



**Samuel Lee, MD**  
**University of Calgary**

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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

SS Lee<sup>1</sup>, E J Heathcote<sup>2</sup>, W Sievert<sup>3</sup>, H Trinh<sup>4</sup>, K Kaita<sup>5</sup>, Z Younossi<sup>6</sup>,  
J George<sup>7</sup>, M Shiffman<sup>8</sup>, P Marcellin<sup>9</sup>, J Sorbel<sup>10</sup>,  
J Anderson<sup>10</sup>, E Mondou<sup>10</sup>, J Quinn<sup>10</sup>, and F Rousseau<sup>10</sup>

<sup>1</sup>University of Calgary, Calgary, AB, Canada; <sup>2</sup>Toronto Western Hospital,  
University of Toronto, Toronto, ON, Canada; <sup>3</sup>Monash University, Melbourne, VIC, Australia;  
<sup>4</sup>San Jose Gastroenterology, San Jose, CA, USA; <sup>5</sup>University of Manitoba Health Science Center, Winnipeg, MB, Canada;  
<sup>6</sup>Inova Fairfax Hospital, Falls Church, VA, USA; <sup>7</sup>Westmead Hospital and University of Sydney, Westmead, NSW, Australia;  
<sup>8</sup>Virginia Commonwealth University Medical Center, Richmond VA, USA; <sup>9</sup>Hopital Beaujon, Clichy, France; <sup>10</sup>Gilead  
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# Introduction

- Tenofovir DF has superior efficacy to adefovir dipivoxil (ADV) in treatment-naïve chronic hepatitis B in 2 pivotal studies
  - At 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) [<69 IU/mL]
- Asians comprised a substantial subset of the patients in these pivotal studies
- Evaluation of efficacy and safety in Asian patients is important given the high prevalence of HBV in this population

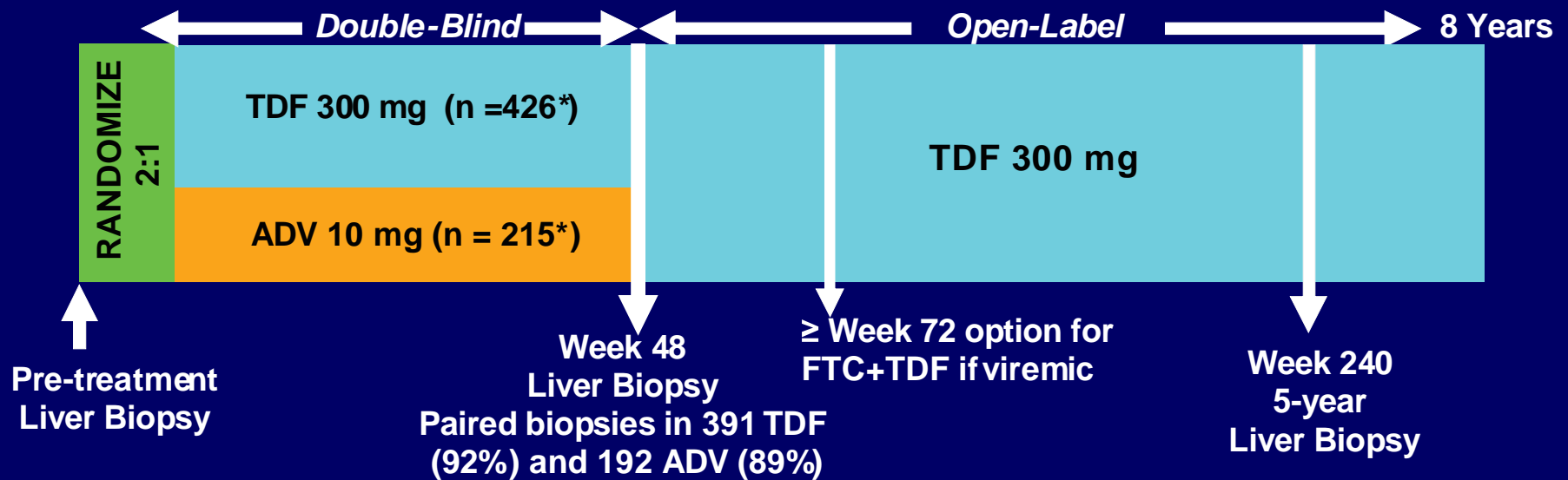
# Objective

- Evaluate efficacy and safety of tenofovir DF among Asian patients with chronic hepatitis B participating in tenofovir DF pivotal studies GS-174-0102 (HBeAg<sup>-</sup>) and GS-174-0103 (HBeAg<sup>+</sup>)

