# Novel Biomarkers as Determinants of HBsAg Loss in Persons with HIV/HBV on Tenofovir

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## BACKGROUND

- Hepatitis B surface antigen (HBsAg) loss is associated with improved clinical outcomes in persons with hepatitis B virus (HBV) infection.
- The association between novel biomarkers, including circulating HBV RNA and hepatitis B core-related antigen (HBcrAg), and HBsAg loss has not been studied in persons with HIV/HBV.

## OBJECTIVE

- To describe qHBsAg trends and assess predictors of HBsAg loss in Euro-B, a multi-cohort collaboration including participants from the Swiss HIV Cohort Study, EuroSIDA and the French HIV/HBV Cohort.

## METHODS

- We included participants with a quantitative HBsAg (qHBsAg) ≥0.05 IU/ml at tenofovir start and at least one qHBsAg measurement after >180 days of follow-up on tenofovir-containing antiretroviral therapy (ART).
- We assessed rates of HBsAg loss, defined as qHBsAg <0.05 IU/ml, and evaluated its predictors using multivariable logistic regression.

**TABLE 1: Characteristics of participants, stratified by ART exposure status at start of tenofovir therapy**

| | ART-naïve | ART-experienced |
|---|---|---|
| | N = 259 | N = 340 |
| Female sex at birth | 55/259 (21.2%) | 55/340 (16.2%) |
| Median age [years] | 40 (34-46) | 41 (36-47) |
| Median follow-up duration [years] | 8.2 (3.7-12.3) | 8.3 (3.5-14.2) |
| Median BMI [kg/m$^2$] | 23.4 (21.2-25.7) | 22.5 (20.7-25.0) |
| CD4+ T-cell count [cells/µl] | 308 (181-438) | 410 (271-587) |
| HIV viral load <50 copies/ml | 58/259 (22.4%) | 242/340 (71.2%) |
| Median qHBsAg [$\log_{10}$ IU/ml] | 3.9 (2.9-4.5) | 3.9 (3.1-4.7) |
| qHBsAg ≤1000 IU/ml | 68/259 (26.3%) | 75/340 (22.1%) |
| Median HBV DNA [$\log_{10}$ IU/ml] | 3.5 (1.7-7.1) | 2.9 (0.0-6.6) |
| HBV DNA <20 IU/ml | 56/259 (21.6%) | 121/337 (35.9%) |
| Median HBcrAg [$\log_{10}$ U/ml] | 5.4 (3.2-8.0) | 6.0 (3.1-8.0) |
| HBcrAg <3 $\log_{10}$ U/ml | 52/250 (20.8%) | 74/337 (22.0%) |
| Median HBV RNA [$\log_{10}$ copies/ml] | 1.5 (0.0-5.9) | 2.2 (0.0-5.8) |
| HBV RNA <10 copies/ml | 113/239 (47.3%) | 122/255 (47.8%) |
| HBeAg positive | 79/177 (44.6%) | 131/222 (59.0%) |

*Data are presented as median (IQR) for continuous measures, and n/total (%) for categorical measures.*

## KEY POINTS:

- 18% of persons with HIV/HBV experienced HBsAg loss during a median follow-up of 8 years.
- A low baseline qHBsAg level at tenofovir start was the strongest predictor of HBsAg loss.
- High HBcrAg levels in HBeAg-negative individuals and low HBV RNA levels in HBeAg-positive individuals were associated with HBsAg loss.

## RESULTS: Rates of HBsAg loss

- qHBsAg <0.05 IU/ml was observed in 66/510 (12.9%) participants after 2 years of tenofovir therapy and in 109/599 (18.2%) at the last follow-up visit after a median of 8.2 years (interquartile range [IQR] 3.6-13.1, Figure 1).

**FIGURE 1: Quantitative HBsAg levels during follow-up.**

Only the 455 (76%) participants with 3 available qHBsAg measurements are shown.

