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ABOUT COVER

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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Randomized Controlled Trial

Tenofovir disoproxil fumarate in Chinese chronic hepatitis B patients: Results of a multicenter, double-blind, double-dummy, clinical trial at 96 weeks

Xiao-Fan Chen, Ya-Nan Fan, Chong-Wen Si, Yan-Yan Yu, Jia Shang, Zu-Jiang Yu, Qing Mao, Qing Xie, Wei Zhao, Jun Li, Zhi-Liang Gao, Shan-Ming Wu, Hong Tang, Jun Cheng, Xin-Yue Chen, Wen-Hong Zhang, Hao Wang, Zhong-Nan Xu, Ling Wang, Jun Dai, Jing-Hang Xu

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statement: The study was reviewed and approved by the Ethics Committees of the 14 study sites, including Peking University First Hospital, China, and all procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments (approval No. 2013L01048).

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Abstract

BACKGROUND

Tenofovir disoproxil fumarate (TDF) is a prodrug of a nucleotide analogue. As an antiviral drug, TDF has been proposed in the first-line treatment of chronic hepatitis B (CHB). Qingzhong, a brand name of TDF, commercialized by Jiangsu Chia-tai Tianqing Pharmaceutical Co Ltd., and Viread, another brand name of TDF, commercialized by GlaxoSmithKline, have both been approved by the State Food and Drug Administration, China.

AIM

To investigate the efficacy and safety of the two TDF agents in the treatment of Chinese CHB patients.

METHODS

This trial was registered at ClinicalTrials.gov with the identifier number of NCT02287857. A total of 330 Chinese CHB patients, among which 232 were hepatitis B e antigen (HBeAg)-positive, were included in this 5-year-long, multicenter, double-blinded, double-dummy, randomized-controlled, non-inferiority phase III trial. The participants were initially randomized into two groups: Group A ($n = 161$), in which the participants received 300 mg Qingzhong once a day for 48 wk; and Group B, in which the participants received 300 mg Viread once a day for 48 wk. Starting from week 49, all the participants in Groups A and B received 300 mg Qingzhong once a day until the 96th week. In this study, the primary endpoint was the decrease in plasma level of hepatitis B virus (HBV) DNA at the 96th week, while the secondary endpoints were suppression of HBV replication, alanine aminotransferase (ALT) normalization, HBeAg loss, and HBeAg seroconversion rates.

RESULTS

For the participants with HBeAg-positive CHB, the decrease in mean HBV DNA level relative to the baseline value was comparable between Groups A and B (5.77 *vs* 5.73 \log_{10} IU/mL, $P > 0.05$) at the 96th week. In addition, similar percentages of HBeAg-positive participants in the two groups exhibited undetectable levels of HBV DNA, HBeAg loss, and HBeAg seroconversion (71.05% *vs* 77.97% , 31.00% *vs* 27.27% , and 20.22% *vs* 15.79% , respectively, in Group A *vs* Group B; $P > 0.05$). For the participants with HBeAg-negative CHB, the decrease in mean HBV DNA level relative to the baseline value was also comparable between Groups A and B (4.46 *vs* 4.70 \log_{10} IU/mL, $P > 0.05$) at the 96th week. In addition, similar percentages of HBeAg-negative participants in the two groups exhibited undetectable levels of HBV DNA (87.23% *vs* 94.12% in Group A *vs* Group B, respectively; $P > 0.05$). Finally, similar percentages of CHB patients (HBeAg-positive or HBeAg-negative) in the two groups exhibited normalization of ALT (80.14% *vs* 84.57% in Group A *vs* Group B, respectively; $P > 0.05$), and similar incidences of adverse events were observed (106 *vs* 104 in Group A *vs* Group B, respectively; $P > 0.05$).

CONCLUSION

Both Qingzhong and Viread are effective and safe in the treatment of Chinese CHB patients according to the results of our clinical trial.

