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ABSTRACTS

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Plenary Presentation

17 February 2017 (Friday)
Plenary Presentation 01
15:45–17:15

PL001

Impact of baseline NS5A polymorphisms on sustained virologic response rates to treatment with daclatasvir plus sofosbuvir with or without ribavirin in patients infected with HCV genotypes prevalent in Asia

Fiona McPhee[1], Dennis Hernandez[1], Maria Jesus Jimenez-exposito[2], Eugene Scott Swenson[1], Nannan Zhou[1]

[1]Bristol-Myers Squibb, Wallingford, CT, USA; [2]Bristol-Myers Squibb, Princeton, NJ, USA

Background: Although hepatitis C virus (HCV) genotype (GT)-1b is the most common genotype in Asia (50–75%), GT-2, -3 and -6 are also highly prevalent (≥10%). Treatment with daclatasvir (DCV) plus sofosbuvir (SOF) ± ribavirin (RBV) results in high sustained virologic response (SVR) rates in a diverse range of patients across genotypes, including prior NS3 protease inhibitor (PI) failures, HCV/HIV coinfection, cirrhosis or advanced fibrosis, and post-liver transplant. We performed a retrospective sub-analysis of resistance-associated substitutions (RAS) observed at baseline and virological failure in these patient populations infected with GT-1b, -2, -3, and -6 who were treated with DCV + SOF ± RBV for 12, 16 or 24 weeks. **Methods:** 257 patients with, and 10 patients without, baseline (BL) NS5A sequences (sensitivity cutoff ≥10%) were assessed in clinical studies AI444040 (7 prior PI failures), ALLY-2 (42 HCV/HIV co-infected), ALLY-3 + (49 advanced fibrosis or compensated cirrhosis), ALLY-1 (43 advanced cirrhosis or post-liver transplant) and ALLY-3 (116 advanced, no/mild, or undefined fibrosis). One patient with a BL sequence (non-virologic failure for treatment-unrelated death), was excluded from the analysis. Next-generation sequencing (sensitivity achieved by 100% (7/7) of patients with prior PI failure; 100% (42/42) with HCV/HIV coinfection; 91% (63/69) with advanced fibrosis (includes 3 PI failures, 10 coinfections, 12 post-transplant); 90% (54/60) with cirrhosis (includes 4 coinfections); 91% (20/22) post-liver transplant, and 100% (125/125) with no/mild fibrosis. By HCV genotype, 98% (49/50) with GT-1b, 93% (13/14) with GT-2, 94% (17W190) with GT-3, and a single patient with GT-6 achieved SVR. Baseline NS5A RAS were detected in 13% (33/257) of patients. SVR was achieved in 85% (28/33) of patients with NS5A RAS: 100% (6/6) GT-1b patients with L31 M or Y93H, 75% (3/4) GT-2 with L31 M, 82% (18/22) of GT-3 with A30 K or Y93H (including all of 8 with no/mild fibrosis), and in the single GT-6 patient with R30S. NS5A RAS were detected at relapse in all 13 virologic failures while no NS5B RAS were detected. **Conclusion:** In this retrospective sub-analysis, high SVR rates (90–100%) were observed after treatment with DCV + SOF ± RBV in challenging-to-treat patient populations infected with HCV genotypes frequently observed in Asia. SVR rates (75–100%) were minimally impacted in the few patients with BL RAS, irrespective of genotype. Emergent NS5A RAS and no NS5B RAS were observed in patients not achieving SVR. These results suggest DCV + SOF ± RBV offers an effective treatment option in a wide range of patient populations.

PL002

Sofosbuvir/velpatasvir for 12 weeks results in high SVR12 rates with a favorable safety profile in asian patients: an integrated subgroup analysis of the ASTRAL-1, ASTRAL-2, and ASTRAL-3 studies

Henry L. Y. Chan[1], Ching-Lung Lai[2], Jordan Feld[3], Nancy Reau[4], LingLing Han[5], Brian Louis McNabb[6], John McNally[6], Diana M Brainard[6], Graham Foster[8], Stuart Roberts[7]

[1]The Chinese University of Hong Kong, Ma Liu Shui, Hong Kong; [2]The University of Hong Kong, Pok Fu Lam, Hong Kong; [3]Toronto General Hospital Liver Center, Toronto, ON, Canada; [4]Rush University Medical Center, Chicago, IL, USA; [5]Gilead Sciences, Foster City, CA, USA; [8]Queen Mary University of London, London, UK; [7]The Alfred Hospital

classes of anti-HBV drugs were also assessed with the HBVcircle system.
Conclusion: Compared with previous reported HBV mouse models which employ other viral vectors to introduce overlength HBV genomes, viral gene expression and associated phenotypes are entirely driven by cccDNA-like viral genomes in the HBVcircle mouse model. Therefore, the HBVcircle is a close mimic of cccDNA, and it represents a novel tool for addressing HBV cccDNA-related biological questions and for anti-HBV drug discovery.

