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Cessation of Nucleos(t)ide Analogue treatment after HBeAg seroconversion is associated with a 4-fold increased risk of relapse in cirrhotic compared to non-cirrhotic patients

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Background: Cessation of Nucleo(s)ide Analogue (NA) therapy after HBeAg seroconversion is associated with high relapse rates. Factors predictive for relapse in Caucasian patients are not well known. We investigated relapse rates and factors predictive for relapse after NA stop in a large multicenter cohort of HBeAg positive Chronic Hepatitis B (CHB) patients. **Methods:** This is a multicenter, pooled analysis of non-immune-suppressed HBeAg-positive, mono-infected CHB patients treated with different NA for ≥ 3 months. Data were collected between 1998 and 2017. Virologic relapse was defined as HBV DNA >2000 IU/mL; biochemical relapse as ALT $>2 \times$ ULN (with ULN = 40 IU/mL). Metavir score was histologically graded at start of treatment. Cox regression model was used to identify predictive factors for HBeAg seroconversion on treatment and relapse after treatment stop. Follow-up time was calculated as respectively time from treatment start to HBeAg seroconversion or last follow-up and time from HBeAg seroconversion to relapse or last follow-up. **Results:** A total of 356 patients (75.3% male; 63% Caucasian; 16% African) were included; 115 (32%) of whom showed HBeAg seroconversion after a median treatment time of 17.7 months.

Rapid, persistent HBV DNA suppression was predictive for HBeAg seroconversion (HR 0.955; $p < 0.001$ per month increment) when results were adjusted for the presence of cirrhosis, HBV DNA and ALT levels at start of treatment in a multivariate Cox regression model. Treatment was stopped in 70 patients (of whom 11 were cirrhotic at baseline) after HBeAg seroconversion and a subsequent median consolidation therapy of 8.8 months. The median follow-up duration after treatment stop was 3.0 years during which 30 patients (43%) showed relapse (16 solely virologic, 14 combined biochemical and virologic), necessitating retreatment in 22 cases. HBeAg seroreversion was observed in 6/30 (20%) relapsed patients. Multivariate Cox regression model showed that the presence of cirrhosis (HR 4.350; $p = 0.027$) at start of treatment predicted relapse after NA stop when results were adjusted for ethnicity and age at NA stop. In addition, relapse after NA stop was accompanied by liver-related death in two patients. **Conclusion:** In a predominant Caucasian population, treatment cessation after HBeAg seroconversion led to relapse in 43% of the patients within a median follow-up duration of 3.0 years. Presence of cirrhosis at start of treatment was associated with a 4-fold increased risk of relapse after treatment stop. Two relapsed patients showed severe clinical events leading to liver-related death.

Disclosures:

Stefan Bourgeois - Advisory Committees or Review Panels: MSD, AbbVie, Gilead; Speaking and Teaching: BMS

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Regulation of antiviral CD8 T cell response by MMP mediated soluble CD100 releasing in HBV infection

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CD100 is the first semaphorin described to have immune functions and serves important roles in T cell responses. Proteolytic cleavage of CD100 from the cell surface by matrix metalloproteinases (MMPs) gives rise to a soluble fragment of CD100 (sCD100), which is also thought to have immunoregulatory properties. In this study, we characterized the expression and the possible role of CD100/sCD100 in regulating antiviral response during HBV infection in patients and HBV-replicating mouse model. We found that surface CD100 expression on T cells of chronic Hepatitis B (CHB) patients was significantly increased compared to that of healthy controls (HC). Meanwhile, CHB patients showed significantly lower concentrations of serum sCD100 than HC. Correspondingly, decreased surface CD100 expression on T cells in PBMCs and elevated serum sCD100 levels were