Key Words: Chronic hepatitis B; Hepatitis B virus infection; Chronic; Tenofovir disoproxil

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Core Tip: This clinical trial compared the efficacy and safety of Qingzhong and Viread, two commercialized tenofovir disoproxil fumarate drugs, in the treatment of Chinese chronic hepatitis B (CHB) patients during a 96-wk period. The decrease in mean hepatitis B virus DNA level relative to the baseline value, the rates of hepatitis B e antigen (HBeAg) loss and HBeAg seroconversion, and the incidence of adverse events were all comparable between patients treated with the two drugs. Our results indicate that both Qingzhong and Viread are effective and safe in the treatment of Chinese CHB patients.

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INTRODUCTION

Hepatitis B virus (HBV) infection poses a serious threat to public health globally. Currently, there are 240000000 people infected by HBV around the world[1], and approximately 650000 people die from liver diseases induced by HBV infection[2]. Specifically, the proportions of liver cirrhosis and hepatocellular carcinoma (HCC) caused by HBV infection are 30% and 45%, respectively[3], in the world, and 60% and 80%, respectively[4], in China. Various types of drugs have been developed to suppress the replication of HBV DNA. Among them, nucleoside/nucleotide analogues (NAs) have been reported to be able to prevent liver decompensation and HCC[5,6].

Tenofovir disoproxil fumarate (TDF) is a prodrug of tenofovir. As an oral antiviral drug, TDF has been proposed for the first-line treatment of chronic hepatitis B (CHB) [7-10]. Before this study, Viread, which was commercialized by GlaxoSmithKline, Shanghai, China, was the only National Medical Products Administration-approved TDF drug in the treatment of Chinese CHB patients. The safety and efficacy of Viread at a dose of 300 mg once daily (q.d.) have been confirmed in previous trials[11-15]. However, the cost of long-term treatment with Viread is high. As a generic TDF drug commercialized by Chia Tai Tianqing Pharmaceutical Group Co. Ltd, Qingzhong was demonstrated to have comparable efficacy and safety with Viread in the treatment of naive Chinese CHB patients during a 48-week trial, thus providing a less expensive option for treating CHB[16]. However, the long-run performance of Qingzhong in the treatment of CHB remains unevaluated. Herein, the virological, serological, and biochemical effects of Qingzhong in the treatment of naive Chinese CHB patients were evaluated in a 96-wk-long clinical trial.

MATERIALS AND METHODS

Study design

This trial includes two stages, and the study design was reported previously[16]. Patients with poor response (which was defined as the HBV DNA level being reduced by less than 1 log₁₀ IU/mL relative to the baseline value after 24 wk of treatment), viral breakthrough (which was defined as the HBV DNA level increasing by more than 1 log₁₀ IU/mL relative to the lowest value during the trial), or genotypic resistance and clinical resistance [which was defined as viral breakthrough on the basis of genotype resistance, regardless of the alanine aminotransferase (ALT) level] were withdrawn from the trial.

Participants

CHB patients from 14 centers in the cities of Beijing, Zhengzhou, Nanjing, Chongqing, Chengdu, Shanghai, and Guangzhou were included in this trial and were followed for more than 5 years from September 2014 to October 2019. The key inclusion and exclusion criteria have been elaborated in a previous report[16].

Endpoints for efficacy evaluation

In this study, the primary endpoint was the decrease in HBV DNA level relative to the baseline value at the 96th week. Secondary endpoints included the proportion of patients with undetectable HBV DNA (< 20 IU/mL), the normalization of serum ALT, hepatitis B surface antigen (HBsAg)/hepatitis B e antigen (HBeAg) loss or seroconversion, and virological breakthrough. These were elaborated in the previous report [16].

Safety analysis

Safety analysis was performed in all the 338 participants who were treated with at least one dose of the TDF drugs during this clinical trial. All types of adverse events (AEs), including serious AEs (SAEs), were monitored. The definitions of SAEs have been elaborated previously[16]. The estimated glomerular filtration rate (eGFR) obtained based on the CKD-EPI CRE (Chronic Kidney Disease Epidemiological Collaboration creatinine equation) formula and the level of urine neutrophil gelatinase-associated lipocalin (NGAL) were used to indicate kidney function change.

