

Vemlidy® (tenofovir alafenamide)

Risk of Hepatocellular Carcinoma Compared with Entecavir

This document is in response to your request for information regarding Vemlidy® (tenofovir alafenamide [TAF]) compared with entecavir (ETV) treatment and the risk of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB).

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Clinical Data on TAF vs ETV and Risk of HCC

Retrospective, Multicenter Study in Korea, Chon et al¹

Study design and demographics

This study evaluated the rates of HCC in treatment-naïve patients with CHB who were treated with ETV, TDF, or TAF between May 2017 and April 2019 in three Korean hospitals. Included patients were ≥19 years old, had ≥6 months of follow-up, did not have a history of HCC or occurrence of HCC within 6 months after enrollment, did not have co-infection with another hepatitis virus or HIV, and did not have decompensated cirrhosis at baseline. The primary outcome was the rate of HCC development. A total of 2082 patients were included in statistical analyses.

Table 1. Baseline Demographics and Characteristics (Chon et al)¹

Key Demographics and Characteristics	TAF (n=389)	ETV (n=1064)	TDF (n=629)	P-Value
Age, mean (SD), years	48.4±11.3	53.3±11.2	48.6±12.1	<0.001
Male, n (%)	208 (53.5)	592 (55.6)	324 (51.5)	0.251
BMI, median (IQR), kg/m ²	23.5 (21.5–25.8)	23.6 (21.5–25.8)	23.2 (21.2–25.4)	0.049
Cirrhosis, n (%)	110 (28.3)	224 (21.1)	115 (18.3)	0.001
AST, median (IQR), IU/L	59 (37–91)	34 (23–62)	46 (27–88)	<0.001
ALT, median (IQR), IU/L	87 (42–147)	35 (20–81)	47 (26–107)	<0.001
Total bilirubin, median (IQR), mg/dL	0.8 (0.6–1)	0.7 (0.5–1)	0.8 (0.6–1.1)	<0.001
Serum albumin, median (IQR), g/dL	4.3 (4–4.5)	4.2 (3.8–4.4)	4.2 (3.9–4.5)	0.006
Platelet count, mean (SD), × 10 ³ /mm ³	190.7±65.7	197.1±84.8	177.5±71.8	<0.001

HBeAg+, n (%)	171 (44)	278 (26.1)	242 (38.5)	<0.001
HBV DNA, median (IQR), log ₁₀ IU/mL	6.5 (5.1–8)	3.8 (1.8–6.2)	4.8 (2.1–7)	<0.001

Results

Over a median (IQR) of 20.9 (14.6–27.8) months of follow-up, 43 patients (2.1%) developed HCC (TAF, n=3; ETV, n=25; TDF, n=15). The cumulative incidence rates of HCC development at 1 and 2 years, respectively, were as follows: TAF, 0.3% and 1.3%; ETV, 0.7% and 2.9%; and TDF, 0.7% and 2.1%. There was no significant difference in the cumulative incidence rate of HCC between the TAF and ETV arms overall ($P=0.138$), among patients with cirrhosis ($P=0.275$), and among patients without cirrhosis ($P=0.384$). Univariate analysis found no significant difference in the risk of HCC development with TAF compared with ETV ($P>0.05$). In a multivariate analysis, older age (HR [95% CI]: 1.044 [1.013–1.076]; $P=0.005$) and male gender (HR [95% CI]: 2.99 [1.429–6.254]; $P=0.004$) were significantly associated with the development of HCC, whereas higher platelet count was associated with a decreased risk of HCC (HR [95% CI]: 0.993 [0.988–0.999]; $P=0.012$).

