Introduction

Tenofovir disoproxil fumarate (tenofovir DF, TDF) is a nucleotide analog with potent antiviral activity in patients mono-infected with HIV and co-infected with HIV-1 and HIV-2. HIV pre-core/core (pre/ptc)/reverse transcriptase (RT) resistance mutations have been identified following administration of other one and two-drug HIV agents (tenofovir, didanosine, nucleoside analogs, etc.).

No amino acid substitutions associated with resistance to tenofovir DF were detected in the HIV pre/ptc/RT during the first 144 weeks of TDF treatment of HBeAg- and HBeAg+ patients in Studies 102 and 103.

Objectives

To identify amino acid substitutions in the HIV pol/RT following up to 192 weeks of therapy with TDF 300 mg twice daily.

To evaluate the effects of these substitutions on the clinical response to TDF monotherapy in chronic hepatitis B.

To determine whether these substitutions alter susceptibility to tenofovir using in vitro analyses and to evaluate the cross-resistance profiles of these substitutions.

Methods

Patients were enrolled in one of two double-blind, randomized studies of TDF [Study 102 (HBeAg+) or Study 103 (HBeAg-)].

- Genotypic analysis by population-diary sequencing of serum HIV pol/RT
- Phenotypic analyses were conducted in HepG2 cells transiently transfected with:• Plasma HBV DNA levels were determined by Roche COBAS TaqMan assay (LLOQ = 169 copies/mL; 29 IU/mL).

- Patients had the option of the duration of the investigation to add emtricitabine (FTC) 150 mg to TDF 300 mg if a new mutation conferring resistance at baseline or transitory. Study 102 was extended

- All patients were enrolled in study 101 (Cov HBeAg+ or negative) and were evaluable for analysis.

- The week 192 visit is out of window or missing HBV DNA values for 2 additional patients who added FTC; both patients had documented non-adherence during year 3 based on CDP data.

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