Laboratory tests

Virological and serological parameters were assessed centrally by Department of Infectious Diseases, Peking University First Hospital. HBV DNA was assayed using the second-generation polymerase chain reaction quantitative assay, and HBeAg and hepatitis B e antibody were assayed by the corresponding Abbott AxSYM microparticle enzyme immunoassays. The biochemical tests were performed by the local laboratory. These have been described in detail previously[16].

Statistical analysis

Continuous variables are expressed as the mean with standard deviation or median with interquartile ranges. Categorical variables are expressed as counts plus percentages. Continuous variables were compared by *t* tests or Wilcoxon rank sum test. Categorical data between the two groups were compared by the Chi-square test or Fisher exact test. A two-tailed *P* value < 0.05 was considered statistically significant. These statistical analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC, United States). The statistical methods were the same as those described in the previous report[16].

RESULTS

Baseline characteristics

Among the 401 patients screened, 341 were included in this trial, and the participants were randomly assigned into either Group A (171 CHB patients) or Group B (170 CHB patients). Among the participants, 338 were blindly treated with at least one dose of the two TDF drugs. After excluding 11 participants[16], the final full analysis set contained a total of 330 participants [161 in group A (HBeAg-positive: 114 *vs* HBeAg-negative: 47) and 169 in group B (HBeAg-positive: 118 *vs* HBeAg-negative: 51)]. As shown in Table 1, the participants in the two groups showed comparable baseline characteristics.

Endpoint outcomes

Virological and serological outcomes: Both TDF drugs exhibited suppressive effects on HBV DNA level early during the trial, and the effects were maintained or enhanced throughout the 96-wk trial period (Table 2). For participants with HBeAg-positive CHB, the mean values of decrease in HBV DNA level relative to the baseline values were 5.77 and 5.73 log₁₀ IU/mL in Groups A and B, respectively, at the 96th week (*P* > 0.05). While for HBeAg-negative participants, the values were 4.46 and 4.70 log₁₀ IU/mL in Groups A and B, respectively, at the 96th week (*P* > 0.05) (Table 3).

Table 1 Baseline demographic and clinical characteristics of the nucleoside-naive chronic hepatitis B Chinese patients

Demographic and clinical characteristics	Group A (n = 161)	Group B (n = 169)	P value
Age, yr			
mean ± SD	35.16 ± 9.34	34.91 ± 9.79	0.8082
Range	19.00-62.00	19.00-64.00	
Male, n (%)	116 (72.05)	134 (79.29)	0.1248
HBV DNA, log ₁₀ IU/mL	6.86 ± 1.13	6.91 ± 1.05	0.6761
HBeAg positive			
mean ± SD	7.27 ± 0.81	7.29 ± 0.71	0.8126
Range	5.00-8.66	5.02-8.47	
HBeAg negative			
mean ± SD	5.87 ± 1.20	6.03 ± 1.17	0.5144
Range	3.42-8.01	3.33-8.16	
HBeAg status, n (%)			
HBeAg negative	114 (70.81)	118 (69.82)	0.8448
HBeAg positive	47 (29.19)	51 (30.18)	
Baseline HBsAg, log ₁₀ IU/mL	161 (100)	169 (100)	0.4979
HBeAb status, n (%)			
HBeAg positive			
HBeAb negative	12 (10.53)	16 (13.56)	0.4776
HBeAb positive	102 (89.47)	102 (86.44)	
HBeAg negative			
HBeAb negative	46 (97.87)	51 (100.00)	0.2236
HBeAb positive	1 (2.13)	0 (0.00)	
Duration of positivity for HBV, yr			
mean ± SD	10.39 ± 8.03	9.76 ± 7.22	0.4575
Range	0.00-40.00	0.50-34.00	
Baseline ALT, U/L, mean ± SD	175.47 ± 92.17	180.05 ± 96.05	0.6592

HBV: Hepatitis B virus; HBeAg: Hepatitis B e antigen; HBeAb: Hepatitis B e antibody; ALT: Alanine transaminase; HBsAg: Hepatitis B surface antigen.

