respectively. The seroprotection rate was significantly higher in Group 1 at 12-month (Group 1 vs. Group 2 vs. Group 3 = 100% vs. 87% vs. 77.8%; P=0.047). There was no difference in the seroprotection rate among the three groups at 1 and 6-month. However, the GMT anti-HBs was significantly higher in Group 1 at 6 and 12-month, (6-month: Group 1 vs. Group 2 vs. Group 3 = 373.3 IU/L, 95% CI 177.8-783.4 IU/L vs. 169.8 IU/L, 95% CI 62.5-462.4 IU/L; vs. 76 IU/L, 95% CI 33.3-174.2 IU/L; P=0.026; (12-month: Group 1 vs. Group 2 vs. Group 3 = 3191.5 IU/L, 95% CI 1207.8-8433.3 IU/L vs. 818.5 IU/L, 95% CI 225.9-2964.8 IU/L; vs. 58.5 IU/L, 95% CI 28.7-118.9 IU/L; P<0.0001). Overall side effects were few and self-limiting with no difference among the three groups. **Conclusion:** Topical imiquimod before intradermal HBVv was highly effective in OBI patients, with significantly higher seroprotection rate and GMT at 12 months after vaccination. This vaccination strategy could effectively prevent hepatitis B virus reactivation in OBI patients.

Disclosures:

James Fung – Novartis: Grant/Research Support

Man-Fung Yuen – Abbvie: Advisory Committee or Review Panel; Arrowhead: Grant/Research Support; Bristol Myers Squibb: Grant/Research Support; Gilead: Advisory Committee or Review Panel; Fujerubio: Speaking and Teaching; Roche: Advisory Committee or Review Panel; MSD: Advisory Committee or Review Panel

The following people have nothing to disclose: Ivan FN Hung, Danny Ka Ho Wong

Disclosure information not available at the time of publication: Wai-Kay Seto, Kwok-Yung Yuen

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Efficacy of Pegylated Interferon α-2a Therapy for HBsAg ≤1500 IU/Ml CHB Patients with a Prior Nas History

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Background: HBsAg clearance with or without seroconversion is a ideal goal of antiviral therapy for chronic hepatitis B virus (CHB) patients. However, the clearance rate is extremely low with nucleos(t)ide analogs (NAs) or interferon monotherapy. We comprehensively evaluated that the efficacy of pegylated interferon α-2a (Peg-IFNα-2a) therapy for HBsAg ≤1500 IU/mL CHB patients with a prior NAs history, which will provide a more optimized treatment plan for CHB patients. **Methods:** 185 HBeAg-negtive CHB patients under persistent virological suppression and HBsAg ≤1500 IU/mL after more than 1 year of NAs therapy were enrolled, which were randomly divided into the trial group (n=85) and the control group (n=100). Patients in trial group received NAs combined with Peg-IFNα-2a treatment for 48 weeks and followed-up for 24 weeks. Patients in control group received NAs monotherapy continuously. HBsAg clearance and seroconversion rates at week 72 were used to evaluate the therapeutic efficacy. **Results:** Per-protocol (PP) analysis showed that HBsAg clearance and seroconversion rate in the trial group were 28.2% and 20.0% at week 48, increased to 40.0% and 32.0% at week 72. However, the HBsAg clearance rate in control group were 1.0% at week 48 and 2.0% at week 72, and no patient achieved seroconversion (Figure 1). In the trial group, the proportions of patients who achieved HBsAg ≤1000 IU/mL, ≤ 100 IU/mL, ≤ 10 IU/mL at week 72 were 100.0%, 76.0%, 58.0%, respectively, while the proportions were 25.0%, 17.0%, 9.0% in the control group, respectively. Baseline HBsAg <500 IU/mL, HBsAg <200 IU/mL at 24 weeks treatment, ALT≥2 ULN at the early 12 weeks treatment were independent predictors of HBsAg clearance. The incidence of common adverse events (including headache, alopecia, and pyrexia) were similar to previous studies and all patients had good tolerance to these treatments in the trial group. **Conclusion:** For HBeAg-negtive CHB patients under persistent virological suppression and HBsAg ≤1500 IU/mL after more than 1 year of NAs therapy, combining with Peg-IFNα-2a therapy for 48 weeks is a more optimized treatment plan for CHB patients.

