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HEPATITIS B SURFACE ANTIGEN LOSS IN ANTIVIRAL-TREATED PATIENTS WITH HBEAG(+) CHRONIC HEPATITIS B (CHB) INFECTION: OBSERVATIONS FROM ANTIVIRAL-NAIVE PATIENTS TREATED WITH ENTECAVIR (ETV) OR LAMIVUDINE (LVD) Robert Gish¹, Ting-Tsung Chang², Ching-Lung Lai³, Robert de Man⁴, Adrian Gadano⁵, Fred Poordad⁶, Jin Zhu⁷, Joanna Yang⁷, Helena Brett-Smith⁷; ¹California Pacific Medical Center, San Francisco, CA; ²National Cheng Kung University Medical College, Tainan, Taiwan; ³Department of Medicine, University of Hong Kong, Hong Kong SAR, China; ⁴Erasmus MC, University Hospital Rotterdam, Hong Kong SAR, Netherlands; ⁵Hospital Italiano, Hepatologia, Buenos Aires, Argentina; ⁶Department of Hepatology and Liver Transplantation, Cedars-Sinai Medical Center, Los Angeles, CA; ⁷Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT

Background: Hepatitis B surface antigen (HBsAg) loss and HBsAg seroconversion are considered an important goal of HBV therapy but are seldom achieved with current treatments. We describe baseline characteristics and Wk 24 treatment responses of patients who demonstrated confirmed HBsAg loss by Wk 120 (on-treatment or during the 24-week follow-up period). **Methods:** A total of 709 nucleoside-naïve, HBeAg(+) patients received ETV 0.5 mg (n=354) or LVD 100 mg (n=355) once daily for a minimum of 52 Wks and maximum of 96 Wks in the randomized, double-blind ETV-022 trial. Entry criteria included: biopsy-confirmed liver disease, serum HBV DNA by bDNA levels ≥ 3 MEq/mL, ALT levels 1.3-10 x ULN and no prior nucleoside therapy >12 Wks. Serum HBV DNA, HBV serology (HBeAg/anti-HBe) and ALT were measured on treatment and through 24 weeks off-treatment. **Results:** HBsAg loss was confirmed in 28/709 (4%) patients (18 for ETV and 10 for LVD) by Wk 120. Baseline characteristics and Wk 24 treatment responses for patients with confirmed HBsAg loss by Wk 120 are presented below. **Conclusions:** Patients with confirmed HBsAg loss by Wk 120 were characterized by genotype A or D, male sex and Caucasian race at baseline and by HBeAg loss and HBeAg seroconversion at Wk 24.

Baseline characteristics	Patients with confirmed HBsAg loss by Wk 120
	Overall (N=28)
Male(%)	23(82%)
Asian(%)	4(14%)
Caucasian(%)	22(79%)
Other(%)	2(7%)
Mean viral load (log ₁₀ copies/ml)	9.8
Genotype A	15(54%)
Genotype B	3(11%)
Genotype C	1(4%)
Genotype D	7(25%)
Knodell necroinflammatory score (mean)	9.1
Mean and Median ALT (U/L)	226, 163
Week 24 Responses	
HBeAg loss	14(50%)
HBeAg seroconversion	12(43%)
ALT normalization (≤ 1 x ULN)	15(54%)
HBV DNA <300 copies/mL	13(46%)

Disclosures:

Robert Gish - Consultant and Speakers Bureau: Bayer, BMS, Eximious F.Hoffmann-LaRoche, Gilead; Consultant and Speakers Bureau: GSK, InterMune, Orthobiotech, Schering-Plough; Consultant and Speakers Bureau: Valeant; Consultant: Amgen, Anadys, Chiron, Corixa, ; Consultant: Human Genome Sciences, Metabasis Therapeutics, ; Consultant: SciClone, United Therapeutics, Pharmasset, Idenix; Consultant: Hepahope, Nucleonics, Innogenetics, XTL; Consultant: Zymogenics
Ting-Tsung Chang - Investigator: BMS
Ching-Lung Lai - Investigator: BMS, LG Lifesciences; Advisory Board: BMS, Idenix Pharmaceuticals, GSK; Speaker Bureau: BMS
Robert de Man - Investigator: BMS, Gilead, GSK
Adrian Gadano - Investigator: BMS; Advisory Board: BMS; Consultant: Idenix/Novartis
Fred Poordad - Investigator: BMS; Speakers Bureau: BMS
Jin Zhu - Employee: BMS
Joanna Yang - Employee: BMS; Employee: BMS
Helena Brett-Smith - Employee: BMS

