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Incidence and Risk Factors for Incomplete HBV DNA Suppression in HIV/HBV-Coinfected Patients Initiating Tenofovir-Based Therapy

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Abstract

Suppression of hepatitis B virus (HBV) DNA to undetectable levels is an important goal for HIV/HBV-coinfected patients receiving anti-HBV-active antiretroviral therapy (ART), and current guidelines recommend that this outcome should be reached by one year of treatment. However, the proportion of patients that fail to achieve an undetectable HBV DNA at this time point and its determinants remain unknown in clinical practice. The objective of this study was to determine the incidence and risk factors for incomplete HBV suppression following one year of tenofovir-based ART. We performed a cohort study among tenofovir-treated HIV/HBV-coinfected patients. Patients had HBV viremia, initiated tenofovir-based ART, and had HBV DNA measured at one

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year of therapy. The primary outcome was incomplete HBV suppression (HBV DNA ≥ 2.6 log IU/mL) at one year. Logistic regression determined odds ratio (ORs) of incomplete HBV suppression for risk factors of interest. Among 133 patients, 54% (95% CI, 46%–63%) had incomplete HBV suppression at one year. Incomplete suppression was associated with higher baseline HBV DNA (OR, 1.46 per log IU/mL increase; 95% CI, 1.1–1.94) and detectable HIV viremia at one year (OR, 2.52; 95% CI, 1.19–5.32). Among 66 patients with suppressed HIV RNA at one year, 28 (42%) failed to achieve an undetectable HBV DNA. Failure to suppress HBV DNA by one year occurred in a sizeable proportion of tenofovir-treated HIV/HBV-coinfected patients. Higher HBV DNA and detectable HIV viremia were risk factors for incomplete HBV suppression.

Keywords

hepatitis B virus; HIV/hepatitis B virus coinfection; HIV; tenofovir; lamivudine

INTRODUCTION

Approximately 6–14% of HIV-infected individuals are coinfecting with chronic hepatitis B virus (HBV) infection [1]. HIV/HBV-coinfected patients are at higher risk for developing complications of HBV-associated liver disease (e.g., cirrhosis, hepatocellular carcinoma) than those with chronic HBV monoinfection [2, 3]. In the developed world, HBV-associated chronic liver disease remains an important cause of non-AIDS morbidity among HIV-infected patients [4].

Current HIV management guidelines consider chronic HBV coinfection to be an indication to initiate antiretroviral therapy (ART), regardless of CD4 T-lymphocyte count and HBV DNA level [5, 6]. Further, since elevated HBV DNA levels are associated with an increased risk of developing cirrhosis [7], hepatic decompensation [8], and hepatocellular carcinoma [9] and may contribute to ART-related hepatotoxicity [10], HBV DNA suppression to an undetectable level is an important therapeutic goal for HIV/HBV-coinfected patients [11–16].

To achieve this goal, initiation of anti-HBV-active ART is recommended among HIV/HBV-coinfected persons, preferably with tenofovir plus either emtricitabine or lamivudine [5, 17–19]. However, HBV therapy with oral nucleos(t)ide analogues is not generally curative, and HBV viremia tends to recur upon withdrawal of antiviral therapy [8, 20]. Therefore, oral HBV treatment is typically maintained indefinitely in HIV-infected patients to provide persistent HBV control [17, 18]. Guidelines for the management of chronic HBV in HIV-infected patients recommend that HBV DNA be fully suppressed by 12 months of tenofovir-based therapy [12, 18, 21]. However, few studies have specifically examined incomplete HBV DNA suppression among HIV/chronic HBV-coinfected patients. As a result, the proportion of tenofovir-treated HIV/HBV patients that fails to suppress HBV DNA and determinants of failure remain unclear in real-world clinical settings. These results are important because they may define potential underlying mechanisms for incomplete HBV suppression among HIV/HBV-coinfected patients and can identify patients who might benefit from closer monitoring of HBV DNA levels, risk factor modification, and possibly intensification of HBV treatment [22]. Our objective was to determine the cumulative incidence and risk factors for incomplete HBV DNA suppression at one year of tenofovir-based ART among HIV/HBV-coinfected patients.