Table 2 Hepatitis B virus DNA levels in trial participants in the two groups (log₁₀ IU/mL)

Group	HBeAg-positive CHB			HBeAg-negative CHB		
	n	72 wk (mean ± SD)	96 wk (mean ± SD)	n	72 wk (mean ± SD)	96 wk (mean ± SD)
A	114	1.55 ± 0.73	1.50 ± 0.70	47	1.38 ± 0.30	1.41 ± 0.36
B	118	1.54 ± 0.61	1.56 ± 0.84	51	1.36 ± 0.25	1.32 ± 0.10
P value		0.8570	0.5579		0.7215	0.1177

HBeAg: Hepatitis B e antigen; CHB: Chronic hepatitis B.

At the 96th week, 71.05% and 77.97% of the HBeAg-positive participants in Groups A and B, respectively, exhibited undetectable HBV DNA levels (< 20 IU/mL) (*P* > 0.05), while 87.23% and 94.12% of the HBeAg-negative participants in Groups A and B, respectively, exhibited undetectable HBV DNA levels (< 20 IU/mL) (*P* > 0.05) (Table 4).

Table 3 Reductions in hepatitis B virus DNA level in trial participants in the two groups (log₁₀ IU/mL)

Group	HBeAg-positive CHB			HBeAg-negative CHB		
	<i>n</i>	72 wk (mean ± SD)	96 wk (mean ± SD)	<i>n</i>	72 wk (mean ± SD)	96 wk (mean ± SD)
A	114	5.72 ± 1.01	5.77 ± 0.99	47	4.49 ± 1.19	4.46 ± 1.19
B	118	5.75 ± 0.84	5.73 ± 1.01	51	4.67 ± 1.22	4.70 ± 1.18
<i>P</i> value		0.8514	0.6843		0.5528	0.3644

HBeAg: Hepatitis B e antigen; CHB: Chronic hepatitis B.

Table 4 Proportions of participants with undetectable levels of hepatitis B virus DNA (< 20 IU/mL) in the two groups

Group	HBeAg-positive CHB			HBeAg-negative CHB		
	<i>n</i>	72 wk	96 wk	<i>n</i>	72 wk	96 wk
A	114	74 (64.91)	81 (71.05)	47	40 (85.11)	41 (87.23)
B	118	81 (68.64)	92 (77.97)	51	48 (94.12)	48 (94.12)
<i>P</i> value		0.5788	0.2326		0.1877	0.3046

Values are presented as *n* (%). HBeAg: Hepatitis B e antigen; CHB: Chronic hepatitis B.

At the 96th week, 31.00% and 27.27% of participants with HBeAg-positive CHB in Groups A and B, respectively, showed HBeAg loss ($P > 0.05$), while 20.22% and 15.79% of participants with HBeAg-positive CHB in Groups A and B, respectively, showed HBeAg seroconversion ($P > 0.05$). However, only one patient in group A experienced HBsAg loss at week 48, while none experienced HBsAg loss between weeks 48 and 96. None of the HBeAg-negative CHB participants exhibited HBsAg seroconversion during the entire trial period (Table 5).

Biochemical outcomes: One hundred and thirteen out of 141 (80.14%) participants in Group A and 137 out of one 162 (84.57%) participants in group B achieved ALT normalization at week 96 ($P > 0.05$) (Table 6).

At week 96, the mean ALT levels for Groups A and B were 29.73 and 30.74 U/L, respectively, showing significant decreases from the baseline values (175.47 and 180.05 U/L in Groups A and B, respectively).

Viral breakthrough

During the first 48 wk of the trial, viral breakthrough was observed in one participant of each group [16], while no participant developed viral breakthrough between weeks 48 and 96.

