



Improved Survival of Hepatocellular Carcinoma (HCC) in HIV-Infected Patients with Undetectable HIV RNA



Imperial College London

Emma Page¹, Eugenia Vispo², David E. Kaplan³, Luciana Kikuchi⁴, Marina Núñez⁵, Mark Nelson¹, Pablo Barreiro², Jorge Daruich⁶, Kristen Marks⁷, Rena Fox⁸, Morris Sherman⁹, Massimo Puoti¹⁰, Norbert Bräu¹¹. The Liver Cancer in HIV Study Group*

¹Chelsea & Westminster Hospital & Imperial College, London, United Kingdom, ²Hospital Carlos III, Madrid, Spain, ³Philadelphia Veterans Affairs Medical Center & University of Pennsylvania, Philadelphia, PA, USA, ⁴Universidade de São Paulo, São Paulo-SP, Brazil, ⁵Wake Forest University, Winston-Salem, NC, USA, ⁶Universidad de Buenos Aires, Buenos Aires, Argentina, ⁷Weill Cornell Medical College, New York, NY, USA, ⁸University of California at San Francisco, San Francisco, CA, USA, ⁹University of Toronto, Toronto, ON, Canada, ¹⁰Università degli Studi di Brescia, Brescia, Italy, ¹¹Bronx Veterans Affairs Medical Center, Bronx, NY & Mount Sinai School of Medicine, New York, NY, USA

Background

- High HIV viral load in HIV/HCV-coinfected patients is associated with faster fibrosis progression.
- The influence of HIV viral load on HCC is unknown

Methods

- Retrospective analysis in 22 centers in 7 countries (dark gray on map):

- North America: Canada and United States
- South America: Argentina and Brazil
- Europe: Germany, Spain and United Kingdom



Sites from countries in light gray are awaiting IRB/EC approval

- All HCC cases in HIV-infected patients from 1995-2009 with data on initial presentation.

N=115 total of 117 patients, of whom 2 had no HCV RNA data

- Diagnosis by AASLD criteria (Bruix & Sherman, Hepatology, 2005)

- Patients were divided into

Undetectable: HIV RNA <400 copies/ml n=68
Detectable: HIV RNA 400+ copies/ml n=47

HCC Tumor Characteristics

	HIV RNA <400 c/ml n=68	HIV RNA 400+ c/ml n=47	P
Hepatic Lesions			
Solitary Tumors	35 (52%)	21 (45%)	0.52
Multiple tumors	28 (41%)	24 (51%)	
Diffusely Infiltrative Tumors	5 (7.4%)	2 (4.3%)	
Median Size Largest Lesion (cm), Range	3.5 (0.5 – 18)	5.6 (2.0 – 20)	0.017
Portal Vein Thrombosis	10 (15%)	9 (19%)	0.53
Extrahepatic Metastases	11 (16%)	8 (17%)	0.91
AFP level			
Median (ng/ml)	231	1,504	0.045
Normal (≤ ULN)	8 (13%)	5 (11%)	0.73

Patient Characteristics

	HIV RNA <400 c/ml n=68 (59%)	HIV RNA 400+ c/ml n=47 (41%)	P
Age (yrs), Mean ± SD	51.4 (±7.9)	51.5 (±8.3)	0.96
Male Sex	63 (93%)	43 (92%)	1.00
Race/Ethnicity			0.13
Black	24 (35%)	26 (55%)	
White	32 (47%)	15 (32%)	
Latino Asian + other	10 (15%) 2 (2.9%)	6 (13%) 0	
Time of HCC Diagnosis Date, Median	Jul-2005	May-2003	<0.001
Etiology of HCC			0.86
Chronic Hepatitis C	49 (72%)	36 (77%)	
Chronic Hepatitis B Non-Viral (Alcohol, NASH)	17 (25%) 2 (2.9%)	10 (21%) 1 (2.1%)	
Alcohol Consumption			0.052
None	26 (40%)	8 (18%)	
Moderate	18 (24%)	16 (36%)	
Excessive Unknown	22 (36%) [2]	21 (47%) [2]	
Liver Function			
Child-Turcotte-Pugh Score, Mean ± SD	6.4	7.3	0.005
Stage A	41 (60%)	19 (40%)	0.004
Stage B	24 (35%)	21 (45%)	
Stage C	3 (4.4%)	7 (15%)	
Initial Presentation			0.070
Screening Without Symptoms (AFP, Imaging)	42 (62%)	21 (45%)	
Symptoms	26 (38%)	26 (55%)	
HIV parameter, Mean (range)			0.13
CD4+ Cells (per mm ³)	319 (5-1423)	320 (9-1000)	