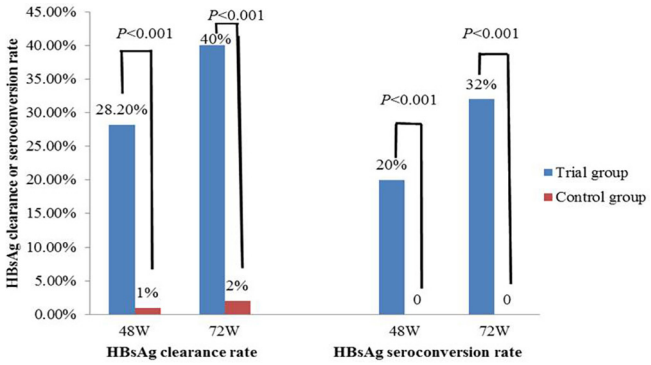

Figure . The HBsAg clearance and seroconversion rates in CHB patients.

Disclosures:

The following people have nothing to disclose: Juanjuan Shi

Disclosure information not available at the time of publication: Fengping Wu, Yaping Li, Mei Li, Wenjun Wang, Xiaoli Jia, Xin Zhang, Shuangsuo Dang

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The Determination of Tenofovir Level in Breast Milk of Nursing Mothers Under Tenofovir Therapy

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Background: In this study, we aimed to determine of tenofovir concentration in maternal plasma, breast milk and plasma of infants and factors affecting drug levels in chronic hepatitis B (CHB) patients using tenofovir disoproxil fumarate (TDF) during breastfeeding period. **Methods:** Patients followed up or transferred to Istanbul University Cerrahpasa Medical Faculty Infectious Diseases and Clinical Microbiology Department for CHB and who had recevied TDF at least for one month during breastfeeding period between 2014-2017 years were enrolled in this study. A total of 11 mother infant pairs had been included in this study. Maternal blood, breast milk and infant blood samples were obtained simultaneously from mother and infant pairs. Tenofovir concentrations were determined by liquid chromatography tandem mass spectrometry (LC-MS / MS) method **Results:** Tenofovir concentrations were determined at a range of 4-600 ng / mL. The median concentrations of tenofovir in maternal plasma and breast milk samples were 88,44 (IQR: 62,47-116,17) ng / mL, 6,69 (IQR: 4,88-7,03) ng /mL, respectively. Tenofovir

concentrations in all of the infant plasma samples were determined as 0 ng/mL. The ratio of tenofovir concentration in breast milk/maternal plasma was determined as 0,07. There was a strong and statistically significant relationship between the concentration of tenofovir in breast milk and maternal plasma (r: 0,7 p <0,05). There was no significant relationship between tenofovir concentrations and age, height and weight of the mothers, infant's age, duration of TDF use and time of the last TDF dose. **Conclusion:** This study demonstrated that TDF use during breastfeeding due to CHB, leads to passage of small amount of tenofovir to the breast milk and no any detectable drug is present in the infant's systemic circulation. These results suggest that use of TDF is safe during the breastfeeding period, but a wider cohort study evaluating whether any side effects will develop or not in the long term in infants is required.

Number of Patients	Concentration of tenofovir in maternal blood (ng/mL)	Concentration of tenofovir in breast milk (ng/mL)	Concentration of tenofovir in infant blood (ng/mL)
1	88.443	6.95	0
2	79.001	4.88	0
3	93.431	4.44	0
4	49.890	5.05	0
5	115.836	8.10	0
6	116.175	7.03	0
7	57.788	6.75	0
8	62.475	5.71	0
9	87.719	4.86	0
10	162.621	10.00	0
11	133.994	6.69	0

Disclosures:

The following people have nothing to disclose: Umran Sumeyse Erturk, Bahar Kacmaz

