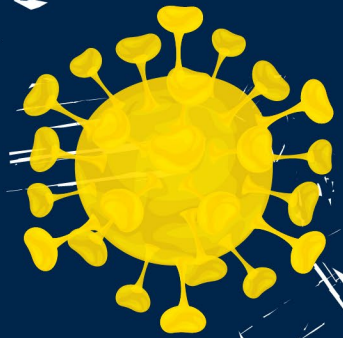
CROI ICAR AWARDS 2024

CROI Affiliated Event for
Italian Young Investigators



CHAIRS:
F. Kirchhoff
(Ulm, Germany, EU)
D. Margolis
(Chapel Hill, North Carolina, USA)

Denver, Colorado
March 4th, 2024
h 06.00 - 07.30 pm

CROI 31st CONFERENCE ON
Retroviruses and **Opportunistic Infections**
MARCH 3-6 2024 DENVER, COLORADO

ICAR 16th NATIONAL CONGRESS
Italian Conference on **AIDS** and **Antiviral Research**
JUNE 19-21 ROME, ITALY

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Transaminase elevations among patients with occult HBV infection on two-drug antiretroviral regimens

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Background

Background:

- Occult hepatitis B virus infection (OHBVI) is a common condition among people with HIV (PWH), with an estimated prevalence ranging from 10 to 45%.
- Concerns have emerged regarding the risk of HBV reactivation in PWH with OHBVI who discontinue antiretroviral agents with anti-HBV activity, especially when CD4+ cell count is low or during immunosuppressive treatment.
- Rates of hepatitis B reactivation may vary depending on the definition and the characteristics of the population, [1,2] and its clinical significance is debated.

Objective:

- To investigate whether OHBVI is associated with an increased risk of transaminase elevation after the discontinuation of tenofovir (TFV) and/or lamivudine/emtricitabine (XTC).

1 Abdullahi et al., Open Forum Infectious Diseases, 2018
2 Denyer et al., ID weeks, 2023

Methods

Patient selection:

Antiretroviral-experienced PWH from the HSG cohort were selected if:

- Switching for the first time to a dual regimen (2DR) between 2018 and 2023
- Discontinued ≥1 drug with anti-HBV activity.
- Had negative HBsAg and available HBcAb and transaminase levels before the switch.

PWH who switched to a 3TC-containing 2DR (Cohort 1) and those who had switched to a 2DR that did not include either TFV or XTC (Cohort 2) were analyzed separately.

Exposure of interest: Presence of OHBVI, defined as a reactive HBcAb serum.

Primary Outcome Measure: Time to grade ≥1 liver function test increase (LFTI), defined as AST or ALT ≥1.25x ULN

Secondary outcomes: Transaminase evolution across time after the switch, rate of LFTI across follow-up

Statistical analysis

- Time to LFTI was compared between patients with or without OBHVI, using Log-rank test and Cox regression, adjusting for the following possible confound: age, gender, HIV risk factor, HCV Ab status, hepatits B surface antibody (HBsAb), alcohol abuse, diabetes, baseline AST/ALT, and CD4 count.
- Mixed linear regression models with random intercepts and slopes were used to compare transaminase trajectories and Generalized Estimating Equation (GEE) model with a random intercept to compare rates of grade≥1 LFTI after the switch, in those with and without OHBVI.
- Multiple imputation by chained equations (MICE) was used to address missingness.

Patients' characteristics

Cohort 1: 167 patients switched to a 3TC-containing 2DR.

— 33 patients (19.8%) discontinued TDF

— 134 patients (80.2%) discontinued TAF

Cohort 2: 118 patients switched to a 2DR without any anti-HBV drugs.

— 11 patients (9.3%) discontinued TDF and FTC

— (61 patients (51.7%) discontinued TAF and FTC.

— 46 patients (39%) discontinued only 3TC.

