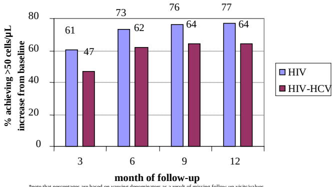
Data Analysis:
❖Summary of relevant baseline characteristics via computation of measures of central tendency and dispersion
❖Comparison of changes over time in CD4 count amongst clinical subgroups of interest using non-parametric Mann-Whitney and Kruskal Wallis tests
❖Computation of a series of multivariable linear regression models:
- differences in CD4 at baseline and CD4 count at 3, 6, 9, 12 months as outcome variables
- Co-infection status, drug use, alcohol use, baseline CD4, PI/NNRTI use as predictors

❖No data was imputed at this stage of analysis

Table 1 Baseline Characteristics

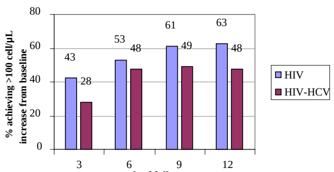
Characteristic	Group: HIV	Group: HIV-HCV	Overall
Sample Size	415	134	549
Age in Years (mean, SD)	43 (9)	42 (8)	43 (9)
Male Sex	305 (73%)	110 (81%)	415 (76%)
Baseline CD4 [cells/µL (mean, SD)]	268 (220)	308 (267)	277 (233)
History Injection Drug Use			
Yes	19(5%)	105(78%)	124(23%)
No	396(95%)	29(22%)	425(77%)
History Excess Alcohol Use			
Yes	132(32%)	52(39%)	184(34%)
No	283(68%)	82(61%)	364(66%)
Antiretroviral Regimen			
NNRTI-based	90 (22%)	20 (14%)	110 (20%)
PI-based	231 (56%)	99 (73%)	330 (60%)
NNRTI and PI Regimen	38 (9%)	4 (3%)	42 (8%)
Nucleoside Only	54 (13%)	13 (10%)	67 (12%)

Figure 1a % achieving a 50 cell/µL increase in CD4 from baseline at each time point



*note that percentages are based on varying denominators as a result of missing follow-up visits/values

Figure 1b % achieving a 100 cell/µL increase in CD4 count from baseline at each time point



*note that percentages are based on varying denominators as a result of missing follow-up visits/values

Figure 2 Change in CD4 from baseline as a function of HCV Status (mean, 95% CI)

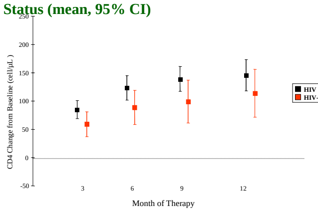


Figure 3a Change in CD4 from baseline as a function of HCV: patients with baseline CD4<200 (mean, 95% CI)

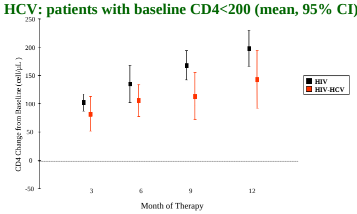


Figure 3b Change in CD4 from baseline as a function of HCV: patients with Baseline CD4 200-349 (mean, 95% CI)

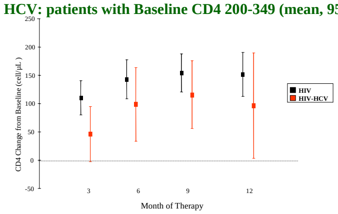


Figure 3c Change in CD4 from baseline as a function of HCV: patients with Baseline CD4 350+ (mean, 95% CI)

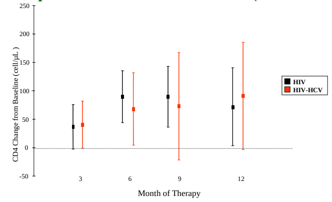


Table 2a: Median (IQR) change from baseline in CD4 count as a function of HCV Status

HCV Status	Median Increase in CD4 Count from Baseline (cells/µL)			
	Month 3	Month 6	Month 9	Month 12
HIV	83 (15-159)	106 (43-192)	131 (56-230)	137 (57-256)
HIV-HCV	45 (-3 to 105)	79 (-5 to 154)	96 (28-173)	92 (26-202)
P Value *	**0.01**	**0.06**	**0.04**	**0.08**

* Mann-Whitney Test

Table 2b: Median (IQR) change from baseline in CD4 count as a function of Baseline CD4 Count

CD4 Count at Baseline	Median Increase in CD4 Count from Baseline (cells/µL)			
	Month 3	Month 6	Month 9	Month 12
CD4<200	86 (35-148)	112 (62-166)	133 (77-227)	169 (108-256)
CD4 200-349	80 (7-164)	106 (59-212)	123 (71-205)	122 (65-245)
CD4 350+	37 (-60 to 145)	87 (-41 to 196)	81 (-59 to 212)	68 (-27 to 186)
P Value *	**0.0007**	**0.07**	**0.01**	**0.0003**

