**Introduction**

- Tenofovir DF (TDF) approved for HIV-1 in 2001 and chronic hepatitis B (CHB) in 2008:
  - 3.5 million patient-years
- Week 48 Phase 3 data showed a significantly greater antiviral activity of TDF compared to adefovir dipivoxil (ADV) in HBeAg-negative patients:
  - 93% vs 63% HBV DNA <400 copies/mL
- TDF treatment in HBsAg-negative patients after Week 48 shown:
  - Both viremic and nonviremic patients on ADV can effectively switch to TDF and achieve or maintain viral suppression (HBV DNA <400 copies/mL) and normal ALT at week 144
- TDF patients treated for 144 weeks maintained HBV DNA <400 copies/mL and normal ALT levels

**Objectives**

- Evaluate the efficacy and safety of up to 4 years of TDF therapy in HBsAg-negative patients

**Methods**

- 100% of patients who entered the open-label extension were included in the analyses of HBV DNA and ALT.
- Patients who added emtricitabine (FTC) were considered failures for all time points following FTC addition.
- Patients discontinued the study early and missing data due to death, safety, tolerability, or efficacy: loss to follow-up; or for any other reason who were failures for the endpoint or had an ongoing AE at the last on-study visit were considered failures.
- Patients who added FTC were considered failures for all time points following FTC addition.
- Includes only those patients who entered the open-label extension.

**Assessments During Year 4**

- HBsAg, HBV DNA, and safety laboratory analyses every 12 weeks
- Resistance surveillance for patients with HBV DNA ≥400 copies/mL (86% IL28B).

**Statistical Methods**

- Long-Term Evaluation, TDF only analysis (LTE-TDF):
  - Patients discontinuing the study early and missing data due to death, safety, tolerability, or efficacy: loss to follow-up; or for any other reason who were failures for the endpoint or had an ongoing AE at the last on-study visit were considered failures.
- Patients who added FTC were considered failures for all time points following FTC addition.
- Includes only those patients who entered the open-label extension.
- Long-Term Evaluation, TDF only analysis (LTE-TDF):
  - Includes only those patients who entered the open-label extension.
  - Employment of intent-to-treat analysis.
  - Patients who added FTC were considered failures for all time points following FTC addition.
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- Patients who added FTC were considered failures for all time points following FTC addition.
- On-Treatment Analysis [observed data, missing data excluding patients with missing data from both the numerator and denominator at each applicable time point for the analyses of HBV DNA and ALT.

**Results**

- **Figure 2. Patient Retention**
  - Tenofovir DF (TDF) approved for HIV-1 in 2001 and chronic hepatitis B (CHB) in 2008:
  - Significantly greater antiviral activity of TDF compared to adefovir dipivoxil (ADV) in HBeAg-negative patients:
  - 93% vs 63% HBV DNA <400 copies/mL
- **Figure 3. HBV DNA remains Suppressed with up to 4 Years of TDF Treatment**
  - % Patients with HBV DNA <400 copies/mL
- **Figure 4. Mean ALT (U/L) Over Time**
  - In ADV-TDF, patient increase at week 180 to peak of 1.3 mg/dL (and concurrent decrease in phosphorus to 0.8 mg/dL)
- **Figure 5. Serum Creatinine Over Time**
  - Randomized TDF
  - Double-Blind TDF
  - Open-Label TDF
- **Figure 6. On-Treatment Analysis**
  - % Patients with Normalized ALT On-Treatment: 80% TDF-TDF; 86% ADV-TDF

**Conclusion**

- With 84% retention at the end of Year 4 TDF demonstrated:
  - Potential antiviral activity with nearly 100% of patients on treatment at week 192 with HBV DNA <400 copies/mL
  - No development of resistance up to Year 4
  - Stable serum creatinine over time
  - Good tolerability over time

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