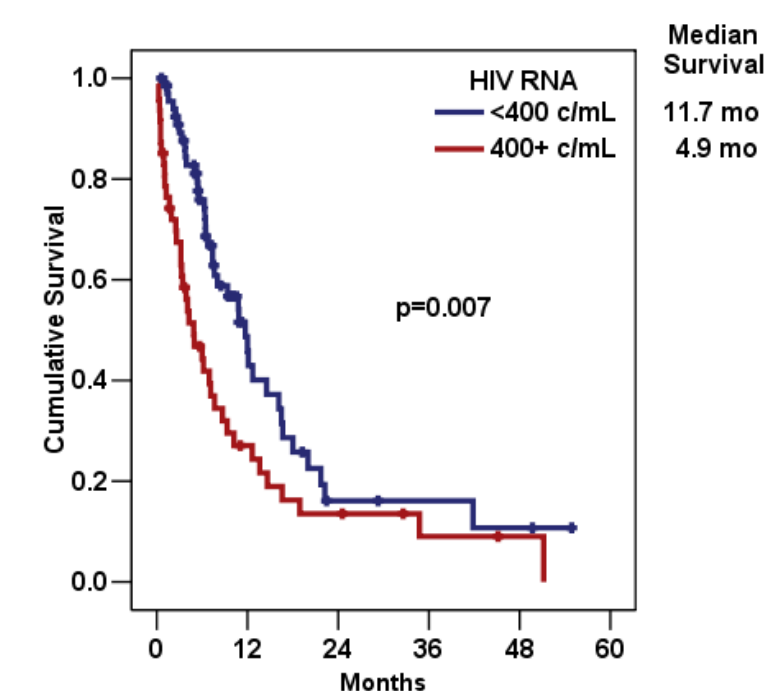
HCC Staging

	HIV RNA <400 c/ml n=68	HIV RNA 400+ c/ml n=47	P
BCLC Stage, n (%)			0.37
A	24 (35%)	10 (21%)	
B	12 (18%)	12 (26%)	
C } Advanced, D } Incurable	25 (37%) 7 (10%)	28 (38%) 7 (15%)	
BCLC Stages C and D	32 (47%)	25 (53%)	0.52
CLIP Score, Mean ±SD	1.65 (±1.3)	2.37 (±1.3)	0.004

HCC Therapy

	HIV RNA <400 c/ml n=68	HIV RNA 400+ c/ml n=47	P
Potentially Curative Therapy	22 (32%)	9 (19%)	0.024
Radiofrequency Ablation (RFA)	9	5	
Ethanol Injections	3	4	
Surgical Resection	8	0	
Liver Transplantation	2	0	
Effective, Non-Curative Therapy	23 (34%)	10 (21%)	0.006
Transarterial Chemoembolization Sorafenib	20 3	9 1	
No Therapy	23 (34%)	28 (60%)	0.12
Any Potentially Curative Therapy	22 (33%)	9 (19%)	0.006
Any Effective Therapy	45 (66%)	19 (40%)	

Survival (all patients)



At Risk:

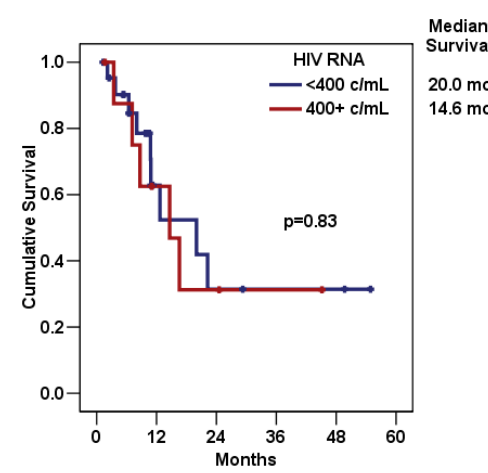
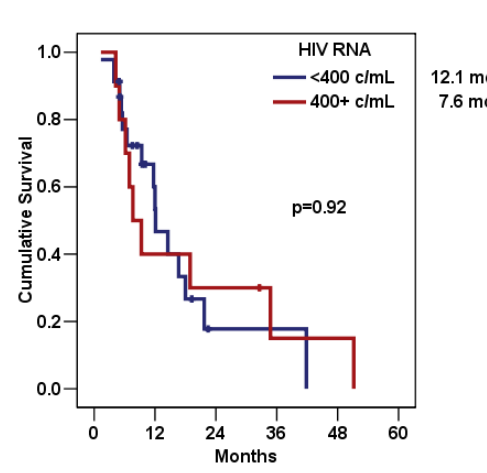
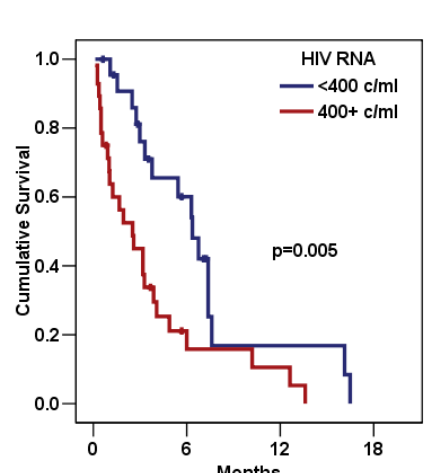
	0	12	24	36	48	60
HIV RNA <400	68	17	4	3	2	
HIV RNA 400+	47	10	5	2	1	

Survival (by HCC Therapy)

None

Effective, Non-Curative

Potentially Curative



Summary and Conclusion

- Undetectable HIV RNA (<400 copies/ml) is associated with better survival
- This phenomenon is only observed in patients receiving no HCC therapy
- Any effective HCC therapy obliterates the beneficial effect of suppressed HIV infection on survival
- In this study, there were only n=79 deaths, precluding a meaningful multi-variable Cox regression analysis
- This will be performed in the future, when the sample size has increased.

* This abstract is dedicated to Edmund J. Bini, MD, MPH (1967 – 2010) who contributed greatly to this study, and who would have been a co-author



To contribute your cases of HCC in HIV patients for further studies, please contact:
 Norbert Bräu norbert.brau@va.gov Tel: (+1) 917-701-3867
 or visit us at www.HCCinHIV.org