*(Kruskal-Wallis test)

Table 2c: Median (IQR) change from baseline in CD4 count as a function of Injection Drug Use History

History of Injection Drug Use	Median Increase in CD4 Count from Baseline (cells/µL)			
	Month 3	Month 6	Month 9	Month 12
Yes	60 (10-113)	77 (-11 to 154)	75 (11-178)	142 (32-220)
No	80 (14-159)	107 (57-191)	134 (58-227)	132 (56-250)
P Value *	0.11	**0.05**	**0.02**	0.55

* Mann-Whitney Test

Table 2d: Median (IQR) change from baseline in CD4 count as a function of Excess Alcohol Use History (>50 grams/day)

History of Excess Alcohol Use	Median Increase in CD4 Count from Baseline (cells/µL)			
	Month 3	Month 6	Month 9	Month 12
Yes	72 (13-139)	105 (26-209)	128 (53-212)	136 (56-230)
No	75 (9.5-148.5)	106 (45-175)	125 (44-225)	123 (41-241)
P Value *	0.99	0.99	0.78	0.46

* Mann-Whitney Test

Table 2e: Median (IQR) change from baseline in CD4 count as a function of Antiretroviral Regimen

Antiretroviral Regimen Composition	Median Increase in CD4 Count from Baseline (cells/µL)			
	Month 3	Month 6	Month 9	Month 12
Neither (Nucleoside-based ART)	23 (-60 to 109)	80 (-9 to 146)	13 (-116 to 116)	1 (-138 to 116)
NNRTI-based HAART	72 (12-110)	96 (17-180)	113 (44-202)	127 (71-186)
Protease Inhibitor-based HAART	78 (19-149)	104 (35-174)	131 (66-213)	133 (55-245)
NNRTI and Protease Inhibitor-containing ART	123 (25-228)	166 (91-223)	184 (77-276)	202 (91-269)
P Value *	**0.007**	**0.02**	**0.002**	**0.003**

* Kruskal Wallis Test

Table 3: Predictors of CD4 Count Recovery-Regression Coefficients and P-values from Multivariable Regression at Each Follow-Up Time

Risk factor	3 months		6 months		9 months		12 months	
	Param. Estimate	P-value	Est. (95% CI)	P-value	Est. (95% CI)	P-value	Est. (95% CI)	P-value
HIV/HIV-HCV status (Ref=HIV)	-92	**0.001**	-15	0.60	-27	0.59	-39	0.33
History IDU								
Yes	81	**0.03**	-20	0.54	-35	0.52	27	0.55
No	Ref		Ref					
History Excess Alcohol Use	9	0.68	-5	0.78	-22	0.49	-16	0.53
Yes	Ref		Ref					
No								
Baseline CD4								
<200	Ref	**0.04**	Ref	0.26	Ref	0.19	Ref	**0.01**
200-350	-12		6		-41		-43	
350+	-60		-30		-64		-85	
ART Regimen								
Nucleoside	-85	0.18	-143	**0.01**	-270	**0.002**	-175	**0.01**
NNRTI-based	-39		-86		-123		-34	
PI-based	-17		-81		-106		-23	
NNRTI and PI	Ref		Ref		Ref		Ref	

***note that sample sizes used for modeling at each time point vary due to patterns of patient follow-up

Conclusions and Discussion

❖HIV mono-infected patients achieved greater CD4 cell recovery at each time point in comparison to HIV-HCV co-infected individuals.

❖HCV positive status and past injection drug use may explain this in the initial 3 months of treatment, but not afterwards. This analysis does not support a direct HCV effect of immune recovery with HAART.

❖Univariate and multivariable analysis suggest that the composition of combination antiretroviral therapy and baseline CD4 are important contributors to the size of CD4 recovery following initiation of HAART.
❖The lower the CD4 count at the start of HAART, the greater the increase in CD4 cell count.
❖Nucleoside-sparing therapy (i.e. NNRTI and PI) may produce greater CD4 recovery.

❖Past alcohol consumption did not effect CD4 cell recovery at any time point.

Limitations and Potential Biases

❖Capture of information regarding drug use and alcohol use is limited/not optimal, and may be prone to misclassification in some cases.
❖Issues of missing data limit the type of analysis that can be pursued at this time.
❖At several time points the absolute number of individuals on nucleoside-only and PI/NNRTI containing ART was small. Those started on PI and NNRTI-containing ART were more likely to be clinical trial participants which may have introduced bias. Further analysis is planned to explore this concern.
❖Retrospective analysis

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