METHODS

Study Design and Patients

We performed a retrospective cohort study among tenofovir-treated HIV/HBV-coinfected patients cared for in HIV clinics at eight centers (five in Philadelphia, PA: Hospital of the University of Pennsylvania, Penn Presbyterian Medical Center, Pennsylvania Hospital, Philadelphia Veterans Affairs Medical Center [PVAMC], and Jonathan Lax Center/Philadelphia Field Initiating Group for HIV Trials [JLC/FIGHT]; two in Atlanta, GA: Emory University Hospital Midtown and Grady Memorial Hospital; and one in Camden, NJ: Cooper University Hospital). The study was approved by the Institutional Review Board of each center.

Patients were eligible for inclusion if they had: 1) HIV infection (HIV antibody and/or RNA positive), 2) initiated tenofovir-based ART between 2001 and 2012, 3) had detectable HBV DNA within one year prior to the start of tenofovir or while on treatment, and 4) had an HBV DNA result recorded at one year (defined as 12 months $\pm$ 5 months) after tenofovir initiation. Patients were excluded if they had an undetectable HBV DNA at the start of tenofovir, had no HBV DNA result within this 7–17 month period, or were no longer receiving tenofovir at the one-year time point at which HBV DNA was determined. At each clinic, patients were identified based on tenofovir prescriptions and detectable HBV DNA. All eligible patients were included.

HBV DNA Assays

HBV DNA was determined using the assay available at each site (Philadelphia: Hybrid Capture II Assay [Digene, Gaithersburg, MD; lower limit of detection 4.79 log IU/mL]; Versant HBV DNA 3.0 Assay [Bayer, Berkeley, CA; lower limit of detection: 2.6 log IU]; Cobas Amplicor HBV Monitor test [Roche Diagnostics, Branchburg, NJ; lower limit of detection: 40 IU/mL]; COBAS AmpliPrep/TaqMan HBV Real-Time Polymerase Chain Reaction v2.0 qualitative test [Roche Diagnostics, Branchburg, NJ; lower limit of detection: 20 IU/mL]; Atlanta and Camden: Cobas Amplicor HBV Monitor test). HBV DNA results reported in copies/mL were converted to IU/mL (5.8 copies/IU for PCR-based assays; 5.6 copies/IU for branched-chain assays; 2.3 copies/IU for signal amplification assays) [23, 24].

Main Outcome Measure

The primary outcome was incomplete HBV DNA suppression, defined as an HBV DNA result ≥ 2.6 log IU/mL at one year (i.e., 12 months $\pm$ 5 months) after initiation of tenofovir-based ART. If multiple HBV DNA results were available within this period, the result closest to 12 months was selected.

We chose incomplete HBV DNA suppression as the main endpoint because detectable and increasing HBV DNA levels are associated with higher risks of cirrhosis, hepatocellular carcinoma, and antiviral resistance [7, 9, 25, 26]. The cut-off point of 2.6 log IU/mL was chosen because this was the most clinically relevant lower limit of detection of the most commonly used quantitative assay available across the sites. The rationale for evaluating outcomes at one year was based on recommendations from HIV/HBV treatment guidelines [12, 18, 21] and clinical trials [27] that suggest that HBV suppression should be achieved by one year of antiviral therapy.

