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The association between hepatitis B infection and malignancies in persons living with HIV: Results from the EuroSIDA study

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Introduction

Little is known about the impact of hepatitis B virus (HBV) infection on extrahepatic malignancies in PLWH. The aims of this study are to investigate

- the association between HBV and all fatal and non-fatal extrahepatic malignancies in PLWH
- to determine the association between antiretrovirals used to treat HIV and HBV, and extrahepatic malignancies

Methods

All persons aged ≥18 with known HBsAg status after the latest of 1 January 2001 and enrolment to the EuroSIDA cohort (baseline) were included; persons were categorised HBV-positive or negative using the latest HBsAg test and followed to their first extrahepatic malignancy or last visit. Poisson regression assessed the association between current HBV status and extrahepatic malignancies, anal, lung or non-Hodgkin's lymphoma (NHL).

Results

The characteristics of the 17,485 PLWH included stratified by baseline HBsAg status are shown in ***Table 1***.

Table 1 Characteristics at baseline

		All		HBV negative		HBV positive	
		N	%	N	%	N	%
All		17485	100.0	16216	92.7	1269	7.3
Gender	Male	12884	73.7	11817	72.9	1067	84.1
HIV risk	MSM	6510	37.2	5961	36.8	549	43.3
	IDU	4786	27.4	4410	27.2	376	29.6
Ethnicity	White	15004	85.8	13956	86.1	1048	82.6
Region	South	4226	24.2	3950	24.4	276	21.7
	Central	4601	26.3	4223	26.0	378	29.8
	North	3509	20.1	3235	19.9	274	21.6
	Central East	2260	12.9	2106	13.0	154	12.1
	East	2305	13.2	2157	13.3	148	11.7
Fibrosis	F4	601	3.4	518	3.2	83	6.5
		Median	IQR	Median	IQR	Median	IQR
Age	years	41	35–49	41	35–49	41	35–48
CD4	/mm³	440	284–634	442	288–638	399	251–576
Nadir CD4	/mm³	179	75–290	180	77–293	148	55–251

MSM; men having sex with men. IDU; intravenous drug user. Baseline was defined as the latest of enrolment to EuroSIDA, known HBsAg status or 1 January 2001information on aspartate transaminase (AST) and platelet counts were used to calculate the AST to platelet ratio (APRI). Hyaluronic acid was available for a small subset. The most recent fibrosis marker measured prior to baseline was used to define fibrosis stage and where >1 marker was measured priority was given to biopsy, Fibroscan, APRI followed by hyaluronic acid.

Results ctd….

- At baseline, 1269 (7.2%) were HBV positive with a median age of 41 years (interquartile range [IQR 35–49) and a median CD4 of 440/mm³ (IQR 284–634). The median follow-up was 7.4 years (IQR 4.2–13.5).
- In total, 1298 persons developed 1360 extrahepatic malignancy events during 151,766 person-years of follow-up (PYFU); incidence rate 8.55/1000 PYFU (95% confidence interval [CI] 8.09–9.92). ***Table 2*** shows the number and crude incidence rates of extrahepatic malignancies overall and stratified by HBV status prior to the malignancy.
- Those HBV DNA positive had an increased incidence of extrahepatic malignancies compared to those HBV-negative and no significant differences between those HBV DNA negative and HBV-negative (Table 2).

