

Impact of Screening on Staging and Survival of Hepatocellular Carcinoma (HCC) in HIV / HBV-Coinfected Patients

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Background

- **Current recommendations for HCC screening in patients chronically infected with the hepatitis B virus (HBV) are based on a randomized controlled trial from China.** (Zhang BH, *J Cancer Res Clin Oncol* 2004)
- **No data are available on the effectiveness of HCC screening in HIV/HBV-coinfected patients.**

Methods

- **Retrospective analysis of consecutive HCC cases in HIV/HBV-coinfected patients 1992 – 2011 with data on initial presentation, identified through local tumour registries.**
- **Subjects recruited from 29 centres in 8 countries:**
 - Canada (3), United States (35), Brazil (4), United Kingdom (3), Germany (2), Spain (6), Australia (1)

N=54, all male

Patients were divided into two groups:

- Screened**

n = 30 (56%)

asymptomatic, diagnosis was made through screening procedure, i.e. abnormal screening AFP or imaging studies
- Not Screened**

n = 24 (44%)

symptomatic, diagnosis was made through work-up of symptoms, not screening results
- **Analysis of tumour characteristics, staging, therapy, and survival**
 - **Estimation of lead time of screened pts. using tumor doubling time method:**

Lead Time (T) = Tumour Doubling Time * 3log (median tumour size not screened/ screened) * 1/ log(2) (Schwartz M, *Cancer*, 1961)

Here: T = 80 days * 3log (8.7 cm/3.8 cm) * 1/ log(2) = 287 days (9.4 months)
 - **Published median HCC tumor doubling time in HIV-negative patients:** 80 days (Cucchetti A, *J Hepatol*, 1992; Okada S, *Hepatogastroenterol*1993)

Patient Characteristics

	Screened N=30	Not Screened N=24	P
Age (yrs), Mean	48.3	50.1	0.38
Male Sex	30 (100%)	24 (100%)	1.0
Alcohol abuse	8 (30%)	5 (23%)	0.59
Child-Turcotte-Pugh Score, Mean	5.90	7.54	0.002
On HIV Therapy	25 (89%)	18 (78%)	0.28
HIV Parameters			
CD4+ Cells (per mm3), Median	310	338	0.96
HIV RNA <400 Copies/mL	22 (76%)	15 (63%)	0.29

HCC Tumour Characteristics

	Screened N=30	Not Screened N=24	P
Hepatic Lesions			
Solitary Tumours	18 (60%)	6 (25%)	0.01
Multiple /Infiltrative Tumours	12 (40%)	18 (75%)	
Median Size Largest Tumour (cm), for Tumor Doubling Time	3.8	8.7	0.002
Eligibility for Liver Transplantation (Milan Criteria)			
	12 (43%)	1 (5%)	0.005
Portal Vein Thrombosis			
	5 (17%)	9 (38%)	0.083
Extrahepatic Metastases			
	2 (7%)	4 (17%)	0.245
Alpha-fetoprotein Level Median (ng/mL),	223	1236	0.071

HCC Staging

	Screened N=30	Not Screened N=24	P
BCLC Stage, n (%)			
A	13 (43%)	1 (4%)	0.001
B	8 (27%)	3 (13%)	
C } Advanced,	7 (23%)	14 (58%)	
D } Incurable	2 (7%)	6 (25%)	
Stages C+D	9 (30%)	20 (83%)	<0.001
CLIP Score, Mean	1.48	2.96	0.001

