Treatment persistence and discontinuation among chronic hepatitis B patients initiating nucleos(t)ide analogues treatment

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Poster 3266

HBV Treatment Patterns

Conclusions

- TAF was found to have higher adherence and longer persistence versus ETV and TDF, especially among patients 65+ years old.
- While half to two-thirds of patients discontinued the index therapy, most restarted before the end of the follow-up.
- These findings have clinical implications for patient engagement, therapy selection, and achieving long-term treatment success and warrant further investigation.

Plain Language Summary

- TAF is an orally bioavailable prodrug of tenofovir, a nucleotide analog that inhibits reverse transcription of HIV and HBV.
- Nucleos(t)ide analogues are recommended as first line treatments for CHB
- Here, we report that combination TAF was found to have higher adherence and longer persistence versus ETV and TDF, more so among patients 65+ years old. Two-thirds of patients discontinued the index therapy, but most restarted before the end of the follow-up.

References

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Introduction

- Chronic hepatitis B virus (CHB) infection is a major cause of cirrhosis and hepatocellular carcinoma worldwide.[1]
- Around 30% of 257 million people who are chronically infected also have chronic disease and active viral replication. They are considered candidates for hepatitis B virus (HBV) treatment with either peg-interferon (IFN) or nucleos(t)ide analogues. [2]
- Effective viral suppression using antiviral drugs has shown to improve patients' survival and quality of life.[3]
- Nucleos(t)ide analogues such as entecavir (ETV), tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) remain as first line treatment in the clinical for patients with HBV.[4]
- TAF has overcome TDF limitations in long-term kidney and bone related side effects, though it is not widely accessible and lengthier studies in real-life settings are lacking.[2]

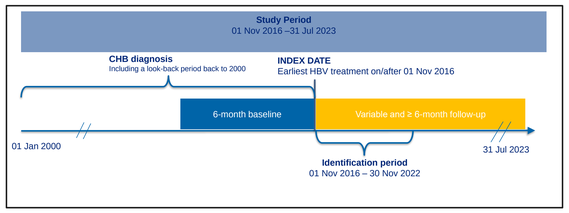
Objective

- This study aimed to describe treatment persistence, discontinuation, switch, and restart of nucleos(t)ide analogues in treatment naïve CHB patients.

Methods

- This was a retrospective study using administrative claims from the Optum Research Database, a database covering most U.S. payer claims, for commercial and Medicare Advantage Part D (MAPD) health plan enrollees.
- Treatment-naïve CHB adult patients initiating TAF, ETV, or TDF between 01Nov2016 and 30Nov2022 were identified. Treatment initiation was considered the index date. (**Figure 1**)
- CHB was defined as having one of the following ICD-9 and ICD-10 Dx diagnosis codes: 070.20, 070.22, 070.30, 070.32, V02.61, B181, and Z2251.
- Persistence was measured as time to the earlier of discontinuation (gap in therapy >30 days), switch (initiation of new nucleos(t)ide analogues), or end of follow-up/study period.
- Adherence was measured as proportion of days covered during the variable length follow-up.
- Descriptive analysis, Kaplan-Meier analysis, and Cox Proportional Hazards (Cox-PH) model adjusting for demographics, and clinical characteristics were conducted.

Figure 1. Study Schematic



[a]Abbreviations: CHB, chronic hepatitis B virus

Results

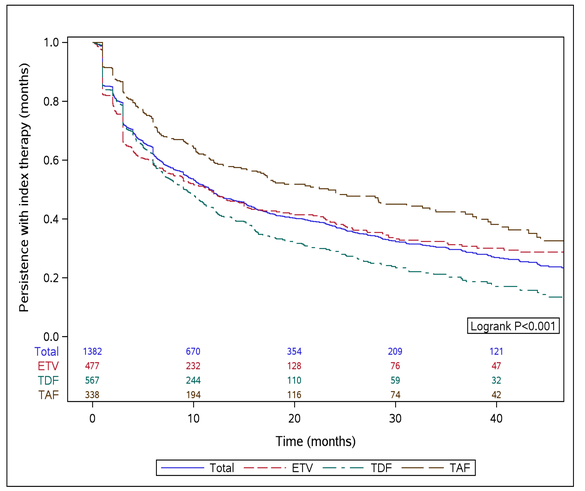
- Among patients receiving HBV antiviral therapy (N=14,935), 4067 adults had a claim with a diagnosis for CHB and at least 6 months baseline and follow-up enrollment in the claims database.
- A total of 1384 treatment-naïve patients met inclusion criteria.
- On index 338(24%) patients initiated TAF, 477(35%) ETV, and 567(41%) TDF. Mean (SD) age (years) was 55(14) for ETV, 54(15) TAF and 52(14) TDF. (**Table 1**)
- Using Kaplan-Meier analysis, median persistence (months) with the index therapy was longest for TAF (23.3), followed by ETV (11.5) and TDF (9.2). (**Figure 2**)

