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Limited Sustained Response and Lack of HBsAg Decline after Stopping Long-Term Nucleos(t)Ide Analogue Therapy in Hbeag Negative Patients with Chronic Hepatitis B: Results of a Prospective, Randomized, Open-Label Phase IV Trial

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Abstract Text

Background: Chronic hepatitis B (CHB) patients often receive life-long therapy with nucleos(t)ide analogues (NA). In this prospective randomized controlled trial we assessed the proportion of patients with sustained response after stopping long-term entecavir (ETV) or tenofovir (TDF) therapy.

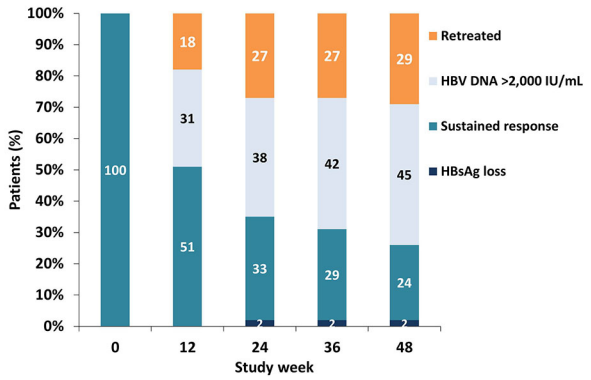
Methods: Patients at the Toronto Centre for Liver Disease were included if they had received ETV/TDF therapy for ≥1 year and achieved virologic suppression (defined as HBeAg seroconversion combined with undetectable HBV DNA ≥ 12 months in HBeAg positive patients, or undetectable HBV DNA ≥ 36 months for start of therapy HBeAg negative patients). Patients were then randomized 2:1 to stop or continue NA therapy for 72 weeks. Patients were retreated in case of persistent HBV DNA>20,000IU/mL, HBeAg seroreversion or HBV DNA>2,000 with ALT>5xULN (clinical relapse). Sustained response (HBeAg-negative, HBV DNA <2,000 IU/mL and normal ALT) at 48 weeks of follow-up was evaluated in both groups.

Results: Of 67 enrolled patients (60% male, 97% Asian), 45 (67%) patients were randomized to stop and 22 (33%) to continue NA therapy. 37/67 (55%) patients lost HBeAg on NA therapy. At randomization the mean duration of NA therapy was 8 (4) years and HBsAg level was 3.0 (0.7) log IU/mL. Sustained response was observed in 11/45 (24%) stop vs. 22/22 (100%) continue patients at week 48 (see Figure). Within the stop group 24/45 (53%) patients continued to have a normal ALT and HBeAg negative status. Fourteen (21%) patients developed ALT >10x ULN and another 7 (10%) had ALT >5x ULN.

HBsAg loss occurred in two patients (1 per group). Mean HBsAg decline from randomization to week 48 was 0.1 (0.0-0.3) vs. 0.0 (0.0-0.1) log IU/mL in stop vs. continue patients (p=0.50) and was not associated with peak ALT values after stopping (p>0.05). Among patients who stopped, 13/45 (29%) required retreatment by week 48 (6 had virologic relapse >20,000IU/mL and 7 had clinical relapse, of which 1 had HBeAg seroreversion). Median (range) time to retreatment was 12 (10-30) weeks. No patient experienced liver decompensation or died.

Conclusion: Forty-eight weeks after stopping NA therapy, only 24% of patients had a sustained response, while 74% had relapse and 2% had HBsAg loss. HBsAg levels in the stop group declined marginally and were not different from the NA continuation group. The findings of this prospective study in mainly Asian patients demonstrate no additional benefit of stopping NA therapy. Week 72 results will be presented at the Meeting.

Sustained response, retreatment and HBsAg loss in stop patients (n=45)



Disclosures

Kin Seng Liem – Merck: Speaking and Teaching

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