# Methods

- 2:1 randomization 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 ( $\geq 2$  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 self-reported on the case report form

# GS-174-0102 (HBeAg-) and GS-174-0103 (HBeAg+) Study Design



\*Combined across both pivotal studies

Eligibility criteria required elevated ALT\*, Knodell necroinflammatory score  $\geq 3$ , 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)

# Asian Patients Participating in Pivotal Studies

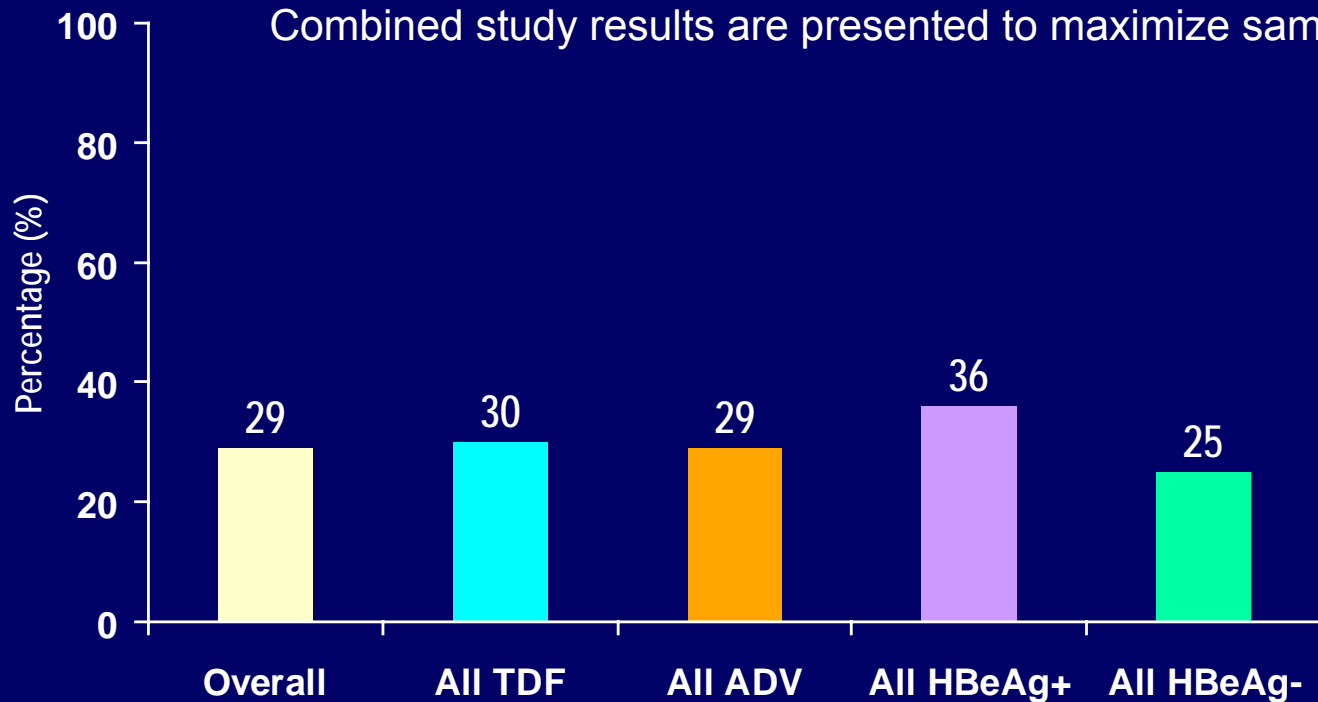
189 Asians were enrolled across the 2 studies