Data Collection

Baseline data were collected from medical records from dates closest to but within 12 months prior to the start of tenofovir and included: age; sex; race; site; body weight; quantitative HBV DNA level (in IU/mL); hepatitis B surface antigen (HBsAg); hepatitis B e

antigen (HBeAg); hepatitis B e antibody (anti-HBe); hepatitis B surface antibody (anti-HBs); hepatitis C virus (HCV) RNA; presence of hepatic decompensation (defined by a recorded diagnosis of ascites, spontaneous bacterial peritonitis, variceal hemorrhage, and/or hepatic encephalopathy); duration of HIV diagnosis; antiretroviral regimen; previous receipt of lamivudine therapy; CD4 cell count; and HIV RNA level (all sites: Versant HIV-1 RNA 3.0 Assay; Bayer, Berkeley, CA; lower limit of detection: 75 copies/mL).

During the initial 17 months on tenofovir-based ART, medical records were reviewed to ascertain continued tenofovir treatment and decompensation events. All HBsAg, HBeAg, anti-HBe, anti-HBs, HBV DNA, and HIV RNA results during this 17-month period were collected. The HIV RNA result nearest to the corresponding HBV DNA result was also collected.

Statistical Analysis

The baseline period was defined as the 12 months prior to the start of tenofovir. Follow-up began on the date of tenofovir initiation. Follow-up continued until the one-year HBV DNA measurement for the primary analysis evaluating the incidence of incomplete suppression at one year. However, in a secondary analysis evaluating the time to achieving an HBV DNA level below 2.6 log IU/mL (described below), follow-up continued until the last HBV DNA result recorded prior to 17 months after tenofovir initiation.

Since some baseline variables had missing data, removing patients with missing observations from analyses leads to a biased sampling of the study population. Thus, we used multiple imputation to decrease the likelihood of missing data affecting the validity of our results [28]. Final estimates in the multivariable model were determined from ten imputed datasets [29].

The incidence of incomplete HBV DNA suppression at one year was determined for the overall cohort and by previous receipt of lamivudine. Two patients with detectable HBV DNA at one year by qualitative assay were classified as having incomplete HBV DNA suppression in the primary analysis. Further, since 10/18 (56%) patients who had an HBV DNA result at one year determined via the Hybrid Capture II assay were undetectable (i.e., HBV DNA <4.78 log IU/mL), it was unknown if these patients actually had achieved suppressed HBV DNA <2.6 log IU/mL. In the primary analysis, multiple imputation was used to estimate incomplete HBV DNA suppression status at one year for these 10 patients. We assessed the robustness of the results of the primary analysis by conducting several sensitivity analyses. First, we performed analyses to examine the incidence of incomplete HBV suppression in which we classified all 10 patients with an undetectable HBV DNA determined via the Hybrid Capture II assay as either having: 1) complete HBV DNA suppression, or 2) incomplete suppression, in separate analyses. Second, we determined the incidence of incomplete HBV suppression among patients who had an HBV DNA level measured within a narrower period of 9–15 months of tenofovir-based therapy (i.e., 12 months $\pm$ 3 months). Finally, we calculated the incidence after excluding patients who had: 1) low-level baseline HBV DNA (<2.6 log IU/mL) on a sensitive assay, and 2) only a positive qualitative HBV DNA recorded at one year.

Differences by incomplete HBV suppression status were assessed using Chi-square tests for categorical data and Wilcoxon rank-sum tests for continuous data. Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of incomplete HBV suppression associated with baseline risk factors of interest. Hypothesized risk factors included younger age, lower CD4 cell count, higher HIV RNA level, and higher HBV DNA level. Potential confounders evaluated included sex, race, weight, HCV coinfection, prior lamivudine therapy, and antiretroviral class.

We also conducted several secondary analyses. We used detectable HIV viremia (HIV RNA ≥ 75 copies/mL) at one year as a surrogate of antiviral non-adherence and assessed its relation with incomplete HBV suppression [30]. Then, among patients with undetectable HIV viremia (HIV RNA <75 copies/mL) at one year, we determined the frequency and characteristics associated with incomplete HBV suppression. Next, to explore differences between responders and non-responders to tenofovir-based therapy, we compared the characteristics of patients who had a ≥ 2 log IU/mL decrease in HBV DNA from baseline to those who did not. Finally, we constructed Kaplan-Meier curves and compared the time to achieving an HBV DNA level below 2.6 log IU/mL by each of the risk factors of interest using log-rank tests. This analysis utilized all HBV DNA results measured over the initial 17 months on tenofovir-based ART.