Disclosure information not available at the time of publication: Bilgul Mete, Resat Ozaras, Nese Saltoglu, Ilker Inanc Balkan, Ali Mert, Onursal Saglam, Berrak Guney, Ozden Aksu Sayman, Fehmi Tabak

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MMP2/MMP9 Mediated CD100 Shedding Is Crucial for Inducing Intrahepatic Anti-HBV CD8 T Cell Response and HBV Clearance

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Background: CD100 is the first semaphorin described to have immune functions and serves important roles in inducing 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 though to have immunoregulatory properties. **Methods:** In this study, we characterized the possible role of CD100 in regulating antiviral response during HBV infection in patients and HBV-replication mouse model. **Results:** We found that chronic Hepatitis B (CHB) patients showed significantly higher membrane CD100 (mCD100) expression on T cells and significantly lower sCD100 levels in serum than healthy controls (HC). Consistently, decreased mCD100 expression on T cells in PBMCs and elevated serum sCD100 levels were observed during the course of HBV clearance in HBV replicating mice but not in HBV-persistent mice. Both in vitro and in vivo sCD100 treatment could induce dendritic cell and liver sinusoidal endothelial cell activation and enhance effector T cell response. Importantly, in vivo sCD100 treatment led to enhanced intrahepatic anti-HBV CD8 T cell response and accelerated viral clearance in HBV-persistent mice. In vitro sCD100 treatment could also enhance HBV-specific CD8 T cells response in CHB patients. Blockade of the interaction between CD100 and its ligand CD72 attenuated anti-HBV CD8 T cell responses in the spleen and liver in HBV replication mice. Next, we further investigated the possible mechanism involved in mCD100 shedding and sCD100 formation during HBV infection. Our results demonstrated that MMP2 and MMP9 are responsible for the cleavage of CD100 from the surface of T cells in CHB patients. Significantly lower serum MMP2 but not MMP9 levels were observed in CHB patients than HC, and a positive correlation between serum sCD100 and MMP2 levels was observed. Consistently, elevated MMP2 expression in the liver was observed during the course of viral clearance in HBV replication mice. Specific inhibition of MMP2 and MMP9 activity resulted in decreased sCD100 levels, attenuated anti-HBV CD8 T cell response and delay HBV clearance in mice. **Conclusion:** In conclusion, our results demonstrate that MMP2/MMP9 mediated mCD100 shedding and sCD100 formation is crucial for the induction of antiviral T cell response and viral clearance during HBV infection. Our study provides a new mechanism to elucidate HBV persistence and a new potential target for developing strategies to overcome T cell tolerance in chronic HBV infection.

Disclosures:

The following people have nothing to disclose: Shangqing Yang, Dongliang Yang

Disclosure information not available at the time of publication: Lu Wang, Jia Liu

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Hepatitis B Patients Under Oral Nucleos(t)Ide Treatment with Intermittent Kidney Function Assessment (The BONIKA-Study) – 1-Year Follow up Data of a Multicenter, Prospective, Observational Trial (NCT-Nr. 02267473)

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Background: Infinite duration of nucleos(t)ide treatment of chronic hepatitis B (HBV) involves vulnerability for longterm toxicity. Monitoring of renal function by creatinine is deficient to detect early renal toxicity (mainly proximal tubular dysfunction) caused by longterm nucleos(t)ide analoga (NUC) treatment of chronic hepatitis B. To elucidate this matter an investigator initiated prospective trial monitoring renal tubular function in serum and urine in a cohort of patients under various oral antiviral HBV treatment was set up. This cohort is monitored on an annually basis. At present the 1-year-Follow-Up (1y-FU) data is completed. **Methods:** Between 10/2014 and 12/2016 HBV monoinfected patients (n=310) under NUC treatment were included after informed consent (t0) and then yearly screened for renal tubular dysfunction (RTD) by analyses of serum phosphate (sPh < 2,6 mg/dl)), serum uric acid (sUA < 3,4 mg/dl), urine alpha-1 microglobuline (uMG > 12 mg/l) and