Safety analysis

Safety analysis was performed in 338 participants. Among the participants in Groups A and B, 62.72% and 61.54%, respectively, experienced AEs during the trial ($P > 0.05$). Therefore, the incidence of AEs was comparable between the two groups.

Among the participants in Groups A and B, 42 and 39, respectively, experienced mild to moderate adverse reactions (ARs). Among these participants, one in group A and two in group B developed hypophosphatemia without pathological fracture. Other ARs observed were abnormal hepatic enzyme levels, fluctuations in complete blood count, and elevations in serum creatinine level. All the ARs were observed during the first 48 wk and no new ARs appeared from week 48 to week 96. Between weeks 48 and 96, however, eight SAEs occurred. Four of the eight SAEs were observed in Group A, including active hepatitis, pregnancy, partner pregnancy, and liver cancer. Among the four SAEs observed in Group A, the active hepatitis SAE resulted in the patient's withdrawal from the trial but was judged as possibly not being caused by the use of TDF drugs. The two pregnancy SAEs were obviously not caused by the use of TDF drugs. The SAE of liver cancer also resulted in the patient's withdrawal, but was not induced by the use of TDF drugs. The other four SAEs occurred in group B, including active hepatitis, pregnancy, frozen shoulder, and adenomyosis. The active

Table 5 Rates of hepatitis B e antigen loss and hepatitis B e antigen seroconversion in participants with hepatitis B e antigen-positive chronic hepatitis B at week 96

	Group	Number of observations	Number of cases	Incidence	P value
HBeAg loss	A	100	31	31.00	0.6482
	B	110	30	27.27	
HBeAg seroconversion	A	89	18	20.22	0.4491
	B	95	15	15.79	

HBeAg: Hepatitis B e antigen.

Table 6 Number of participants who exhibited alanine aminotransferase normalization in the two groups

	Group	Number of observations	Number of cases	P value
72 wk	A	145	120	1.0000
	B	162	133	
96 wk	A	141	113	0.3637
	B	162	137	

hepatitis SAE resulted in the patient's withdrawal and was judged as possibly being induced by the use of TDF drugs. The other three SAEs were not caused by the use of TDF drugs. No discontinuations due to ARs or AEs happened, and no deaths occurred.

In total, 233 participants (109 in Group A and 124 in Group B) had available eGFR data (Table 7) and urine NGAL levels (Table 8). The eGFRs of the two groups were not significantly different at each evaluation point during the trial ($P > 0.05$). However, when compared with the values at baseline, both the value of eGFR and the level of urine NGAL were significantly lower in all the participants at week 96 ($P < 0.05$).

DISCUSSION

As one of the antiviral agents used for the first-line treatment of CHB, TDF has many advantages, such as better curative effect and lower resistance rate. A large number of studies have confirmed that TDF can significantly suppress HBV DNA replication, even in patients resistant to other NAs. Before Qingzhong was approved, the only choice for the treatment of CHB patients in China was Viread, but the cost of long-term treatment with Viread is high; therefore, a more affordable TDF drug with comparable performance may provide a better choice for CHB patients in China. Qingzhong is such a TDF drug. Therefore, in this 96-wk-long clinical trial, we comparatively evaluated the efficacy and safety of Qingzhong and Viread in Chinese CHB patients and did not observe any significant differences between the two drugs ($P > 0.05$).

Specifically, both HBeAg (+) and HBeAg (-) participants exhibited similar degrees of decrease in HBV DNA level after being treated with the two TDF drugs for 96 wk. At week 48, viral breakthrough was observed in one participant from each group, but no participant experienced viral breakthrough between weeks 48 and 96. The two patients who experienced viral breakthrough were treated with entecavir at the dose of 0.5 mg q.d. and were withdrawn from the study. These results suggest that continuous suppression of HBV DNA replication is beneficial to slow down the disease progression of CHB, as revealed by our COBAS TaqMan HBV assay, which has a lower limit of detection as low as 20 IU/mL. In addition, we observed comparable HBeAg loss and HBeAg seroconversion rates between Groups A and B. In summary, in terms of efficacy, our results demonstrated noninferiority between Qingzhong and Viread.

