Lamivudine Is Not Effective in the Treatment of Non-Cirrhotic HBeAg (-) Chronic Hepatitis B Patients with Low Level Viremia

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351 LAMIVUDINE IS NOT EFFECTIVE IN THE TREATMENT OF NON-CIRRHOTIC HBeAg (–) CHRONIC HEPATITIS B PATIENTS WITH LOW LEVEL VIREMIA

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Background: A subgroup of non-cirrhotic e-minus chronic hepatitis B (CHB) patients shows persistent ALT abnormalities despite undetectable HBV DNA by hybridization assays. The effect of antiviral treatment in these patients is not well established. Very sensitive real-time PCR assays may have an impact in the evaluation of the treatment in these pts.
Patients and Methods: 18 HBeAg (–), HBV DNA < 5 pg/ml CHB patients with persistently elevated ALT levels were included. Fourteen of them received 1 year lamivudine treatment (150 mg/qd) while remaining 4 patients had at least 1 year of follow-up without any treatment. Four of 14 treated patients had also more than 1 year of follow-up period before lamivudine treatment. Hence, we compared 14 treatment periods with 8 control periods in a total of 18 patients. HBV DNA was measured by real-time PCR (100 copy/ml) at baseline and at the end of the treatment/control periods.
Results: Mean baseline HBV DNA levels of treatment vs. control periods were similar ($3.9 \times 104 \pm 9.6 \times 104$ vs. $8.4 \times 105 \pm 2.3 \times 106$, respectively). None of the lamivudine treated but two control patients had >2 log decrease at the end of the treatment/control periods. Two of 14 (14%) treated patients had ALT normalization while no change in ALT was observed during 8 control periods.
Conclusion: Lamivudine is not effective in the treatment of e-minus CHB patients with low level viremia. Lamivudine does not seem to further enhance the immune response-mediated inhibition of viral replication in these patients.

352 ADEFOVIR DIPIVOXIL SAFETY AND PHARMACOKINETICS IN SUBJECTS WITH HEPATITIS B VIRUS INFECTION AND IN HEALTHY SUBJECTS

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Background: Adefovir Dipivoxil (ADV) is being evaluated for the treatment of chronic hepatitis B (HBV) infection. The safety and pharmacokinetics (PK) of ADV in subjects with HBV were investigated and the effect of dosing with and without food was assessed. Food may alter ADV absorption.
Objectives: To evaluate the safety and PK of ADV in HBV patients, and evaluate the effect of food on ADV PK.
Methods: Fourteen HBV subjects received once daily oral dosing of ADV 10 mg, with PK samples measured after single and multiple doses. Eighteen normal subjects received 2 single doses of ADV 10 mg with and without a high fat meal (separated by 1 week washout), with PK measured after each dose. Safety was assessed via adverse events (AEs) and laboratory parameters.
Results: Fourteen HBV subjects (9 males, 5 females, mean age 40 Range: 23–68 years) and 18 normal subjects (10 males, 8 females, mean age 29 Range: 18–41 years) completed the studies. No serious AEs or discontinuations occurred with either group. ADV was well tolerated in all subjects. ADV PK in HBV subjects were similar following single (AUC 210 ng*hr/mL, Cmax 17.5 ng/mL) and multiple (AUC 204 ng*hr/mL, Cmax 18.3 ng/mL) dosing Cmax and AUC in HBV patients after single and multiple dosing were not different to those seen in healthy subjects (AUC 192 ng*hr/mL, Cmax 20.4 ng/mL).
Conclusion: ADV pharmacokinetics were similar in HBV and healthy subjects. There was no significant food effect, therefore ADV may be taken without regard to meals.

353 A DRUG-DRUG INTERACTION STUDY BETWEEN ADEFOVIR DIPIVOXIL AND LAMIVUDINE, ACETAMINOPHEN, IBUPROFEN AND TRIMETHOPRIM/SULFAMETHOXAZOLE

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Background: Coadministration of adefovir dipivoxil (ADV) and lamivudine (LAM) for the treatment of HBV-infection is currently being evaluated. In Phase 3 clinical trials of ADV, the most frequently coadministered medications were acetaminophen (APAP), ibuprofen (IBU) and antibiotics, including trimethoprim/sulfamethoxazole (TMP/SMX). It is important to understand the drug interaction potential of these agents with ADV, especially as APAP can cause hepatotoxicty and IBU can result in renal impairment.
Objectives: To determine whether coadministration of ADV 10 mg with LAM 100 mg QD, APAP 1000 mg QID, IBU 800 mg TID, or TMP/SMX 160/800 mg BID affected the steady-state pharmacokinetics (PK) of either drug such that dosing modifications would be required.
Methods: Each subject was randomized to an interaction cohort and the order of three treatments (ADV alone, ADV+test drug, test drug alone), each treatment separated by a 7-day washout. Alterations in PK (Cmax and AUC) were assessed using equivalence testing (coadministered vs. dosed alone).
Results: The PK of LAM, APAP, IBU, TMP/SMX were equivalent when dosed with ADV. There were no alterations in the PK of ADV when coadministered with these agents, except for when coadministered with IBU, where small increases in the Cmax (33%), AUC (23%), and urinary recovery (23%) were observed, without a change in renal clearance, suggesting enhanced bioavailability of adefovir.
Conclusions: The PK of ADV and LAM, APAP, and TMP/SMX were unaltered by their coadministration. IBU PK was unaffected by ADV. The small increase in adefovir exposure when dosed with IBU is not of sufficient magnitude to necessitate a change in dose.

354 EFFICACY OF A SHORT-SCHEDULE/HIGH DOSE HEPATITIS B VACCINATION IN DRUG USERS

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Objectives: To evaluate the response rates and compliance to 4 vaccination programs of Hepatitis B vaccination in drug users.
Methods: 908 cocaine/heroin users were randomised to 4 groups (2 schedules (standard (0, 4, 24 weeks) or shorter (0, 2, 4 weeks)) and 2 doses of vaccine (Recombivax 10 microg or 40 microg). Response was defined as levels of anti-HBsAg >10 IU/L. Compliance was determined as having received 3 injections of the vaccine.
Results: Compliance to the vaccination was better in the short schedule groups (73.7% vs 46.6%; $p < 0.001$; N = 771). Amongst these, 389 came back for anti-HBs measurement. Their overall response rate was 77.9%, lower than in the general population. The short schedule/high dose group developed comparable response rates to the standard schedule and dose group (82.4% vs 81.5%); the short schedule/standard dose had lower response rates (57.3%).

	Standard calendar	Short calendar
10 microg	81.5%	57.3%
40 microg	93.0%	82.4%

Chi2: 38.825 ($p < 0.000$)

Multivariate analysis showed that the 40 microg dose was positively associated to the response (OR: 4.731; CI 2.579–8.678) while HCV (OR: 0.300; CI 0.155–0.581) the short schedule (OR: 0.316; CI 0.174–0.573) and age