Results

Table 1. Baseline Demographics and Clinical Characteristics by Index Medication

	All Patients (N=1,382)		
	ETV (N=477)	TDF (N=567)	TAF (N=338)
Mean age (SD), years	55.2 (13.9)	51.7 (13.7)	53.8 (13.8)
Sex, n (%)			
Male	310 (65.0)	349 (61.6)	193 (57.1)
Race, n (%)			
White	102 (21.4)	95 (16.8)	59 (17.5)
Black	72 (15.1)	54 (9.5)	35 (10.4)
Hispanic	25 (5.2)	26 (4.6)	19 (5.6)
Asian	239 (50.1)	333 (58.7)	194 (57.4)
Unknown/missing	39 (8.2)	59 (10.4)	31 (9.2)
Osteoporosis, n (%)	28 (5.9)	28 (4.9)	28 (8.3)
Taking osteoporosis medication, n (%)	21 (4.4)	17 (3.0)	16 (4.7)
CKD, n (%)	45 (9.4)	24 (4.2)	27 (8.0)
Charlson comorbidity score, mean (SD)	2.4 (1.2)	2.1 (1.1)	2.4 (1.1)
Variable follow-up days, mean (SD)	954.0 (609.1)	901.4 (582.5)	904.7 (543.5)

Figure 2. Persistence by Index Medication



[a]Abbreviations: ETV, entecavir; TDF, tenofovir disoproxil; TAF, tenofovir alafenamide

[1]Persistence ended by first event to occur: discontinuation, switch or end of study period.
[2]Patients required to have at least 6 months continuous enrollment and 6 months of follow-up. Patients' follow-up time ended by death, end of continuous enrollment, liver transplant or study period end, July 31, 2023, which ever happened first.
Among patients 65+, median persistence (months) with TAF was 38.0, 9.0 for ETV and 6.9 for TDF. (**Figure 3**)

Table 2. Criteria Ending Persistence During Variable Follow-up by Index Medication

	All Patients (N=1,382)		
	ETV (N=477)	TDF (N=567)	TAF (N=338)
Discontinuation of index therapy,[1] n (%)	288 (60.4)	364 (64.2)	165 (48.8)
Switch from index therapy, n (%)	17 (3.6)	43 (7.6)	25 (7.4)
End of study,[2] n (%)	172 (36.1)	160 (28.2)	148 (43.8)
Discontinuation with restart, n (%)	173 (60.1)	214 (58.8)	93 (56.4)

[a]Abbreviations: ETV, entecavir; TDF, tenofovir disoproxil; TAF, tenofovir alafenamide
[1]Persistence ended by first event to occur: discontinuation, switch or end of study period.
[2]Patients required to have at least 6 months continuous enrollment and 6 months of follow-up. Patients' follow-up time ended by death, end of continuous enrollment, liver transplant or study period end, July 31, 2023, which ever happened first.

Table 3. Cox-PH Risk of Non-Persistence

	HR	Lower 95% CI	Upper 95% CI	P-value
Index Med.				
TAF	Ref.	-	-	-
ETV	1.341	1.113	1.616	0.002
TDF	1.617	1.352	1.935	<0.001

[a]Abbreviations: ETV, entecavir; TDF, tenofovir disoproxil; TAF, tenofovir alafenamide

Additional covariates (not shown) include: age, gender, region, **race/ethnicity**, **index year**, osteoporosis, CKD, **Charlson score**, disorders of lipid metabolism, hypertension, diabetes without complications, disease of urinary system, other nutrition/endocrine/metabolic disorders, eye disease, **disease of the heart**, non-traumatic joint disorders, upper GI disorders, baseline all cause HCRU (**ER visits**, IP stays, ambulatory visits, **pharmacy fills**), and **all-cause total cost**.

Bold = P<0.05

- Among patients 65+, median persistence (months) with TAF was 38.0, 9.0 for ETV and 6.9 for TDF. (**Figure 3**)
- Across all three cohorts, persistence was more likely to end due to discontinuation vs. switching; TAF: 48.8% vs. 7.4%; ETV: 60.4% vs. 3.6%; TDF: 64.2% vs. 7.6%. (**Table 2**)
- Following discontinuation, most patients (56%-60%) restarted their index therapy. (**Table 2**)
- Compared to TAF, the rate of discontinuation/switch was higher for ETV (HR=1.34, p<0.01) and TDF (HR=1.62, p<0.01). (**Table 3**)
- Mean adherence with the index medication was highest for TAF (0.74) followed by ETV (0.63) and TDF (0.59). (**Not pictured**)

Limitations

- Due to the nature of the claims analysis, the reasons for discontinuation could not be specified, but could relate to various factors including efficacy, side effects, cost, and other reasons.
- Patients who were considered censored because they disenrolled from the health plan may not represent the broader population.
- Clinical improvement or decline by index treatment or switch/restart were not assessed.
- Future research should more fully examine subsequent treatment patterns including time to restart and subsequent switches in therapy.