	Cohort 1 (N=167)			Cohort 2 (N=118)		
Parameter	**No OHBVI (108)**	**OHBVI (59)**	**p**	**No OHBVI (78)**	**OHBVI (40)**	**p**
Male gender (n, %)	85 (78.7)	50 (84.8)	0.343	53 (68)	29 (72.5)	0.611
Age (mean; SD)	45.6 (11.1)	54.6 (11.9)	<0.001	48.7 (12.4)	56 (8.5)	0.001
Born in Italy (n, %)	96 (88.9)	46 (78)	0.059	64 (82.1)	34 (85)	0.686
Risk Factors (n, %)✤			0.019			0.005
Heterosexual	53 (53.5)	22 (44)		40 (62.5)	15 (42.8)	
MSM	44 (44.4)	22 (44)		22 (34.4)	10 (28.6)	
Intravenous drug use	1 (1.01)	6 (12)		2 (3.1)	7 (20)	
Other	1 (1.01)	0		0	3 (8.6)	
HCV Ab positive (n, %)▲	10 (9.3)	10 (17.5)	0.037	6 (8)	10 (26.3)	0.008
Alcohol abuse (n, %)*	13 (14.1)	11 (22.9)	0.349	13 (20.6)	6 (15.8)	0.089
Diabetes (n, %)	11 (10.2)	8 (13.6)	0.512	5 (6.4)	6 (15)	0.180
BMI (median; IQR)✦	24.6 (22.2-27.9)	25.9 (23.5-29.1)	0.099	25 (21.3-27.7)	26.1 (21.5-28.1)	0.611
Grade≥1 LFTI within 2 years (n, %)	15 (13.9)	5 (8.5)	0.455	8 (10.3)	5 (12.5)	0.760
Calendar year (n, %)			0.058			0.185
2018-2019	2 (1.9)	6 (10.2)		6 (7.7)	5 (12.5)	
2020-2021	64 (59.3)	34 (57.6)		23 (29.5)	17 (42.5)	
2022-2023	42 (38.9)	19 (32.2)		49 (62.8)	18 (45)	
Baseline CD4 count (median cells/mm3; IQR)	781 (562-970)	764 (429-938)	0.389	808 (514-1120)	721 (367-1055)	0.264
Type of therapy (n; %)	3TC+DTG (108; 100)	3TC+DTG (59; 100)		RPV + DTG (29; 37.2%) RPV + CAB (38; 48.7) Other (11; 14.1)	RPV + DTG (19; 47.5) RPV + CAB (13; 32.5) Other (8; 20)	

✤ Risk factor: N=149 (Cohort 1) and N=99 (Cohort 2); ▲ HCV Ab status: N=165 (Cohort 1) and N=115 (Cohort 2); * Alcohol abuse: N=140 (Cohort 1) and N=101 (Cohort 2); ✦ BMI: N=161 (Cohort 1) and N=114 (Cohort 2)

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Risk of grade ≥1 transaminase elevation

Cohort 1

— 20 patients (12%) developed grade ≥1 LFTI.

— Incidence of grade ≥1 LFTI:

- With OHBVI: 4.59 per 100 person-years.
- Without OHBVI: 7.47 per 100 person-years.

— No significant difference was observed in time to event according to OHBVI (log-rank test P=0.259).

— Using Cox regression, no association was found between OHBVI and risk of LFTI (HR 0.56; 95%CI 0.2-1.5; p=0.266), also after adjusting for possible confounders.

Cohort 2

— 13 patients (11%) developed grade ≥1 LFTI.

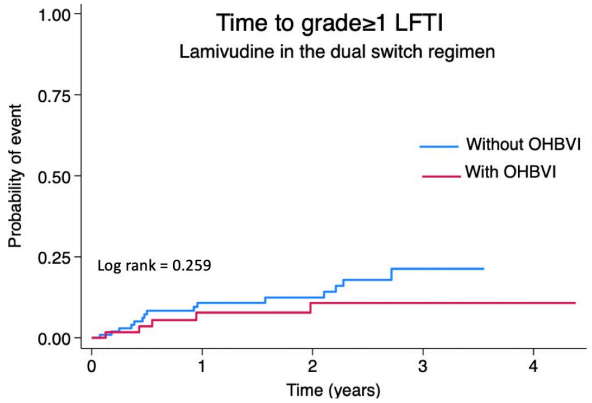
— Incidence of grade ≥1 LFTI:

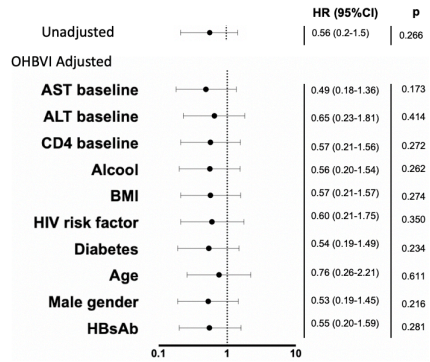
- With OHBVI: 8.04 per 100 patient-years.
- Without OHBVI: 8.68 per 100 patient-years.

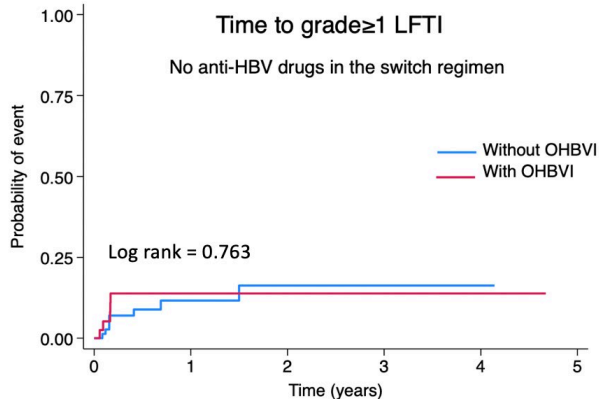
— No significant difference was found in time to event based on OHBVI (log-rank test P=0.763).