A sample size of 133 patients provided 80% power to detect a 20% difference in incomplete HBV suppression between those with and without each hypothesized risk factor. Data were analyzed using Stata 11.0 (Stata Corporation, College Station, Tx).

RESULTS

Patient Characteristics

Across the sites, 155 tenofovir-treated HIV/HBV viremic patients were identified between 2001 and 2012. Twenty-one had HBV DNA results determined outside the 7–17 month follow up window period, and one prematurely discontinued tenofovir within 6 months because of the development of renal insufficiency. Therefore, after excluding these 22 patients, 133 HIV/HBV-coinfected patients were included in the final study sample.

The baseline cohort characteristics are summarized in Table 1. The sample was predominantly male, of black race, and had a median age of 43 years. The median baseline HBV DNA level was 8.0 log IU/mL. Sixty-two percent were HBeAg-positive, and 17% were coinfecting with chronic HCV. No patient had hepatic decompensation diagnosed either at baseline or during follow-up.

Incidence of Incomplete HBV DNA Suppression

The median time to viral suppression in the overall cohort was 12 months (IQR, 10–14). Overall, incomplete HBV DNA suppression occurred in 54% (95% CI, 46%–63%) of patients. The median HBV DNA level for patients who had incompletely suppressed HBV DNA at one year was 5.0 log IU/mL. Table 2 reports the results of the sensitivity analyses, which demonstrate incidences of incomplete suppression similar to the primary analysis.

The incidence of incomplete HBV suppression among lamivudine-naïve patients ($n=31$) was 45% (95% CI, 26%–64%). Incomplete HBV suppression occurred more frequently in patients who previously received lamivudine than those who were lamivudine-naïve (57% vs. 45%), but this difference was not statistically significant ($p=0.25$).

There was no difference in the median time from start of follow-up to time of HBV DNA measurement between those who did and not achieve HBV DNA suppression (12 [IQR, 10–13] versus 11 [IQR, 10–14] months), nor was there an association between duration of tenofovir therapy within the 7–17 month period and incomplete suppression (OR, 1.03; 95% CI, 0.90–1.17).

Risk Factors for Incomplete HBV DNA Suppression

Patients with incomplete HBV DNA suppression at one year were younger, had higher baseline HBV DNA levels, and more commonly received emtricitabine or lamivudine in

combination with tenofovir (Table 1; Figure 1). There were no statistically significant differences in baseline CD4 count or baseline HIV RNA levels between those with and without HBV suppression (Figure 1). The frequency of previous lamivudine use was also similar between the groups.

After controlling for all other hypothesized risk factors as well as HCV coinfection and prior lamivudine use, higher baseline HBV DNA level (OR, 1.46 per log IU/mL increase; 95% CI, 1.1–1.94) remained significantly associated with incomplete HBV suppression. Patients with a baseline HBV DNA level >7.7 log IU/mL (the cohort median baseline level) had a substantially higher odds of incomplete suppression than those at or below this baseline HBV DNA level (adjusted OR, 3.21; 95% CI, 1.39–7.43). Younger age (OR, 1.30 per 5 year decrease; 95% CI, 0.96–1.75), higher HIV RNA level (OR, 0.89 per log IU/mL increase; 95% CI, 0.57–1.39), and lower CD4 count (OR, 1.20 per 100 cells/mm³ decrease; 95% CI, 0.97–1.49) were not associated with incomplete suppression. Black race was also not associated with incomplete suppression. Results of the primary analysis were unchanged when type of tenofovir regimen (i.e., tenofovir plus emtricitabine or lamivudine versus tenofovir plus another nucleoside analogue), treatment start date, or time on tenofovir therapy were included in the model.