Table 2 Association between current HBsAg status and extrahepatic malignancies

		Events	PYFU	Rate/1000 PYFU	95% CI	Univariable IRR	Univariable 95% CI	Univariable p	Multivariable IRR	Multivariable 95% CI	Multivariable p
	HBV neg.	1199	142377	8.42	7.94–8.90	1.00			1.00		
	HBV pos.	99	9389	10.54	8.47–12.62	1.30	1.06–1.60	0.011	1.25	1.01–1.54	0.040
% FU time on TDF/TAF + XTC[1]											
0	HBV neg.	503	68394	7.35	6.71–8.00	1.00			1.00		
	HBV pos.	41	3620	11.33	7.86–14.79	1.54	1.12–2.12	0.0078	1.45	1.04–2.01	0.026
1-50	HBV neg.	367	42153	8.71	7.82–9.60	1.00			1.00		
	HBV pos.	39	3837	10.16	6.97–13.35	1.17	0.84–1.62	0.36	1.15	0.82–1.62	0.40
>50	HBV neg.	329	31831	10.34	9.22–11.45	1.00			1.00		
	HBV pos.	19	1932	9.84	5.92–15.36	0.95	0.60–1.51	0.83	0.95	0.59–1.53	0.84
HBV neg.[1]		1199	142377	8.42	7.94–8.90	1.00			1.00		
HBV pos.	HBV DNA neg.	29	3262	8.89	5.65–12.13	1.06	0.73–1.53	0.77	1.09	0.75–1.58	0.66
HBV pos.	HBV DNA pos.	40	3290	12.16	8.39–15.93	1.44	1.05–1.98	0.020	1.37	1.00–1.89	0.050

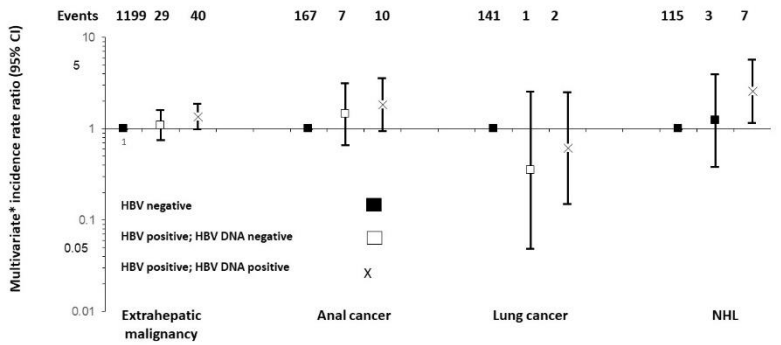
Three separate multivariable models are shown. For the comparison of those currently HBV positive and negative, the model was adjusted for gender, region of Europe, ethnicity, HIV exposure group, hepatitis C antibody status, HIV viral load, CD4 and CD4 nadir, baseline date, prior AIDS, cardiovascular disease, chronic kidney disease, hypertension, smoking status, diabetes mellitus, liver fibrosis, BMI, and age (all fixed at baseline). [1]Multivariable model was adjusted for age, HIV viral load, CD4, baseline date, smoking status and fibrosis, all fixed at baseline.

- Among those with known malignancy type, anal (188 events), lung (147 events) and NHL (131 events) were the most commonly occurring extrahepatic malignancies.
- Figure 1 shows the multivariate incidence rate ratio of each of these extrahepatic malignancies in those currently HBV positive and HBV DNA positive versus those negative.

Results ctd….

- For anal cancer, those HBV positive had marginally significantly higher rates of anal cancer when persons were HBV DNA positive compared to those HBV-negative, which was not seen for those HBV DNA negative compared to HBV negative.
- For NHL, those HBV-DNA positive had a significantly increased incidence of NHL compared to those HBV negative.

Figure 1
Adjusted incidence rate ratios of extrahepatic malignancies, anal cancer, lung cancer and non-Hodgkins lymphoma (NHL): Impact of HBV DNA



* Adjusted for baseline, age CD4, HIV viral load, fibrosis and smoking status at baseline

Limitations

- Limited information on HBV DNA and HDV and no information on other viruses, such as EBV or HPV.
- Few events in some strata and wide confidence intervals.

Conclusion:

- We found increased rates of extrahepatic malignancies in HBsAg-positive participants, which was most pronounced in those HBV-DNA positive, and for NHL. If confirmed, these results may have implications for increased cancer screening in PLWH with chronic HBV.

***Full study group and funding information available at https://chip.dk/Research/Studies/EuroSIDA/Study-group**