Poster Number

481

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Four Years Efficacy and Safety of Tenofovir Disoproxil Fumarate (TDF) in Asians with HBeAg-Positive and HBeAg-Negative Chronic Hepatitis B

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Introduction

- Tenofovir DF has demonstrated durable activity in 2 pivotal studies in chronic hepatitis B through 192 weeks (4 years) of treatment.
- Asian patients comprised a substantial subset of the participants in these studies
- Evaluation of efficacy and safety in Asian patients was considered important given the prevalence of HBV infection in this population

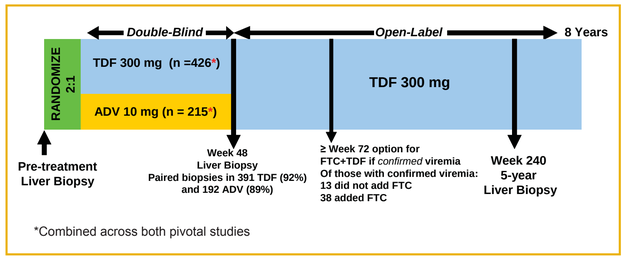
Objective

- To evaluate the efficacy and safety of tenofovir DF among Asian patients with chronic hepatitis B participating in tenofovir DF pivotal Studies 102 (HBeAg–) and 103 (HBeAg+)

Methods

- Patients were randomized 2:1 to double-blind tenofovir DF (TDF) 300 mg or adefovir dipivoxil (ADV) 10 mg once daily for 48 weeks
- Open-label tenofovir DF commenced at week 48 for those patients completing the double-blind phase
- Virologic (HBV DNA < 400 copies/mL [69 IU/mL]), biochemical, and serologic response were prospectively evaluated
- HBV DNA and safety laboratory parameters were performed every 4 weeks in year 1, every 8 weeks in year 2, and every 12 weeks thereafter with annual resistance surveillance
- Asian ethnicity was determined by self-report as recorded on the case report form

Figure 1. GS-US-174-0102 (HBeAg–) and GS-US-174-0103 (HBeAg+) Study Design



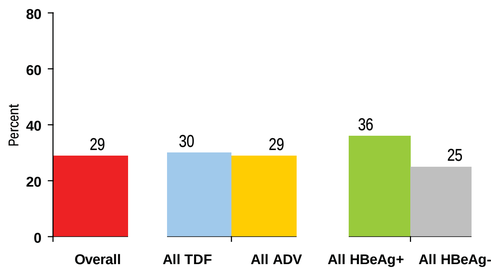
*Combined across both pivotal studies

Eligibility criteria required elevated ALT†, Knodell necroinflammatory score ≥ 3, and viremia with HBV DNA > 10^5 copies/mL with the Roche COBAS TaqMan assay (LLOQ=169 copies/mL [29 IU/mL])

(†Upper normal limit [ULN] 34 U/L for women; 43 U/L for men)

Figure 2. Asian Patients Participating in Pivotal Studies

- 189 Asians and 452 non-Asians were enrolled across the 2 studies
- Asians comprised ~30% of all patients
  - 127/426 (30%) on TDF
  - 62/215 (29%) on ADV
- Combined study results are presented to maximize sample size
- Of 178 Asian patients eligible to continue in the Open-Label extension, 163 entered the Open-Label phase and 89% completed 192 weeks



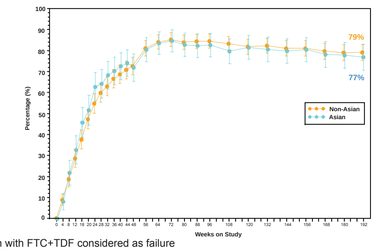
Results

Table 1. Baseline Characteristics

Characteristic	Asian (n = 189)	Non-Asian (n = 452)
Age, yr (SD)	40 (10.9)	40 (12.4)
Weight, Kg (SD)	64.8 (13.3)	79.0 (16.6)
Male, n (%)	129 (68.3)	344 (76.1)
HBV DNA, $\log_{10}$ copies/mL (SD)	7.66 (1.43)	7.66 (1.52)
HBeAg+, n (%)	95 (50.3)	171 (37.8)
Knodell necroinflammation score (SD)	8.5 (2.1)	7.8 (2.3)
Cirrhosis (Knodell=4)	18%	20%
ALT, U/L (SD)	142 (133.5)	143 (106.7)
Genotype A	6%	21%
B	38%	1%
C	52%	4%
D	3%	70%

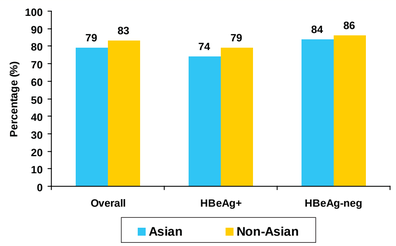
Values are means for continuous variables. ALT ULN= 34 U/L for women; 43 U/L for men

Figure 3. Percentage of Patients with HBV DNA < 400 copies/mL (69 IU/mL) (LTE-TDF)



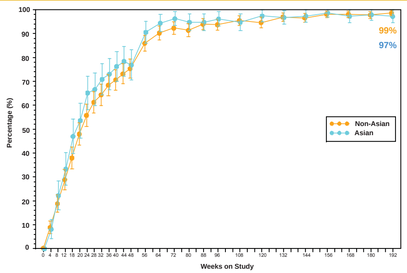
Long-term evaluation with FTC+TDF considered as failure
Error bars are 95% CIs.