Multicenter Cohort Study in Korea, Lee et al²

Study design and demographics

This study evaluated the rates of HCC in treatment-naïve patients with CHB who were treated with ETV or TAF between 2012 and 2019 at three academic hospitals. Included patients were ≥ 19 years old with well-preserved liver function; had ≥ 6 months of follow-up; did not have a history of HCC or decompensated cirrhosis at enrollment or occurrence of other clinical events (death or orthotopic liver transplant) within 6 months of enrollment; did not change antiviral treatment from ETV to TDF/TAF or from TDF/TAF to ETV; did not have co-infection with another hepatitis virus; and did not have a history of organ transplantation or other significant medical illnesses, such as malignancy with advanced stage. A total of 1810 patients were included in statistical analyses.

Table 2. Baseline Demographics and Characteristics (Lee et al)²

Key Demographics and Characteristics	Total (N=1810)	ETV (n=1525)	TAF (n=285)	P-Value
Age, mean (SD), years	52.8±11.3	52.3±11.4	49.5±11.4	<0.001
Male, n (%)	1085 (59.9)	915 (60.0)	170 (59.6)	0.912
Hypertension, n (%)	403 (22.3)	356 (23.3)	47 (16.5)	0.011
Cirrhosis, n (%)	539 (29.8)	443 (29.0)	96 (33.7)	0.116
AST, mean (SD), IU/mL	75±133.6	76.4±131.8	83.8±121.7	<0.001
ALT, mean (SD), IU/mL	80.5±165.6	84.4±165.7	105.1±165.3	<0.001
Total bilirubin, mean (SD), mg/dL	1.1±1.9	1.1±1.9	1.0±1.5	<0.001
Serum albumin, mean (SD), g/dL	4.0±0.6	4.0±0.6	4.1±0.5	<0.001
Platelet count, mean (SD), $\times 10^3/\text{mm}^3$	178.8±81.3	178.9±78.6	179.4±62.9	<0.001
HBeAg+, n (%)	685 (37.8)	523 (34.3)	162 (56.8)	<0.001
HBV DNA, mean (SD), log ₁₀ IU/mL	4.3±2.5	4.1±2.4	5.3±2.5	<0.001

Results

There was no significant difference in the follow-up duration between the ETV and TAF groups [mean (SD), months, 37.3 (17.2) vs. 35.3 (18.7); $P=0.094$]. Among the whole cohort, 89 patients (4.9%) developed HCC (TAF, n=10; ETV, n=79). The annual HCC incidence was

not statistically significantly different between the ETV and TAF groups (1.67 vs. 1.19 per 100 person-years, $P=0.255$). Univariate analysis found no significant difference in the risk of HCC development with TAF compared with ETV (adjusted HR=0.646 [95% CI:0.331–1.258]; $P=0.198$). In the multivariate analysis, prognostic factors of male gender (adjusted HR [95% CI]: 3.796 [2.159–6.674]; $P<0.001$), hypertension (adjusted HR [95% CI]: 3.042 [1.935–4.783]; $P<0.001$), liver cirrhosis (adjusted HR [95% CI]: 1.801 [1.184–2.739]; $P=0.006$), fibrosis-4 index score (adjusted HR [95% CI]: 1.084 [1.029–1.142]; $P=0.002$), and albumin level (adjusted HR [95% CI]: 0.954 [0.633–1.438], $P=0.823$) were independently associated with the development of HCC.

References

1. Chon HY, Ahn SH, Kim YJ, et al. Efficacy of entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide in treatment-naïve hepatitis B patients. *Hepatol Int.* 2021;15:1328-1336.
2. Lee H W, Cho Y Y, Lee H, et al. Impact of tenofovir alafenamide vs. entecavir on hepatocellular carcinoma risk in patients with chronic hepatitis B. *Hepatol Int.* 2021;15:1083–1092.

Abbreviations

CHB=chronic hepatitis B
ETV=entecavir
HBeAg=hepatitis B
envelope antigen

HCC=hepatocellular
carcinoma
HR=hazard ratio
TAF=tenofovir alafenamide

TDF=tenofovir disoproxil
fumarate

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Vemlidy US Prescribing Information available at:

www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vemlidy/vemlidy_pi

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

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