Abstract 566

Tenofovir and the Incidence of Hepatocellular Carcinoma in HIV/HBV-coinfected Persons

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BACKGROUND

- Hepatocellular carcinoma (HCC) is a leading cause of death in HIV/hepatitis B virus (HBV)-coinfected patients.
- Current screening recommendations are based on incidence estimates in untreated HBV-infected patients and might be inadequate for HIV/HBV-coinfected individuals on tenofovir (TDF)-based antiretroviral therapy (ART).
- We explored the impact of TDF on HCC incidence in a large collaboration of HIV cohorts including the Swiss HIV Cohort Study, Athena Observational Cohort Study, EuroSIDA and ANRS CO3 Aquitaine Cohort.

OBJECTIVES

- To evaluate the incidence of HCC in HIV/HBV-coinfected individuals from a large European HIV cohort collaboration and assess related risk factors.
- To determine the impact of TDF on the incidence of HCC in sub-populations categorized by age groups, sex and liver cirrhosis.
- To explore the relationship between time off TDF and the incidence threshold for HCC screening (2 cases per 1,000 person-years, Bruix et al. *Hepatology 2011*) in different sub-populations.

METHODS

Study population and definitions

- The Swiss HIV Cohort Study (SHCS), Athena Observational Cohort Study, EuroSIDA and ANRS CO3 Aquitaine Cohort are observational HIV cohorts with systematic screening of HBV infection at inclusion or initiation of ART.
- We included all HBsAg-positive adults with complete ART history available.
- Follow-up time was measured from date of inclusion to database closure, date of HCC diagnosis, death or loss to follow-up, whichever occurred first.
- We defined the cumulative time off TDF (either without any HBV-active ART or including only lamivudine) as the main HBV therapy exposure variable. A binary variable was created according to the median follow-up (FUP) time on TDF (4 years).
- Liver cirrhosis was defined according to histology or as an AST-to-platelet ratio index (APRI) >2.0 at any time-point during follow-up.

Statistical analyses

- HCC incidence was described for the full population and compared between sub-groups according to the main demographic and clinical characteristics.
- We evaluated the association between cumulative time off TDF and the incidence of HCC using multivariable Poisson regression, adjusted for age, sex, time-updated CD4 cell counts, ethnicity, hepatitis C virus (HCV) infection and liver cirrhosis.

RESULTS

Table 1: Demographic and clinical characteristics of participants at ART start

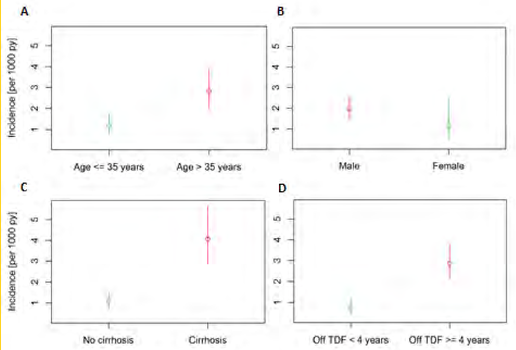
Demographic characteristics	N=3.599
Median age at baseline (IQR)	36 (31-44)
Female sex (%)	590 (16.4)
Caucasian (%)	2,878 (80.0)
HIV transmission group (%)	
MSM	1,803 (52.7)
IDU	587 (17.1)
Other	1,034 (30.2)
Cohort (%)	
Aquitaine	610 (17.0)
Athena	1,353 (37.6)
EuroSIDA	829 (23.0)
SHCS	807 (22.4)

Clinical characteristics	N=3.599
Median baseline CD4 count (IQR)	323 (180-500)
Anti-HCV positive (%)	836 (23.2)
Cirrhosis (%)	830 (23.1)
Best HBV therapy (%)	
None	376 (10.4)
XTC	655 (18.2)
TDF	2,568 (71.4)

IQR: interquartile range, MSM: men who have sex with men, IDU: injection drug use, SHCS: Swiss HIV Cohort Study, HCV: hepatitis C virus, HBV: hepatitis B virus, XTC: lamivudine or emtricitabine, TDF: tenofovir

- Overall, 40.3% of the cumulative FUP time was spent on TDF, 30.5% on XTC (lamivudine or emtricitabine) only and 29.2% on ART without HBV activity.
- Over 32,673 patient-years (py), 60 individuals (1.7%) developed an HCC, resulting in an overall incidence of 1.84 per 1,000 py (95% confidence interval [CI] 1.40-2.36).

Figure 1: Incidence of HCC according to age (A), sex (B), cirrhosis (C) and TDF treatment (D)



- The incidence of HCC was highest in patients with >4 years of FUP off TDF (incidence rate ratio [IRR] 4.04, 95% CI 2.10-7.77, Figure 1).
- In adjusted analyses, there was an increase in incidence of HCC per year off TDF (adjusted IRR [aIRR] 1.13, 95% CI 1.08-1.19), and patients with cirrhosis (aIRR 3.56, 95% CI 2.09-6.07) or aged >35 years (aIRR 3.56, 95% CI 2.09-6.07) remained at higher risk of HCC.
- During TDF therapy, the risk of HCC remained stable per additional year of FUP (aIRR 0.96, 95% CI 0.87-1.07, Figure 2).
- Time spent without TDF had a strong impact on HCC incidence, especially in older patients and in the presence of cirrhosis (Figure 3).

Figure 2: Effect of cumulative time on treatment regimens on HCC incidence
(shaded areas: 95% confidence intervals)

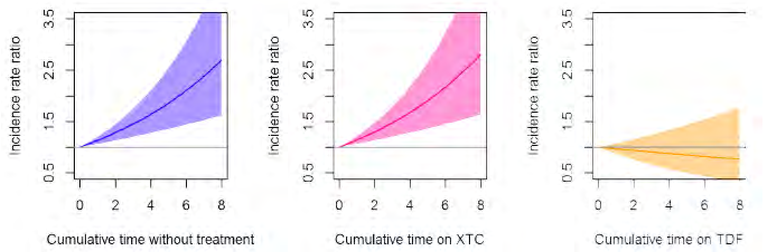
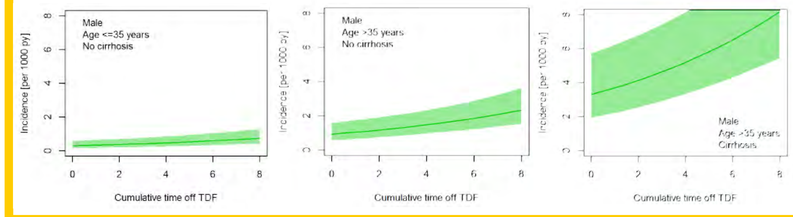


Figure 3: Incidence of HCC for sub-populations, by time off TDF (estimates for men only)



CONCLUSIONS

- Approximately 2% of patients developed an HCC over a median follow-up of 8.4 years.
- HCC incidence increased with the length of FUP off TDF and was three times higher in cirrhotic compared to non-cirrhotic patients.
- HCC screening strategies in HIV/HBV-coinfected individuals on TDF need to be tailored to the individual risk profile and time spent without TDF therapy.

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