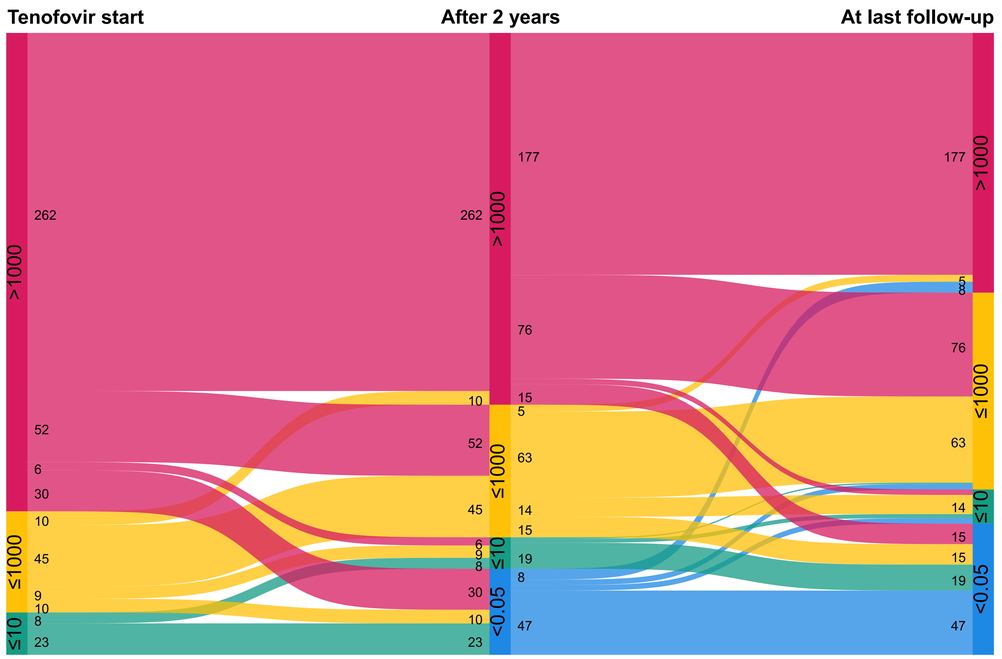
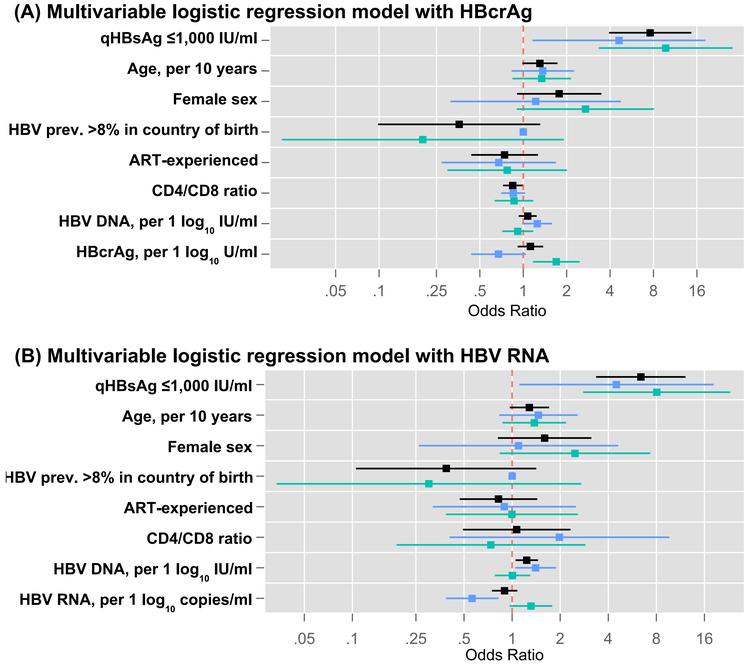



**FIGURE 2: Predictors of HBsAg loss.**




*Main analyses included 466 participants (model with HBcrAg) and 387 participants (model with HBV RNA). In HBeAg-positive individuals, 178 participants in the model with HBcrAg and 126 in the model with HBV RNA were included. In HBeAg-negative participants 177 participants in the model with HBcrAg and 156 in the model with HBV RNA were included.*

## CONCLUSIONS

- We found high rates of HBsAg loss among persons with HIV/HBV, with the majority of events occurring during the first two years of tenofovir-containing ART.
- Only low baseline qHBsAg levels were consistently associated with HBsAg loss in both multivariable logistic regression models.
- In HBeAg-positive participants, lower qHBsAg levels, lower HBV RNA levels, and higher HBV DNA levels, but not HBcrAg were associated with HBsAg loss. In HBeAg-negative participants, lower qHBsAg and higher HBcrAg, but not HBV RNA were associated with HBsAg loss.

## AUTHOR CONTACT INFORMATION

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**Funding:** This study has been financed within the framework of the Swiss HIV Cohort Study, supported by the Swiss National Science Foundation (grant #201369), by SHCS project #809 and by the SHCS research foundation. The data are gathered by the Five Swiss University Hospitals, two Cantonal Hospitals, 15 affiliated hospitals and 36 private physicians (listed in http://www.shcs.ch/180-health-care-providers). EuroSIDA has received funding from ViiV Healthcare LLC, GlaxoSmithKline R&D Limited, Janssen Scientific Affairs, Janssen R&D, Bristol-Myers Squibb Company, Merck Sharp and Dohme Corp., Gilead Sciences and the European Union's Seventh Framework Program for research, technological development and demonstration under EuroCoord grant agreement #260694). The study is also supported by a grant (grant #DNRF126) from the Danish National Research Foundation and by the International Cohort Consortium of Infectious Disease (RESPOND). This work is supported by the French National Research Agency Investissements d'Avenir program (CirB-RNA project – ANR-17-RHUS-0003) to FZ and ML and received funding through an investigator-initiated trial grant from Gilead Sciences (CO-SW-985-5602) and from the NEAT-ID Foundation. LB was supported by the «Young Talents in Clinical Research» program of the Swiss Academy of Medical Sciences and G. and J. Bangerter-Rhyner Foundation (grant YTCR 13/19). GW was supported by a Professorship from the Swiss National Science Foundation (PP00P3_211025).