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

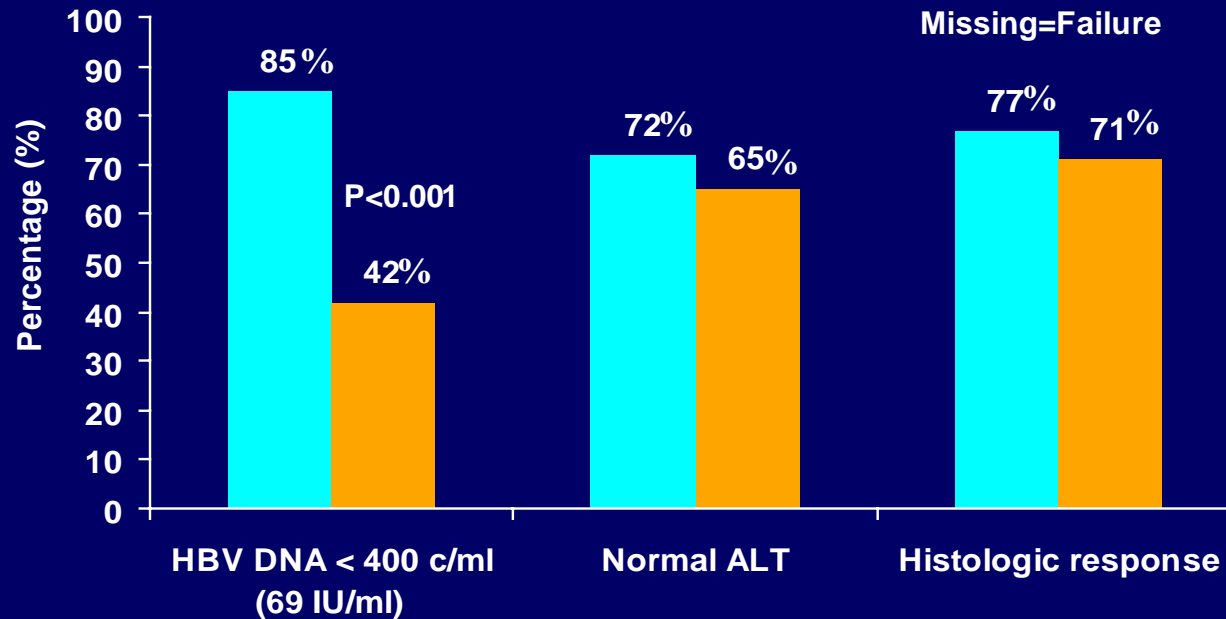


# Asian Patients: Baseline Characteristics

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

Values are means (SD). ALT ULN = 34 U/L for women; 43 U/L for men

# Results–Efficacy at Week 48 in Asians



P-value displayed if significant

