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## TENOFOVIR DISOPROXIL FUMARATE (TDF) AND ADEFOVIR DIPIVOXIL (ADV) ARE EFFECTIVE IN CHRONIC HEPATITIS B VIRUS (HBV) INFECTION IN SUBJECTS WHO ARE CO-INFECTED WITH HIV: HBV AND HIV DRUG RESISTANCE RESULTS OF ACTG PROTOCOL A5127

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**BACKGROUND:** TDF is a frequent component of HAART, and has anti-HBV activity. We analysed HBV and HIV drug resistance findings within A5127, a randomized, double-blind, placebo-controlled trial of TDF versus ADV in HBV- and HIV-co-infected subjects on stable HAART with serum HBV DNA  $\geq 100,000$  copies/ml and plasma HIV-1 RNA  $\geq 10,000$  copies/ml within 12 weeks prior to entry.

**METHODS:** 52 subjects received daily either ADV 10 mg or TDF 300 mg added to ongoing HAART for up to 96 weeks. The primary endpoint was reached and the study closed following a prespecified interim review. Sequencing from overlapping surface antigen and domains B-E of reverse transcriptase region of plasma HBV was performed (TruGene, RUO Version 1.0, Bayer). HIV *pol* genotyping (TruGene, Bayer) was done if plasma HIV RNA was  $\geq 500$  copies/ml.

**RESULTS:** At baseline, 75% of subjects had plasma HIV RNA  $< 50$  copies/ml and 98% had compensated liver disease; median CD4 count was  $467/\text{mm}^3$ ; median serum HBV DNA ( $\log_{10}$  copies/ml) was 8.85 (ADV arm) and 9.45 (TDF arm). 94% of enrolled subjects were 3TC-experienced. At interim analysis, mean DAVG<sub>48</sub> ( $\log_{10}$  copies/ml) was -3.12 on ADV and 4.03 on TDF. The 99.9% lower bound on the difference confirmed the noninferiority of TDF (*Conf Retroviruses Opportunistic Infect* 2005 Feb 22-25;12: [abstract 124](#)). At baseline, 47 (90%) subjects had a YMDD mutation in rt Domain C (either M204V or M204I) and had HBV genotypes: 38 (73%) A, 3 (6%) D, 2 (4%) F, and

9 (17%) G. 106 of 117 (91%) samples from all available timepoints had HBV YMDD rt codon substitutions; 102 of these 106 (96%) had compensatory L180 rt codon substitutions. No TDF-described A194T or ADV-associated A181V or N236T HBV substitutions were seen at entry or over maximum of 96 weeks. No HIV RT K70E mutations were detected. One subject (TDF arm) with low but detectable HIV during A5127 had HIV RT K65K at entry and K65R detected at week 48.

**CONCLUSIONS:** Both TDF and ADV were effective for HBV. No known or novel TDF- or ADV-associated HBV drug resistance mutations were detected during TDF or ADV therapy of HBV-infected subjects with HIV co-infection.

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