In a Kaplan-Meier analysis, age >43 years ($p<0.03$) and baseline HBV DNA <8 log IU/mL ($p<0.001$) were associated with a shorter time to achieving an HBV DNA level below 2.6 log IU/mL (Figure 2).

At one year of tenofovir therapy, incomplete HBV suppression was more common among patients with detectable HIV viremia than those with suppressed HIV RNA (64% versus 42%; OR, 2.52; 95% CI, 1.19–5.32). However, when detectable HIV viremia at one year was included in the multivariable model evaluating risk factors for incomplete HBV suppression, the point estimates for odds ratios generated in prior models did not change significantly.

Among the 66 patients with undetectable HIV RNA at one year and presumed high levels of antiretroviral adherence, 28 (42%; 95% CI, 30%–55%) had incomplete HBV suppression (median HBV DNA at one year, 3.4 [IQR, 1.6–6.6] log IU/mL). Patients with undetectable HIV RNA at one year and incomplete HBV suppression had lower median age (43 versus 47 years; $p=0.04$) and higher median baseline HBV DNA levels (8.4 versus 7.2 log IU/mL; $p=0.03$) than patients with undetectable HIV RNA and suppressed HBV DNA at one year, but there was no difference in baseline CD4 counts between these groups (354 versus 306; $p=0.5$).

Change in HBV DNA and Response to Tenofovir-Based Therapy

The median change in HBV DNA level from baseline was -4.1 (IQR, -2.3 to -5.4) log IU/mL. Among 89 patients who had both a quantitative HBV DNA result at baseline and one-year, 79% (95% CI, 69%–87%) had a ≥ 2 log IU/mL decrease in HBV DNA from baseline to one year. Of the hypothesized risk factors evaluated in the primary analysis, only baseline HBV DNA remained associated with response to tenofovir-based ART.

DISCUSSION

Our study demonstrates that in clinical practice, incomplete HBV suppression occurred in more than half of HIV/HBV-coinfected patients at one year of tenofovir-based therapy. We observed similar results in sensitivity analyses that varied the inclusion criteria and definitions of incomplete HBV DNA suppression. No statistically significant differences in the cumulative incidence of incomplete HBV suppression were observed according to

previous receipt of lamivudine. High baseline HBV DNA was the only risk factor independently associated with incomplete suppression. In secondary analyses, detectable HIV viremia at one year, likely reflecting antiviral non-adherence, was associated with incomplete HBV suppression. Yet, a large proportion of patients with undetectable HIV RNA at one year of tenofovir-based ART also had incomplete HBV suppression. Thus, non-adherence is unlikely to explain all of this virologic failure.

The incidence of incomplete HBV suppression in this study exceeded that observed in the majority of previous observational cohort studies of HIV/HBV-coinfected patients [31–38]. Differences in the study populations (e.g. race, prior exposure to anti-HBV therapy), methods used to measure HBV DNA, and time points at which HBV DNA results were evaluated might have accounted for the higher incidence of incomplete HBV suppression in this study.

Guidelines for the management of HIV/HBV coinfection recommend that coinfecting patients achieve an undetectable HBV DNA level by either 24 weeks[18] or 48 weeks[21] of anti-HBV-active ART. However, given the high incidence of incomplete HBV suppression at one year of tenofovir-based ART observed among the patients in this study, and the findings of other studies that suggest that more than 12 months may be needed to fully suppress HBV DNA in the setting of HIV [36, 39], future guidelines might consider recommending a longer duration on anti-HBV-active ART before considering additional interventions. For patients who do not achieve an undetectable HBV DNA level on combination tenofovir plus either emtricitabine or lamivudine, providers could consider adding entecavir in patient with fully suppressed HIV RNA, to augment HBV DNA suppression. They might also consider initiating a 48-week course of pegylated interferon alfa, to attempt to achieve HBV virologic response.