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HUMAN ANTIGEN PRESENTING CELLS STIMULATE HBV SPECIFIC CTL AND TH CELLS IN THE TRIMERA MOUSE MODEL Reddy Vuyyuru, Nina Blust, Sabine Herzog-Hauff, Soheila Tavakoli, Peter R. Galle, Wulf Bocher; Department of Internal Medicine, University Hospital, Mainz, Germany

Introduction: The strength and breadth of antiviral T cell response is correlated with disease outcome from hepatitis B. Thus, induction of HBV-specific T cells by therapeutic vaccination might represent a new therapeutic strategy, as demonstrated in the humanized trimera mouse model. However, although recipient mice are lethally irradiated, mouse derived antigen presenting cells (APC) might persist together with transferred human B cells, monocytes and dendritic cells (DC). Thus, it was hypothesized that murine APC might crosspresent vaccine derived epitopes to human T cells. **Methods:** To study this issue, Balb/c mice were lethally irradiated, reconstituted with nod.scid mouse bone marrow and transplanted with human PBMC from healthy volunteers or chronic HBV carriers. Donor PBMC were transferred either unmanipulated or depleted for total HLA DR+ APC, CD14+ monocytes, CD19+ B cells or BDCA-1+/-4+ DC. Vaccination of such trimera was performed i.p. with the Th cell antigens tetanus toxoid and recombinant HBV core (Hbc) antigen, or with the synthetic CTL epitopes HBc18-27 and EBV280-288. Antigen specific human Th cell and CTL frequencies were analysed 10 days after vaccination in peritoneal cells by IFN γ ELISpot. **Results:** Very strong Hbc and EBV specific Th cell and CTL responses were induced in vaccinated trimera mice implanted with total PBMC. Depletion of total DR+ APC, or BDCA-1+/-4+ DC led to abrogation of Th cell and CTL responses, demonstrating the need of DC for T cell stimulation in trimera mice. In contrast, monocyte and B cell depletion only partly reduced Hbc and EBV specific T cell responses. **Conclusions:** All three human APC populations contribute to effective stimulation of HBV specific human T cell responses in trimera mice, although only DC are indispensable. Mouse derived APC seem not to play a functionally relevant role in this mouse model. Thus, effective vaccination approaches in trimera mice should be predictive of similar responses in patients.

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The following people have nothing to disclose: Reddy Vuyyuru, Nina Blust, Sabine Herzog-Hauff, Soheila Tavakoli, Peter R. Galle, Wulf Bocher

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COMBINATION OF ADEFOVIR DIPIVOXIL WITH LAMIVUDINE VS. ADEFOVIR ALONE IN LAMIVUDINE-RESISTANT HBEAG-NEGATIVE CHRONIC HEPATITIS B PATIENTS Irene N. Rapti¹, Evangelini Dimou¹, Panayota Mitsoula², Stephanos J. Hadziyannis^{1,2}; ¹Liver Unit, Henry Dunant Hospital, Athens, Greece; ²Hepatitis Research Laboratory, Evgenidion Hospital, Athens University, Athens, Greece

Background: Adefovir dipivoxil (ADV) is effective in most lamivudine resistant (LAM-R) chronic hepatitis B (CHB) patients but ADV resistance develops particularly in HBeAg(+) pts. There are no prospective data on the long-term comparisons of adefovir alone vs. its combination with LAM in HBeAg(-)CHB. **Aim:** To evaluate prospectively the long-term efficacy of the combination treatment with ADV and LAM vs. LAM alone in LAM-R HBeAg(-) CHB patients. **Patients and methods:** 46 HBeAg(-) patients, from a single centre, with histologically confirmed CHB resistant to LAM, were randomly allocated in a two arm study of the efficacy and possible development of ADV resistance of ADV+LAM combination therapy vs. ADV monotherapy. At baseline and during treatment HBV-DNA was tested by a R-T PCR assay (sensitivity level <1000 copies/ml), genotyped and sequenced for LAM and ADV resistant mutations. **Results:** All patients were Caucasian [median age 55.5 years (range 39-76); M/F: 41/5]. Median duration of LAM before development of resistance was 31 months (range 12-84). The majority (26/46) of the pts had either M204I or M204I/L180M mutation, the rest had M204V/L180M. 18 pts had cirrhosis on liver histology. Median HBV-DNA levels before start of ADV treatment were 1.1E+07 cps/ml (range 15500-6.4E+08). Thirty-two pts were treated with combination of ADV and LAM, and 14 with ADV alone. Median hitherto duration