■ TDF

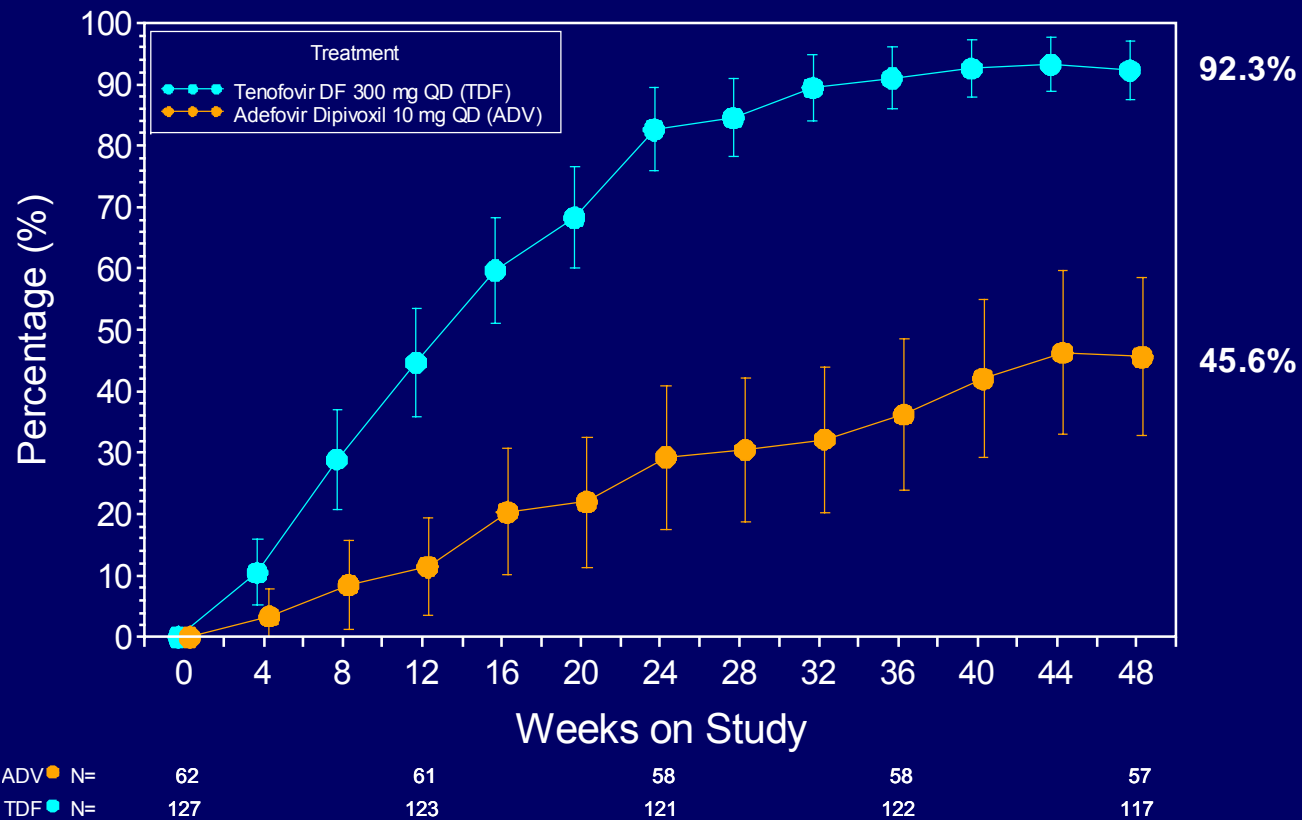
■ ADV

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)

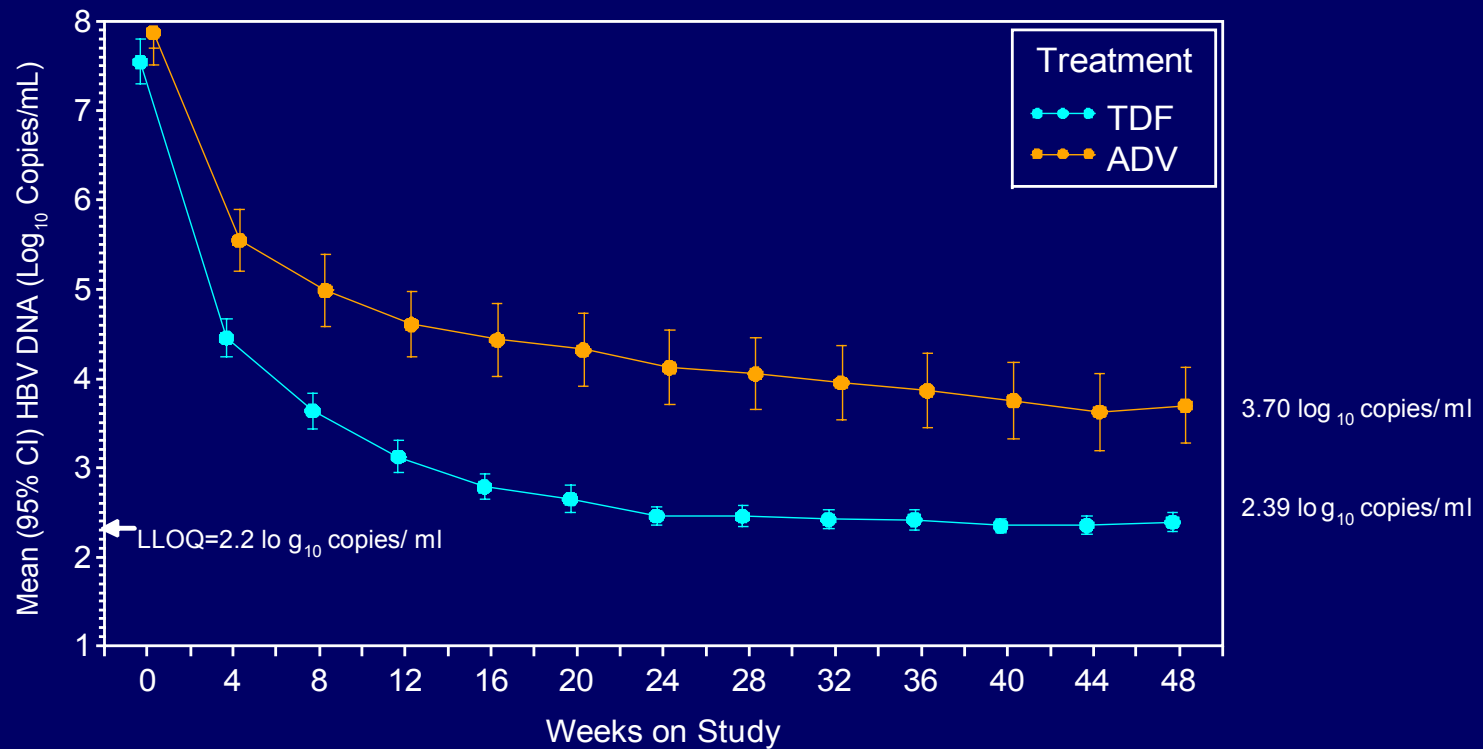
# Observed Percentage of Asian Patients With HBV DNA < 400 copies/mL (69 IU/mL)



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).