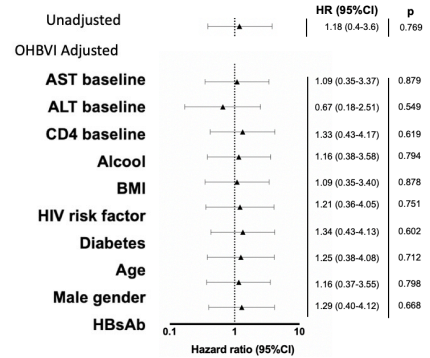
— No association between OHBVI and risk of LFTI (HR 1.18; 95%CI 0.4-3.6; p=0.769). No change in association after adjustment.

No instances of grade ≥3 LFTI were observed in both cohorts.









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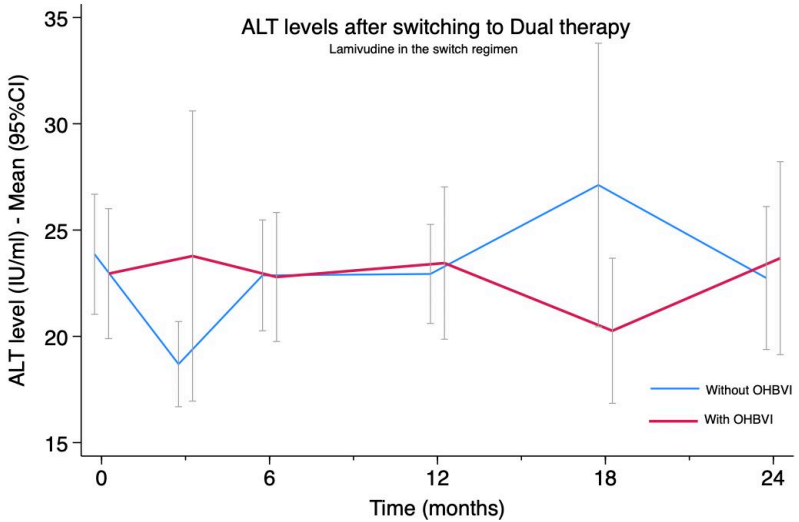
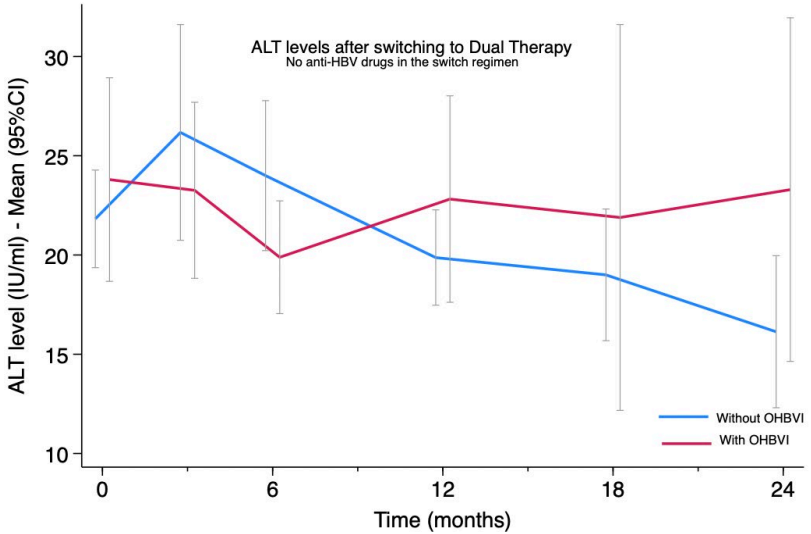
Transaminase dynamics after regimen switch

Mixed-effects model



— No significant difference in ALT levels in Cohort 1 (adjusted coeff 1.64; 95% CI -0.46 to 3.73)



— OHBVI associated with significantly lower mean ALT levels in Cohort 2 (adjusted coeff -2.57; 95% CI -4.99 to -0.13).

Limitations

—The observational nature of the analysis does not allow to exclude residual confounding or selection bias.

—The analysis focused solely on transaminase elevation, as a proxy of clinically relevant possible HBV reactivation.

—Relatively short term observation of transaminase elevation may not reflect long term consequences of a possible reduced control of HBV replication in hepatocytes.

Conclusions

—Occult HBV infection was not significantly associated with transaminase elevation in a cohort of PWH who discontinued anti-HBV drugs and switched to a dual regimen.

—This (lack of) effect was similar in those discontinuing TFV but maintaining XTC and in those switching to a regimen without neither TFV or XTC.

—This real-life observation offers reassurance regarding the safety of transitioning to dual therapy in patients with occult HBV infection.

Thank you for your attention!

Acknowlegedments
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