Figure 4. Percentage of Patients with HBV DNA < 400 copies/mL (69 IU/mL) at Week 192 (ITT)



P ≥ 0.2 for all comparisons; includes FTC+TDF virologic response given additional subsetting. 7 Asian patients (3.7%) started FTC+TDF (none in year 4), 1 discontinued, and 4 of 6 remaining on study had HBV DNA <400 copies/mL

Figure 5. Percentage of Patients with HBV DNA < 400 copies/mL (69 IU/mL) (On-Treatment Analysis)



Error bars are 95% CIs.

Figure 6. Mean HBV DNA Over Time ($\log_{10}$ copies/mL)

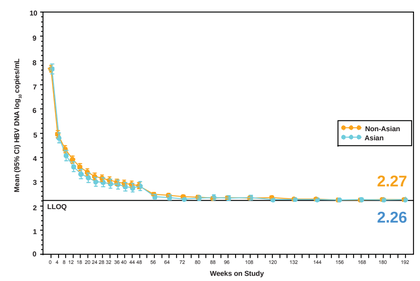
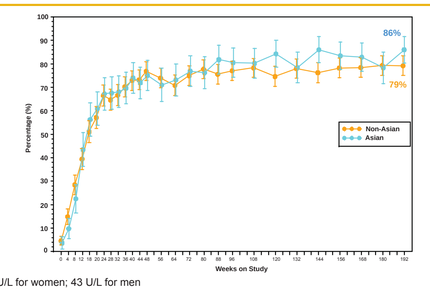


Figure 7. Percentage of Patients with Normal ALT (On-Treatment Analysis)



ALT ULN= 34 U/L for women; 43 U/L for men
Error bars are 95% CIs

Figure 8. Mean ALT Over Time

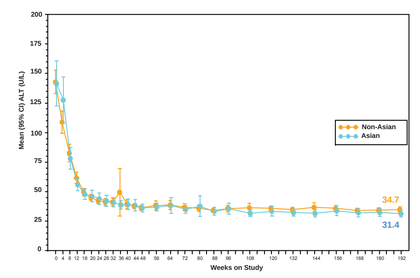
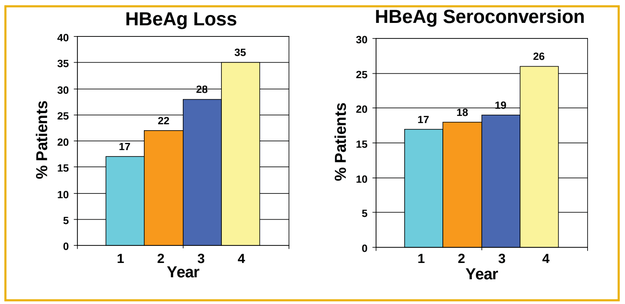


Figure 9. Serologic Response Among Asian Patients (On-Treatment Analysis)



No Asian patient lost HBsAg (23 non-Asians lost HBsAg). At Year 4 among non-Asians 45%/34% of those with Year 4 results had HBeAg loss/anti-HBe

Table 2. Safety and Tolerability During Open-Label TDF Treatment

Parameter	Asians* (n = 163)	Non-Asians* (n = 422)
Grade 3/4 AEs	17 (10.4%)	50 (11.8%)
AEs causing discontinuation	2 (1.2%)	5 (1.2%)
Serious AEs	10 (6.1%)	61 (14%)
Phosphorus < 2 mg/dL	1 (0.6%)	6 (1.4%)
Creatinine ≥ 0.5 mg/dL increase	1 (0.6%)	4 (0.9%)
CrCl < 50 ml/min	0 (0%)	1 (0.2%)

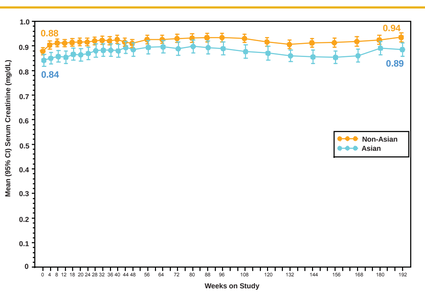
*Incidence of events during open-label TDF treatment across studies/original arms'
Among Asians 2 patients had AEs resulting in discontinuation: osteoporosis diagnosed by DXA (no baseline DXA, no fracture); sepsis in the setting of poorly differentiated nasopharyngeal carcinoma (fatal)

Table 3. Grade 3/4 Laboratory Values During Open-Label TDF Treatment

Parameter	Asians* (n = 163)	Non-Asians* (n = 422)
Any Grade 3/4 Abnormality	24 (14.7%)	67 (15.9%)
ALT	4 (2.5%)	11 (2.6%)
AST	4 (2.5%)	11 (2.6%)
Prothrombin time	3 (1.8%)	18 (4.3%)
Urine glucose	9 (5.5%)	17 (4.0%)
Creatine Kinase	7 (4.3%)	6 (1.4%)

*Incidence of events during open-label TDF treatment across studies/original arms
Note: Includes Grade 3/4 laboratory parameters occurring in > 1 Asian patient

Figure 10. Serum Creatinine Over Time



TDF Resistance Surveillance

- Comprehensive Week 192 resistance surveillance is presented in Poster 1365

Conclusions

- **TDF demonstrated durable antiviral activity, good tolerability, and no development of resistance over 192 weeks with no differences between Asian patients and non-Asian patients**
- **Antiviral efficacy and safety results in the Asian subset were similar to the overall studies**

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