Although NAs can delay the progression of CHB to a certain extent, patients with CHB may eventually develop HCC. In our clinical trial, Participant 315 was found to have developed liver cancer at week 96 and was excluded from the study. Although

Table 7 Estimated glomerular filtration rate values in participants in the two groups

	Group	The median of eGFR	P value
Baseline	A	113.25 ± 19.11	0.651
	B	115.54 ± 18.68	
48 wk	A	111.87 ± 19.22	0.808
	B	115.35 ± 15.54	
96 wk	A	110.00 ± 17.90	0.164
	B	110.49 ± 16.92 ¹	

¹In group B, there was a significant difference in estimated glomerular filtration rate between the baseline value and the value at 96 wk ($P < 0.05$). eGFR: Estimated glomerular filtration rate.

Table 8 Urine neutrophil gelatinase-associated lipocalin levels in trial participants at baseline and at week 96

	Urine NGAL	Z	P value
Baseline	1.69 ± 2.38	3.79	< 0.01
96 wk	3.73 ± 11.48		

NGAL: Neutrophil gelatinase-associated lipocalin.

the HCC of the participant was determined to be unrelated with the use of TDF drugs, it reminded us to closely monitor liver cancer development in CHB patients, even in antiviral treatment responders. In addition, kidney function changes should also be monitored during the long-term treatment with TDF drugs.

Our clinical trial has some limitations. First, the trial only lasted 96 wk. Therefore, we could not obtain longer-term data. As a result, we cannot guarantee the longer-term safety of the drugs based on the observed incidence of AEs. Fortunately, after this study, the patients could participate in an additional 3-year-long open-label trial with Qingzhong. Second, only one patient developed HCC during our 96-wk-long trial. Therefore, more data will be needed to establish the relationship between long-term treatment of CHB with NAs and the incidence of HCC. To address this issue, the authors are carrying out a study on the relationships among entecavir, TDF/tenofovir alafenamide, and HCC incidence in CHB patients.

CONCLUSION

This 96-wk-long phase III trial demonstrated noninferiority between Qingzhong and Viread in terms of effectiveness and safety in the treatment of Chinese patients with HBeAg (+) and HBeAg (-) CHB. Hence, Qingzhong may become a more affordable choice for long-term treatment of Chinese CHB patients with TDF drugs in the future.

ARTICLE HIGHLIGHTS

Research background

Tenofovir disoproxil fumarate (TDF) is a prodrug of a nucleotide analogue. As an antiviral drug, TDF has been proposed in the first-line treatment of chronic hepatitis B (CHB). The National Medical Products Administration has approved two brand names of TDF, namely, Qingzhong, which was commercialized by Jiangsu Chia-tai Tianqing Pharmaceutical Co Ltd., and Viread, which was commercialized by GlaxoSmithKline.

Research motivation

The safety and efficacy of Viread have been confirmed in previous trials. However, the cost of long-term treatment with Viread is high. As a generic TDF drug, Qingzhong

exhibited comparable efficacy and safety with Viread in the treatment of naive Chinese CHB patients during a 48-wk trial, thus providing a less expensive option for treating CHB. However, the long-run performance of Qingzhong in the treatment of CHB remains unevaluated.

Research objectives

To investigate the efficacy and safety of the two TDF agents in the treatment of Chinese CHB patients.

Research methods

This is a 5-year-long, multicenter, double-blinded, double-dummy, randomized-controlled, non-inferiority phase III trial, in which 330 Chinese CHB patients were finally included. The decrease in plasma level of hepatitis B virus (HBV) DNA was continuously monitored. In addition, viral suppression, alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) loss rates, and HBeAg seroconversion rates were also determined.