# Asian Patients: Mean HBV DNA by Week of Study



ADV ● N= 62  
TDF ● N= 127

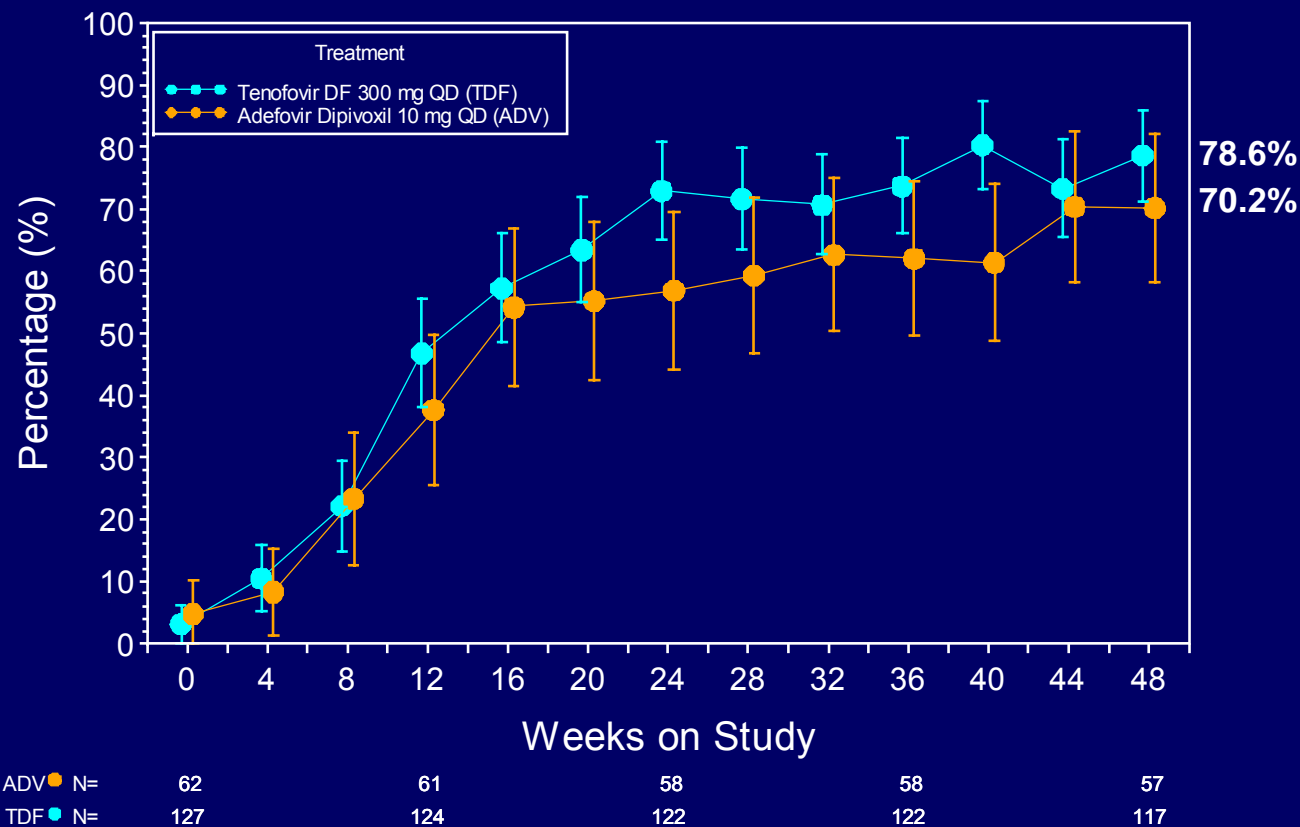
61  
122

58  
120

58  
120

57  
116

# Observed Percentage of Asian Patients With ALT Within Normal Range



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

# 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	11 (8.7%)	3 (4.8%)
AST	3 (2.4%)	2 (3.2%)
Amylase	7 (5.5%)	0 (0%)
Grade 4: ALT	3 (2.4%)	1 (1.6%)
Creatine kinase	3 (2.4%)	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 had a fracture on TDF

# TDF Resistance Surveillance in Asians

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

\*Defined as a confirmed  $1\log_{10}$  increase in HBV DNA and/or confirmed HBV DNA  $\geq 400$  copies/mL after having  $< 400$  copies/mL

# Conclusions

- **TDF demonstrated superior HBV DNA suppression relative to ADV in Asian patients at 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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