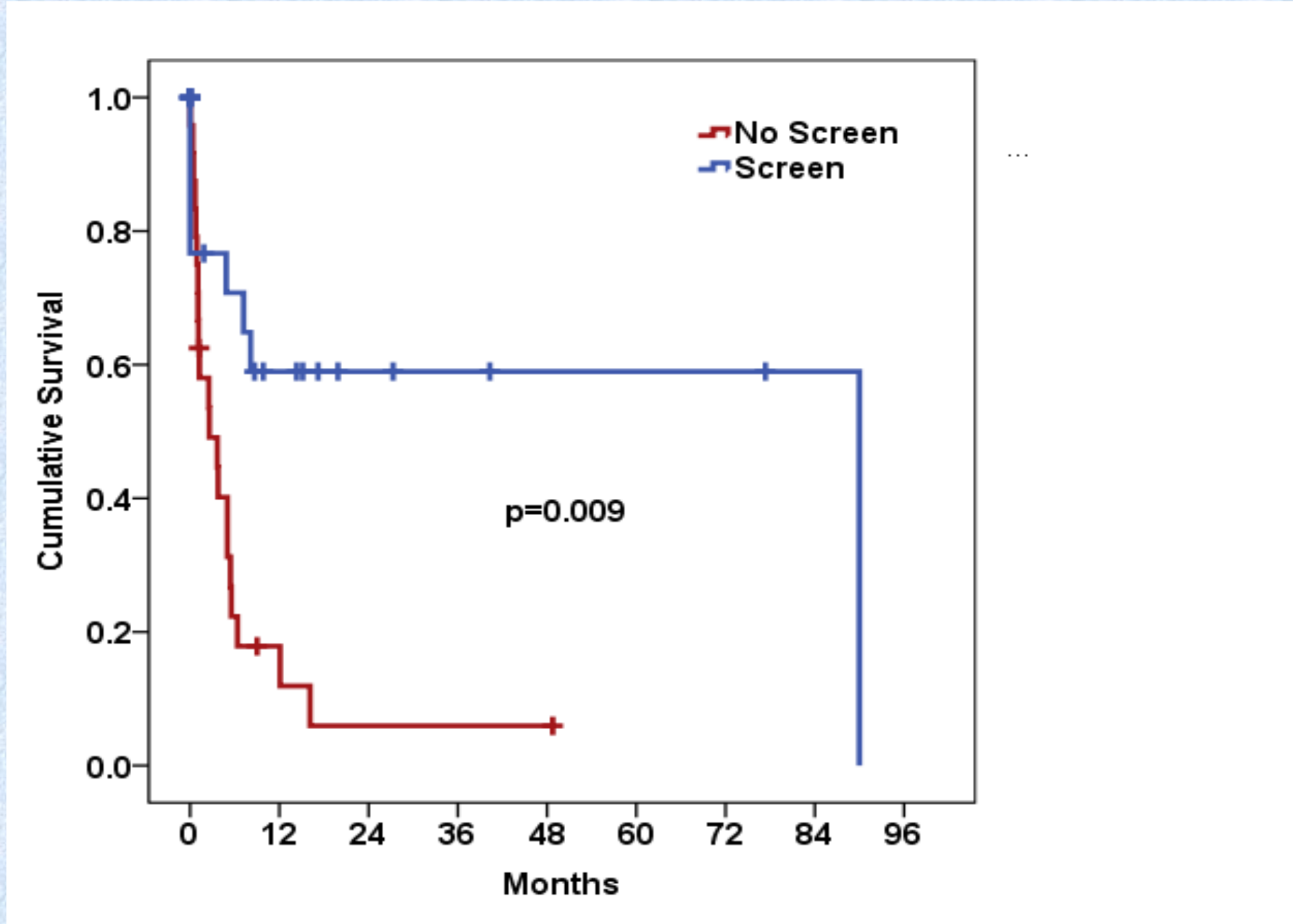
BCLC, Barcelona Clinic Liver Cancer; CLIP, Cancer of the Liver Italian Program

HCC Therapy

	Screened N=30	Not Screened N=24	P
Potentially Curative Therapy	17 (57%)	1 (4%)	<0.001
Radiofrequency Ablation	3	0	
Ethanol Injections	2	0	
Surgical Resection	9	1	
Liver Transplantation	3	0	
Effective, Non-Curative Therapy	6 (20%)	5 (21%)	
Transarterial Chemoembolization / (TACE)	5	1	
Sorafenib	1	2	
Sorafenib + TACE	0	2	
Ineffective or no Therapy	7 (23%)	18 (75%)	

Survival

adjusted for lead time of 9.4 months in screened patients



At Risk								
Screen	30	8	4	3	2	2	1	0
No Screen	24	3	1	1	1	0	0	0
	Median Survival			1-Year	2-Year	Estim. Survival		
Screen	90 months			59%	59%			
No Screen	2.6 months			18%	6%			

Multi-Variable Cox Regression Analysis

Risk Factor	Univariate Hazard Ratio for Death	Univariate P	Multi-Variable Hazard Ratio for Death	95% Confidence Interval	Multi- variable P
HIV RNA (per log10 copies/mL)	1.39	0.012	1.21	1.21-2.27	0.002
HCC Screening	0.16	<0.001	0.26	0.09-0.74	<0.001
Age at diagnosis (per year)	1.09	0.001	1.08	1.02-1.14	0.006
CTP Score (per unit)	1.28	0.002			
Effective HCC Therapy	0.20	<0.001			
AFP (per 1000 ng/mL)	1.002	0.049			
BCLC stages A&B vs. C&D	0.46	0.038			
AST / ALT ratio (per unit)	1.51	0.037			

CTP, Child-Turcotte-Pugh; AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer

Summary and Conclusion

- **Many HIV/HBV-coinfected patients with HCC were not diagnosed through screening**
- **An HCC diagnosis through screening was associated with earlier HCC stages, more HCC therapy, and independently predicted better survival**



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To contribute your cases of HCC in HIV patients

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