We found that 42% of HIV/HBV-coinfected patients who initiated tenofovir-based ART had incomplete HBV suppression at one year despite having an undetectable HIV RNA at this time. The mechanisms that might explain this observation remain unclear. One possibility is that given the high baseline HBV DNA levels present in HIV/HBV-coinfected individuals, one year might not be sufficient to achieve HBV suppression, and more time might be needed to reach this outcome. A recent cohort study of HIV/HBV patients in France demonstrated a prolonged time to undetectable HBV DNA levels despite high levels of anti-HBV-active ART adherence [37]. Another possibility is that the levels of anti-HBV antiviral adherence needed to achieve HBV suppression might be higher than that needed for HIV suppression. Alternatively, other host, genetic, and viral factors might influence incomplete HBV suppression during HBV therapy and should be explored in future studies.

We observed that higher baseline HBV DNA level was associated with incomplete HBV suppression. High HBV DNA levels may make achieving HBV suppression with oral nucleos(t)ide analogue therapy more difficult because of inadequate drug potency, a feature observed in the treatment of other chronic viral infections [40]. Further, higher HBV DNA levels might reflect an impaired innate or adaptive host immune response, which could contribute to inadequate HBV suppression [41, 42].

This study has several potential limitations. First, the retrospective study design did not allow all possible risk factors to be collected and evaluated in analyses. In particular, HBV genotype, HBV genotypic resistance mutations, quantitative HBsAg levels, and duration of prior lamivudine use were not routinely available in medical records, though these variables may also be associated with HBV treatment response in HIV/HBV-coinfected patients [37, 43, 44]. Further, we only had limited data on baseline laboratory tests of liver inflammation and hepatic function, which may affect response to antiviral therapy in chronic HBV.

Second, there is the potential for misclassification of outcomes. The study design did not permit HBV DNA testing with the same assay and at the same time during treatment among all patients. However, we did require HBV viral loads to be obtained in a pre-specified window to reduce misclassification of outcomes. We also conducted a number of sensitivity analyses that showed similar results to our primary analysis.

Although we assessed the study outcome closest to one year after the start of tenofovir, in certain HIV/HBV cohorts, longer duration of therapy may be required before full suppression occurs in the majority of patients [36, 39]. Continued follow-up and analysis of tenofovir-treated HIV/HBV cohorts will be required to assess long-term HBV virologic response rates.

Finally, patients were included from sites in mainly urban settings, potentially limiting the generalizability of the results. However, our study sample was demographically similar to other U.S.-based HIV/HBV cohorts [45, 46].

Our study has a number of strengths. We evaluated outcomes adjusted for prior lamivudine use and therefore possible resistance to this agent. Further, we examined incomplete HBV suppression among patients with undetectable HIV viral loads who were presumably adherent to their antiretroviral regimens to help isolate biological determinants of response. Finally, our sample included a high proportion of African-American patients (68%), who have rarely been included in observational studies of HIV/HBV coinfection.

In conclusion, our study found that the majority of HIV/HBV-coinfected patients who initiated tenofovir-based ART failed to achieve an undetectable HBV DNA by one year of therapy, and a sizable proportion failed to reach this endpoint despite HIV suppression. Future studies should evaluate additional host, viral, and genetic risk factors associated with incomplete HBV suppression and examine long-term clinical biochemical, histological, and serological outcomes of incomplete HBV suppression in HIV/HBV patients.

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Abbreviations

HBV	hepatitis B virus
HCV	hepatitis C virus
ART	antiretroviral therapy
HBsAg	hepatitis B surface antigen
HBeAg	hepatitis B e antigen
anti-HBe	hepatitis B e antibody
anti-HBs	hepatitis B surface antibody

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Figure 1.

