0-008

Adding adefovir compared with switching to entecavir in patients with lamivudine-resistant chronic hepatitis B (ACE study) - a multicenter prospective randomized study: final results

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Background: Management of lamivudine resistant chronic hepatitis B remains to be important issue, as inappropriate choice of treatment may cause multi-drug resistance. This study is designed to prospectively compare the efficacy of two strategies, combination of lamivudine and adefovir vs. entecavir monotherapy in patients with lamivudine resistance for a long term period.

Methods: 219 chronic hepatitis B patients who had been receiving lamivudine, and developed virologic and biochemical breakthrough were consecutively enrolled at 9 university hospitals between April 2007 and March 2009. Patients were followed up until March 2011.

Results: Baseline characteristics of the patients were not different between the groups. At month 24, HBV DNA PCR negativity (<60 IU/mL) was higher (56.7% vs. 40%, respectively; p=0.025) and degree of HBV DNA reduction was significantly greater in the adefovir and lamivudine combination group (n=110) compared to entecavir group (n=109) through the end of month 24 (-4.88 vs. -3.82 log IU/mL, respectively, p<0.001, repeated-measures ANOVA). Mean HBV DNA level was significantly lower in the adefovir and lamivudine combination group compared to the entecavir group through 24 month of the study for adefovir and lamivudine combination group respectively (3.45 [LdT+ADV] vs. 3.68 [LVD+ADV] log10 IU/mL; p=0.470). At week 12 and 24, the mean reduction in HBV DNA levels from baseline with LdT plus ADV were significantly higher than LVD plus ADV (-0.72 vs. +0.10 log10 IU/mL at week 12, -0.75 vs. -0.18 log10 IU/mL at week 24; p<0.001 and p=0.002, respectively). At week 12 and 24, more patients in the LdT+ADV-switch group than in the LVD+ADV-switch group had undetectable HBV DNA levels (6/27 (22.2%) vs. 0/26 (0%) at week 12, 10/30 (33.3%) vs. 3/30 (10.0%) at week 24; p=0.013 and p=0.029, respectively). One patient with LdT plus ADV treatment achieved HBeAg seroconversion. During treatment periods, there was no adverse event in both groups.

Conclusions: In this interim analysis, switching from LVD plus ADV to LdT plus ADV resulted in increased virological efficacy in HBeAg-positive LVD-resistant CHB patients with suboptimal virological response to LVD plus ADV.

Keyword: Hepatitis B virus (HBV); Chronic hepatitis B; Antiviral resistance; suboptimal response; Telbivudine; Lamivudine

0-009

A prospective randomized trial of switching to telbivudine plus adefovir in HBeAg-positive lamivudine-resistant chronic hepatitis B patients who have suboptimal response to lamivudine plus adefovir: interim analysis at 24 weeks.

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Background/Aims: Telbivudine (LdT) showed greater antiviral suppression than lamivudine (LVD) in phase II and III clinical trials. The present prospective randomized trial assessed the antiviral efficacy and safety of continuation of LVD plus adefovir (ADV) versus switch to LdT plus ADV in patients with HBeAg-positive LVD-resistant chronic hepatitis B (CHB) who shows suboptimal response to combination of LVD plus ADV therapy.

Methods: 110 HBeAg-positive CHB patients who received LVD plus ADV therapy for at least 6 months and remained HBV DNA detectable were 1:1 randomized to switch to LdT 600mg plus ADV 10mg daily or continue LVD 100mg plus ADV 10mg daily. 60 patients (LdT+ADV, n=30; LVD+ADV, n=30) completed the 24-week treatment period. HBV DNA levels, HBeAg status, liver biochemistry and safety were monitored.

Results: Duration of prior LVD plus ADV treatment was 17.8 (LdT+ADV) and 14.9 months (LVD+ADV) respectively (p=0.221). No difference was seen in baseline HBV DNA levels between two groups (3.45 [LdT+ADV] vs. 3.68 [LVD+ADV] log10 IU/mL; p=0.470). At week 12 and 24, the mean reduction in HBV DNA levels from baseline with LdT plus ADV were significantly higher than LVD plus ADV (-0.72 vs. +0.10 log10 IU/mL at week 12, -0.75 vs. -0.18 log10 IU/mL at week 24; p<0.001 and p=0.002, respectively). At week 12 and 24, more patients in the LdT+ADV-switch group than in the LVD+ADV-switch group had undetectable HBV DNA levels (6/27 (22.2%) vs. 0/26 (0%) at week 12, 10/30 (33.3%) vs. 3/30 (10.0%) at week 24; p=0.013 and p=0.029, respectively). One patient with LdT plus ADV treatment achieved HBeAg seroconversion. During treatment periods, there was no adverse event in both groups.

Conclusions: In this interim analysis, switching from LVD plus ADV to LdT plus ADV resulted in increased virological efficacy in HBeAg-positive LVD-resistant CHB patients with suboptimal virological response to LVD plus ADV.

Keyword: Hepatitis B virus (HBV); Chronic hepatitis B; Antiviral resistance; suboptimal response; Telbivudine; Lamivudine

0-010

Optimal management of clevudine resistant chronic hepatitis B: a multicenter cohort study