Research results

Among the 330 CHB patients involved in this trial, there were 232 HBeAg(+) CHB participants. For these participants, the decrease in mean HBV DNA level relative to the baseline value was comparable between Groups A and B at the 96th week. In addition, similar percentages of participants in the two groups exhibited undetectable levels of HBV DNA, HBeAg loss, and HBeAg seroconversion at the 96th week. Similar results were observed for the remaining 98 HBeAg(-) CHB participants: Similar degrees of reduction in mean HBV DNA level relative to the baseline and similar percentages of participants who had undetectable levels of HBV DNA were observed between the two groups at the 96th week. Finally, the two groups of participants [participants with both HBeAg(+) and HBeAg(-) CHB] presented with similar rates of ALT normalization and similar incidences of adverse events.

Research conclusions

This 96-wk-long phase III trial demonstrated the effectiveness and safety of utilizing Qingzhong in the treatment of Chinese patients with HBeAg (+) and HBeAg (-) CHB—the TDF drug showed comparable efficacy and safety with Viread. Hence, with its lower cost, Qingzhong may become a better choice for Chinese CHB patients who need long-term treatment with TDF drugs in the future.

Research perspectives

Since this study only elaborated the performance of Qingzhong during a 96-wk period, the longer-term safety and efficacy of the TDF drug remain unsure. Therefore, the longer-term performance of Qingzhong in the treatment of CHB patients warrants further attention.

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REFERENCES

- 1 **Schweitzer A**, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. *Lancet* 2015; **386**: 1546-1555 [PMID: 26231459 DOI: 10.1016/S0140-6736(15)61412-X]
- 2 **Tsai NC**, Marcellin P, Buti M, Washington MK, Lee SS, Chan S, Trinh H, Flaherty JF, Kitrinos KM, Dinh P, Charuworn P, Subramanian GM, Gane E. Viral suppression and cirrhosis regression with tenofovir disoproxil fumarate in Asians with chronic hepatitis B. *Dig Dis Sci* 2015; **60**: 260-268 [PMID: 25179493 DOI: 10.1007/s10620-014-3336-7]
- 3 **Liaw YF**. HBeAg seroconversion as an important end point in the treatment of chronic hepatitis B. *Hepatol Int* 2009; **3**: 425-433 [PMID: 19669245 DOI: 10.1007/s12072-009-9140-3]
- 4 **Wang FS**, Fan JG, Zhang Z, Gao B, Wang HY. The global burden of liver disease: the major impact of China. *Hepatology* 2014; **60**: 2099-2108 [PMID: 25164003 DOI: 10.1002/hep.27406]
- 5 **Sundaram V**, Kowdley K. Management of chronic hepatitis B infection. *BMJ* 2015; **351**: h4263

