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Effectiveness of Tenofovir Alafenamide in Patients with Chronic Hepatitis B Treated in Usual Clinical Practice: Results from the TARGET-HBV Observational Cohort Study

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INTRODUCTION

- Antiviral therapy for chronic hepatitis B (HBV) has improved outcomes and substantially reduced the incidence of complications of cirrhosis and hepatocellular carcinoma.
- Tenofovir alafenamide (TAF), approved in 2016, has demonstrated efficacy and an improved safety profile in phase 3 trials.

OBJECTIVE

- To evaluate the characteristics and clinical outcomes of patients being treated with TAF as either initial therapy or after switching from a prior antiviral agent.

METHODS

- TARGET-HBV is a longitudinal, observational cohort study of patients with HBV managed according to local practice standards at 26 academic and community sites in the United States. (Figure 1) The study design includes a retrospective phase which reflects a 3-year retrospective collection evaluation of patients on TAF and allows for a future prospective data collection phase.
- Presented here are the retrospective data from the medical records of the first 499 patients enrolled into the retrospective phase of the study, thus the enrolled population includes adult patients with HBV who are currently taking TAF.
- After written informed consent was obtained, adult patients on TAF for chronic HBV and without hepatitis delta or HIV coinfection were enrolled in TARGET-HBV.
- Data were acquired from health records from the previous 3 years, including medical history, narratives, laboratory and radiological reports, and pharmacy records, to assess virologic response, measures of liver disease severity, and changes in renal function.
- Baseline demographics are presented in Table 1.

Figure 1: TARGET-HBV Study Sites

RESULTS

- In this planned interim analysis, 499 patients were enrolled at 26 sites (15 academic/11 community) in the U.S. Median age=55 yrs, 66% male, 66% Asian, and 82% had been treated with at least one antiviral agent (predominantly tenofovir disoproxil fumarate) prior to starting TAF (Table 1).

Table 1. Baseline Demographics

		Enrolled Participants	n (N = 499)
Age at Study Entry (Years), *Median (range)*		55.0 (25.0 - 87.0)	499
Gender, n (%)	*Female*	171 (34.3)	499
Race, n (%)	*White*	100 (20.5)	488
	Black or African American	45 (9.2)	
	American Indian or Alaska Native	2 (0.4)	
	Asian	322 (66.0)	
	Other	19 (3.9)	
	Not Available	11	
Ethnicity, n (%)	*Hispanic or Latino*	26 (5.4%)	485
	Not Hispanic or Latino	451 (93.0%)	
	Other	8 (1.6%)	
	Not Available	14	
BMI (kg/m² at Enrollment), *Median (range)*		25.0 (16 – 50)	481
Prior Therapies, n (%)*	*Adefovir*	57 (11.4)	
	Emtricitabine/Tenofovir DF	14 (2.8)	
	Entecavir	102 (20.4)	
	Lamivudine	53 (10.6)	
	Peginterferon	23 (4.6)	
	Telbivudine	6 (1.2)	
	Tenofovir DF	361 (72.3)	
	No Prior	88 (17.6)	

TAF = Tenofovir alafenamide; Tenofovir DF = Tenofovir Disoproxil Fumarate
**Participants may have had more than 1 prior therapy.*

- Median duration of TAF dosing was 98 wks (range, 2-186 wks) and only 10 patients (2%) discontinued TAF (insurance coverage [3], patient request [1], renal insufficiency/disease [1], tolerability [3], cost concerns [1], unknown [2]; patients can have more than 1 reason for discontinuing).
- Reasons for switching to TAF included perceived safety profile of TAF (27%), physician choice (19%), abnormal renal function (9%), risk of bone disease (5%), patient request (3%), copay assistance program for TAF (4%), insurance no longer covers previous therapy or provides greater coverage for TAF (1% each), or no reason recorded (28%) (Figure 2).
- Most recent lab data prior to starting TAF: 76% HBeAg-, 58% undetectable HBV DNA, median ALT=29 IU and creatinine clearance=90mL/min.
- Among those with paired follow up lab data 12-18 months after switching to TAF, compared to pre-TAF:
  - 43/77 (56%, 95% CI [44.1,67.2]) with abnormal ALT (>40 U/L) normalized ALT
  - 23/36 (63.9%, 95% CI [46.2, 79.2]) with detectable HBV DNA had undetectable HBV DNA
  - 5/82 (6%) with paired HBsAg had lost HBsAg (Figure 3)
- There was no median change in creatinine clearance among those with paired measurements (Figure 4).

