Poster Number

980

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Tenofovir Disoproxil Fumarate (TDF) versus Adefovir Dipivoxil (ADV) in Asians with HBeAg-Positive and HBeAg-Negative Chronic Hepatitis B Participating in Studies 102 and 103

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Introduction

- Tenofovir DF has shown superior efficacy to adefovir dipivoxil in treatment-naïve patients with chronic hepatitis B in 2 pivotal studies
  - After 48 weeks of tenofovir DF treatment 76% of HBeAg-positive patients and 93% of HBeAg-negative patients had HBV DNA <400 copies/mL (c/mL)
- Asian patients comprised a substantial subset of the participants in these pivotal studies
- Evaluation of efficacy and safety in Asian patients was considered important given the prevalence of HBV infection in this population

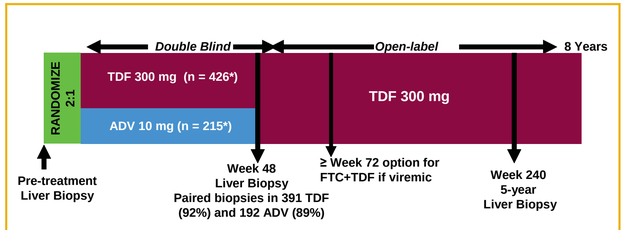
Objective

- To evaluate the efficacy and safety of tenofovir DF among Asian patients with chronic hepatitis B participating in tenofovir DF pivotal studies GS-174-0102 (HBeAg–) and GS-174-0103 (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 in studies GS-174-0102 (HBeAg–) and GS-174-0103 (HBeAg+)
- Virologic (HBV DNA < 400 c/mL [69 IU/mL]) and histologic response (≥ 2 point decrease in Knodell necroinflammation without worsening fibrosis) were prospectively evaluated
- HBV DNA and safety laboratory parameters were performed every 4 weeks through Week 48 with annual resistance surveillance
- Asian ethnicity was determined by self-report as recorded on the case report form

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



*Combined across both pivotal studies

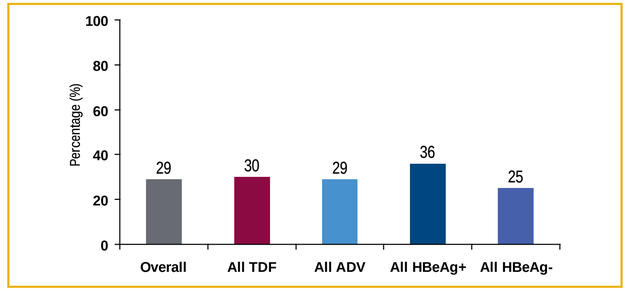
Eligibility criteria required elevated ALT*, Knodell necroinflammatory score ≥ 3, and viremia with HBV DNA > 10^5 copies/mL with the Roche COBAS TaqMan assay (LLOQ=169 copies/mL [29 IU/mL])

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

Methods (cont'd)

Figure 2. Asian Patients Participating in Pivotal Studies

- 189 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



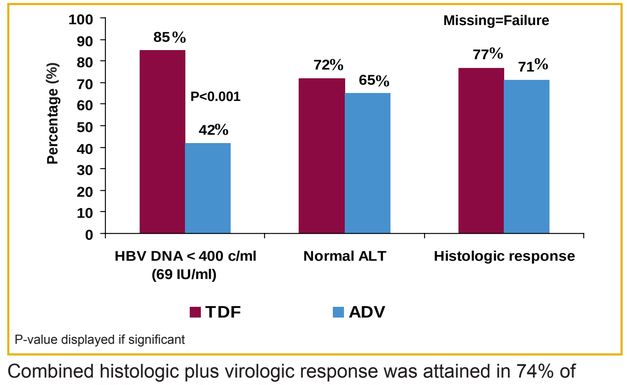
Results

Table 1. Asian Patients: Baseline Characteristics

Characteristic	TDF (n = 127)	ADV (n = 62)
Age (yr) (SD)	40 (10.8)	40 (11.2)
Weight Kg (SD)	63.1 (11.8)	68.5 (15.3)
Male n (%)	84 (66)	45 (73)
HBV DNA $\log_{10}$ copies/mL	7.55 (1.43)	7.88 (1.43)
HBeAg+ HBeAg–	62 (49%) 65 (51%)	33 (53%) 29 (47%)
Knodell necroinflammation Cirrhosis (Knodell=4)	8.5 (2.1) 17%	8.5 (2.1) 21%
ALT U/L (SD)	137.1 (131.3)	150.7 (138.6)
Genotype A B C D	7 (6%) 44 (35%) 64 (50%) 7 (6%)	4 (6%) 26 (42%) 30 (48%) 1 (2%)