- [PMID: 26491030 DOI: 10.1136/bmj.h4263]
- 6 **Yu SJ**, Kim YJ. Hepatitis B viral load affects prognosis of hepatocellular carcinoma. *World J Gastroenterol* 2014; **20**: 12039-12044 [PMID: 25232241 DOI: 10.3748/wjg.v20.i34.12039]
 - 7 **European Association for the Study of the Liver**. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol* 2017; **67**: 370-398 [PMID: 28427875 DOI: 10.1016/j.jhep.2017.03.021]
 - 8 **Terrault NA**, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016; **63**: 261-283 [PMID: 26566064 DOI: 10.1002/hep.28156]
 - 9 **Sarin SK**, Kumar M, Lau GK, Abbas Z, Chan HL, Chen CJ, Chen DS, Chen HL, Chen PJ, Chien RN, Dokmeci AK, Gane E, Hou JL, Jafri W, Jia J, Kim JH, Lai CL, Lee HC, Lim SG, Liu CJ, Locarnini S, Al Mahtab M, Mohamed R, Omata M, Park J, Piratvisuth T, Sharma BC, Sollano J, Wang FS, Wei L, Yuen MF, Zheng SS, Kao JH. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. *Hepatol Int* 2016; **10**: 1-98 [PMID: 26563120 DOI: 10.1007/s12072-015-9675-4]
 - 10 **Society of Infectious Diseases**, Chinese Medical Association, Chinese Society of Hepatology, Chinese Medical Association. [The guidelines of prevention and treatment for chronic hepatitis B (2019 version)]. *Zhonghua Ganzang Bing Zazhi* 2019; **27**: 938-961 [PMID: 31941257 DOI: 10.3760/cma.j.issn.1007-3418.2019.12.007]
 - 11 **Marcellin P**, Heathcote EJ, Buti M, Gane E, de Man RA, Krastev Z, Germanidis G, Lee SS, Flisiak R, Kaita K, Manns M, Kotzev I, Tchernev K, Buggisch P, Weilert F, Kuras OO, Shiffman ML, Trinh H, Washington MK, Sorbel J, Anderson J, Snow-Lampart A, Mondou E, Quinn J, Rousseau F. Tenofovir disoproxil fumarate vs adefovir dipivoxil for chronic hepatitis B. *N Engl J Med* 2008; **359**: 2442-2455 [PMID: 19052126 DOI: 10.1056/NEJMoa0802878]
 - 12 **Heathcote EJ**, Marcellin P, Buti M, Gane E, De Man RA, Krastev Z, Germanidis G, Lee SS, Flisiak R, Kaita K, Manns M, Kotzev I, Tchernev K, Buggisch P, Weilert F, Kuras OO, Shiffman ML, Trinh H, Gurel S, Snow-Lampart A, Borroto-Esoda K, Mondou E, Anderson J, Sorbel J, Rousseau F. Three-year efficacy and safety of tenofovir disoproxil fumarate treatment for chronic hepatitis B. *Gastroenterology* 2011; **140**: 132-143 [PMID: 20955704 DOI: 10.1053/j.gastro.2010.10.011]
 - 13 **Pan CQ**, Trinh H, Yao A, Bae H, Lou L, Chan S; Study 123 Group. Efficacy and safety of tenofovir disoproxil fumarate in Asian-Americans with chronic hepatitis B in community settings. *PLoS One* 2014; **9**: e89789 [PMID: 24594870 DOI: 10.1371/journal.pone.0089789]
 - 14 **Buti M**, Tsai N, Petersen J, Flisiak R, Gurel S, Krastev Z, Aguilar Schall R, Flaherty JF, Martins EB, Charuworm P, Kitrinis KM, Subramanian GM, Gane E, Marcellin P. Seven-year efficacy and safety of treatment with tenofovir disoproxil fumarate for chronic hepatitis B virus infection. *Dig Dis Sci* 2015; **60**: 1457-1464 [PMID: 25532501 DOI: 10.1007/s10620-014-3486-7]
 - 15 **Marcellin P**, Zoulim F, Hézode C, Causse X, Roche B, Truchi R, Pauwels A, Ouzan D, Dumortier J, Pageaux GP, Bourlière M, Riachi G, Zarski JP, Cadranel JF, Tilliet V, Stern C, Pétour P, Libert O, Consoli SM, Larrey D. Effectiveness and Safety of Tenofovir Disoproxil Fumarate in Chronic Hepatitis B: A 3-Year, Prospective, Real-World Study in France. *Dig Dis Sci* 2016; **61**: 3072-3083 [PMID: 26821154 DOI: 10.1007/s10620-015-4027-8]
 - 16 **Liang RY**, Xu JH, Si CW, Wang S, Shang J, Yu ZJ, Mao Q, Xie Q, Zhao W, Li J, Gao ZL, Wu SM, Tang H, Cheng J, Chen XY, Zhang WH, Wang H, Xu ZN, Wang L, Dai J, Yu YY. A randomized, double-blind, double-dummy, controlled, multicenter study of Qingzhong (tenofovir disoproxil fumarate) vs Viread for the treatment of chronic hepatitis B: First-stage results at week 48. *Medicine (Baltimore)* 2019; **98**: e16778 [PMID: 31415381 DOI: 10.1097/MD.00000000000016778]



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