Figure 2. Reasons for Switching to TAF

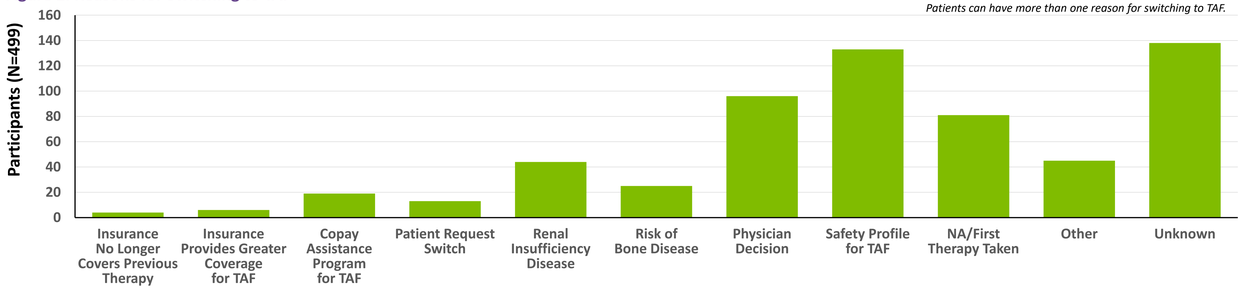
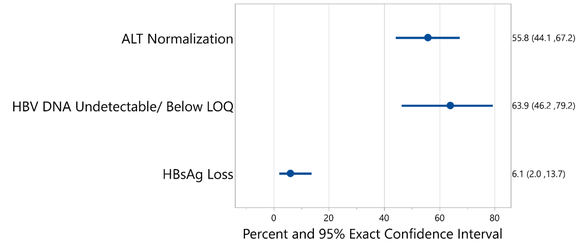
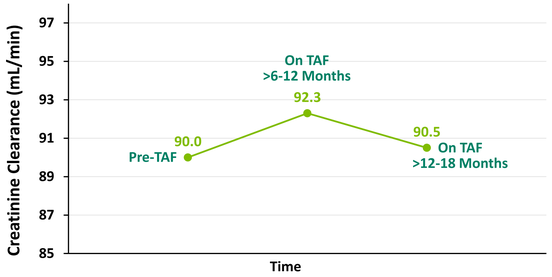


Figure 3. Proportion of Normal ALT, Undetectable HV DNA and HB Surface Antigen Loss in Patients with Abnormal Values Prior to Switching to TAF (paired values pre-TAF to >12-18 months post TAF)



Pre-TAF measures were assessed from the last test on or before TAF dosing; measures are also from the last test within >12 to 18 months. ALT is considered normalized when it is less than or equal to 40 IU/L.

Figure 4. Median Creatinine Clearance Pre-TAF and On-TAF within >6-12 and <12-18 Months



CONCLUSIONS

- Among patients with TAF use in the TARGET-HBV cohort, switching to TAF from another antiviral regimen was well tolerated and associated with further improvement in serum ALT in 56% and a decrease in HBV DNA to undetectable levels in 64% of patients.
- Creatinine clearance did not change after 12-18 months of therapy with TAF.
- These results compare favorably to those reported in phase 3 clinical trials.

Reference: Chan HL et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*, 2016.

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