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

Figure 3. Results- Efficacy at Week 48

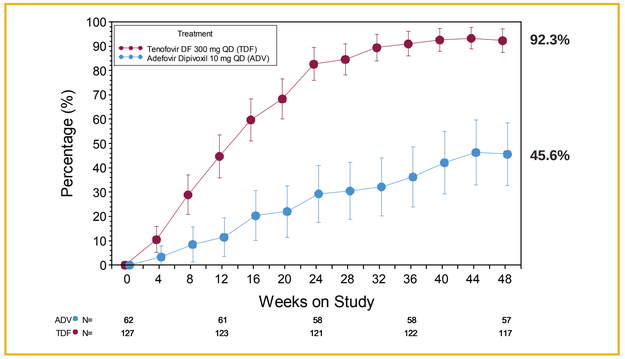


P-value displayed if significant

Combined histologic plus virologic response was attained in 74% of Asians on TDF and 34% on ADV (p < 0.001)
No patient lost HBsAg
16% developed anti-HBe in both treatment arms (last observation carried forward)

Results (cont'd)

Figure 4. Observed Percentage of Asian Patients With HBV DNA < 400 copies/mL (69 IU/mL)



Error bars are 95% confidence intervals (CI).

In the missing=failure analysis at Week 24, 78.7% of TDF-treated Asian patients and 27.4% of ADV-treated Asian patients had HBV DNA < 400 c/mL (69 IU/mL).

Figure 5. Asian Patients: Mean HBV DNA by Week of Study

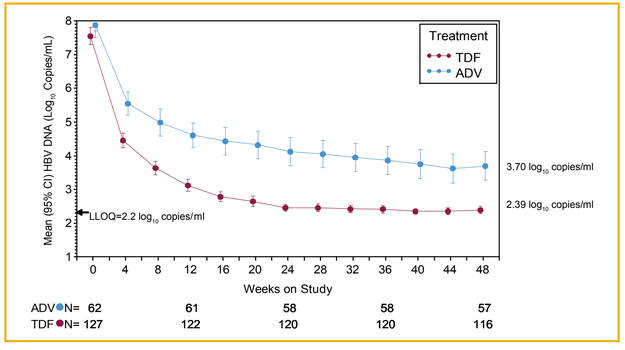
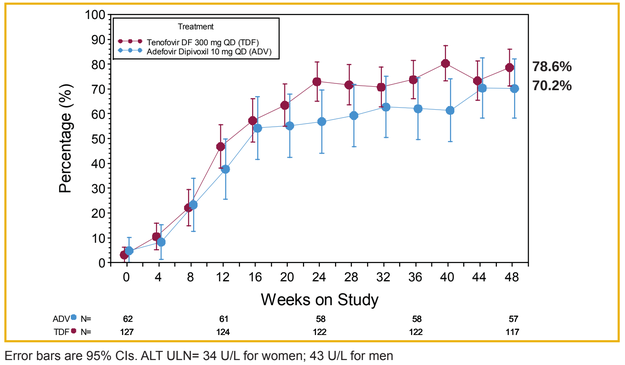


Figure 6. Observed Percentage of Asian Patients With Normal ALT



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

In the missing=failure analysis at Week 24, 70.1% of TDF-treated Asian patients and 53.2% of ADV-treated Asian patients had normal ALT

Table 2. Safety and Tolerability in Asian Patients Through Week 48

Parameter	TDF (n = 127)	ADV (n = 62)
Grade 2 AEs	27 (21.3%)	17 (27.4%)
Grade 3 AEs	7 (5.5%)	3 (4.8%)
Grade 4 AEs	4 (3.1%)	1 (1.6%)
Serious AEs	6 (4.7%)	2 (3.2%)
Grade 3: ALT AST Amylase	11 (8.7%) 3 (2.4%) 7 (5.5%)	3 (4.8%) 2 (3.2%) 0 (0%)
Grade 4: ALT Creatine kinase	3 (2.4%) 3 (2.4%)	1 (1.6%) 2 (3.2%)
Phosphorus < 2 mg/dl	0 (0%)	0 (0%)
Creatinine ≥ 0.5 mg/dl increase	0 (0%)	0 (0%)
CrCl < 50 ml/min	0 (0%)	0 (0%)

Specific Grade 3 or 4 laboratory analytes included if present in > 2 Asian patients in either arm

No Asian patient on TDF had treatment-emergent fracture

TDF Resistance Surveillance:

- No HBV polymerase/reverse transcriptase amino acid substitutions associated with resistance to tenofovir were detected at Week 48 in any patient (see Poster 977 for details to Week 96)
- Across both pivotal studies 10 Asian patients had HBV DNA ≥ 400 copies/mL (≥ 69 IU/mL) at Week 48, which included 4 Asians with a virologic breakthrough* 3 of whom were non-adherent

(*Confirmed 1 $\log_{10}$ increase in HBV DNA from nadir or increase to ≥ 400 copies/mL)

Conclusions

- **TDF demonstrated superior HBV DNA suppression relative to ADV in Asian patients following 48 weeks of randomized treatment**
- **Efficacy, safety and resistance analyses were consistent with the results of the overall studies following 48 weeks of randomized treatment**

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