Distribution of age (Figure 1a), baseline CD4 T lymphocyte count (Figure 1b), baseline HIV RNA level (Figure 1c), and baseline HBV DNA level (Figure 1d) by incomplete HBV suppression status at one year of tenofovir-based antiretroviral therapy. Each box represents the 25th and 75th percentiles (i.e., interquartile range) of the variable, and each dashed line within the box represents the median of that variable for the group. Whiskers extend from each box to values 1.5 times the interquartile range. The dashed line across each figure represents the overall median value of each risk factor.

Figure 2. Kaplan-Meier curves evaluating time to HBV DNA <2.6 IU/mL, by age group (<43 years versus ≥43 years; Figure 2a) and baseline HBV DNA level (<8 log IU/mL versus ≥8 log IU/mL; Figure 2b).

Table 1

Baseline characteristics of the 133 HIV/hepatitis B virus-coinfected patients in the study sample, by HBV suppression status.*

Characteristic	All Patients	HBV DNA Suppressed	HBV DNA Incompletely Suppressed	P-Value
Median age (yrs, IQR)	43 (39–48)	45 (39–50)	42 (36–46)	0.01
Male sex (% , 95% CI)	88 (82–94)	90 (82–98)	86 (78–95)	>0.5
African-American race (% , 95% CI)	68 (60–76)	62 (49–75)	74 (63–84)	0.39
Median baseline body weight (kg, IQR)	77 (66–87)	79 (66–87)	74 (66–87)	>0.5
Median duration of HIV diagnosis (yrs, IQR)	8.1 (2.6–13.5)	8.7 (1.1–15.1)	8.1 (3.1–13.4)	>0.5
Positive hepatitis B e Ag status (% , 95% CI)	86 (79–93)	78 (66–90)	93 (85–100)	0.06
Median baseline HBV DNA (log IU/mL, IQR)	7.7 (6.2–8.7)	7.0 (5.2–8.2)	8.2 (6.7–8.8)	0.01
Hepatitis C virus coinfection (% , 95% CI)	18 (11–24)	24 (13–36)	12 (4–20)	>0.5
Median baseline CD4 cell count (cells/mm ³ , IQR)	258 (73–420)	284 (73–485)	249 (67–385)	0.22
Median baseline HIV RNA (log copies/mL, IQR)	4.3 (3–5)	4.3 (2.7–5.3)	4.4 (3.2–5)	>0.5
NRTI backbone (% , 95% CI)				
Tenofovir + Emtricitabine	64 (56–72)	74 (62–86)	55 (44–67)	Ref.
Tenofovir + Lamivudine	26 (18–33)	22 (11–33)	29 (18–40)	0.19
Tenofovir + Other	10 (5–16)	4 (0–10)	16 (7–25)	0.04
Previous lamivudine therapy (% , 95% CI)	76 (68–83)	71 (59–83)	80 (70–90)	0.25
Previous antiretroviral therapy (% , 95% CI)	79 (72–86)	76 (64–87)	81 (72–91)	0.45

HBV= hepatitis B virus; IQR=interquartile range

* Multiple imputation used to account for missing data.

Table 2

Sensitivity analyses evaluating the incidence of incomplete HBV DNA suppression.

Sensitivity Analysis	Incidence of Incomplete HBV DNA Suppression (95% Confidence Interval)
Included patients with HBV DNA measured between 7–17 months (primary analysis; n=133)	54% (46%–63%)
Classified 10 patients with HBV DNA <4.79 IU/mL on Hybrid Capture II assay as having incomplete HBV DNA suppression (n=133)	56% (48%–65%)
Classified 10 patients with HBV DNA <4.79 IU/mL on Hybrid Capture II assay (Digene) as having suppressed HBV DNA (n=133)	49% (40%–58%)
Included patients with HBV DNA measured between 9–12 months (n=71)	52% (42%–62%)
Exclusion of 3 patients with low-level baseline HBV DNA (<2.6 log IU/mL) on a sensitive assay (n=130)	57% (48%–66%)
Exclusion of 2 patients with only a positive qualitative HBV DNA result recorded at one year (n=131)	54% (45%–62%)