PP1234

Modulation of Tim-3 expression on T cells by antigen-dependent and independent induction in patients with chronic hepatitis B virus infection

Jie Dong[1], Xiao-Fei Yang[1], Ye Zhang[1], Jian-qi Lian[1]

[1]Department of Infectious Diseases, Tangdu Hospital, Fourth Military Medical University, Xi'an

Background: T-cell immunoglobulin domain and mucin domain-containing molecule-3 (Tim-3) were upregulated on viral specific T cells and contributed to the T cells exhaustion during chronic hepatitis B virus (HBV) infection. However, the modulation of Tim-3 expression was still not fully elucidated.
Methods: To evaluate the potential viral and inflammatory factors involved in the inductor of Tim-3 expression on T cell, 76 patients with chronic HBV infection [including 40 chronic hepatitis B (CHB) and 36 asymptomatic HBV carriers (AsC)] and 20 of normal controls (NCs) were enrolled. Tim-3 expression on $CD4^+$ and $CD8^+$ T cells were assessed in response to HBV-encoding antigens, HBV peptide pools, and common γ-chain (γc) cytokines stimulation by flow cytometry.
Result: HBV peptides and anti-CD3/CD28 directly induced Tim-3 expression on T cells. γc cytokines also drive Tim-3 upregulation on both $CD4^+$ and $CD8^+$ T cells in patients with chronic HBV infection. However, γc cytokines did not enhance the Tim-3 induction by either anti-CD3/CD28 or HBV peptides stimulation. Furthermore, γc cytokines-mediated Tim-3 induction could not be abrogated by γc cytokine receptor-neutralizing antibody.
Conclusion: The current results suggested that elevation of Tim-3 expression on T cells could be regulated by both antigen-dependent and independent manner in patients with chronic HBV infection. The role of γc cytokines in modulation of inhibitory pathway could be evaluated as immunotherapies in humans.

PP1235

Is there any association between interferon gamma (IFN-\) gen polymorphism (+874 A/T, rs2430561) and hepatitis B virus infection?

Ozlem Kandemir[1], Gulay Borekci[2], Irem Bekalp[3], Aysegul Cetinkaya[3], Nurcan Aras[3]

[1]Mersin University Faculty of Medicine Clinical Microbiology and Infectious Diseases, Mersin, Turkey; [2]Mersin University Faculty of Health, Mersin, Turkey; [3]Mersin University Faculty of Medicine, Medical Biology, Mersin, Turkey

Background: Genetic polymorphisms in cytokines have been shown to affect HBV infection. The aim of this study is to determine the association of polymorphisms in the interferon-γ gene (+874 A/T, rs2430561) and HBV infection.
Methods: A total of 126 subjects, 78 with hepatitis B infection and a control group of 48 healthy subjects were included in the study. Twenty-three were asymptomatic carriers and 55 were chronic hepatitis B infection of total 78 patients. DNA isolation from patients' blood samples were made using the DNA isolation kit (Roche, Switzerland) and genomic DNAs were obtained. Real-time polymerase chain reaction (RT-PCR) method was applied by using specific primers and probe with Light SNiP kit (TIB MOLBIOL, Germany) to determine the single nucleotide polymorphism (SNP) in the gene region of IFN γ (+874 A/T, rs2430561). The results were interpreted according to the amplification curve as mutant, heterozygous and homozygous wild-type.
Result: The genotype frequencies of IFN γ +874 AA, TT and AT were found as 54.7, 71.1, 61.7% in patients with HBV infection and 45.3, 28.9, 38.2% in control groups, respectively ($p = 0.323$). The frequencies of these genotypes were detected 34.8, 34.7, 20.6% in asymptomatic carriers and 65.2, 65.3, 79.4% in chronic hepatitis B patients, respectively ($p = 0.423$). In addition, no significant differences were found between control groups and asymptomatic carriers and chronic hepatitis B groups ($p = 0.342$ and $p = 0.387$ respectively).
Conclusion: In this study, although IFN γ (+874 A/T) rates in total patients and in patients with chronic hepatitis B were found higher than control groups and asymptomatic carriers respectively, these findings were not statistically significant. More researches with higher number of patients were required for more significant results.

PP1236

Study of liver pathological and biochemical indexes of patients with chronic hepatitis B complicated with pulmonary tuberculosis: a clinical analysis of 83 cases

Shuquan Cheng[1]

[1]The Third People's Hospital of Guilin, Guilin

Background: To analyze the relationship between the liver pathological changes with the related serological indexes of chronic hepatitis B (CHB) complicated with pulmonary tuberculosis (PTB) in patients of mildly elevated ALT ($40 < ALT < 80$ UL).
Methods: 83 CHB with PTB patients were divided into groups according to the different liver inflammation grades and fibrosis stages, the serum liver function indexes, hepatitis B virus load (HBV-DNA), and the difference of T lymphocyte subsets in liver tissues in these groups were compared.
Results: 1. Pathology of hepatic tissues changes showed, 83 cases of patients with mild inflammation (<G2) accounted for 25.3%, mild fibrosis (<S2) accounted for 43.4%, inflammation with two or more (≥G2) accounted for 74.7%, fibrosis with two or more (≥S2) accounted for 56.6%, among them, 7 cases were patients with cirrhosis (S4). 2. The degree of inflammation of the liver (G) and fibrosis (S) were positively correlated with serum aspartate aminotransferase (AST), total bilirubin (TBIL) (rank correlation coefficient is positive, $P < 0.05$), negative correlation with cholinesterase (CHE) (Spearman rank correlation coefficient was negative, $P < 0.05$), and of no significant correlation with alanine aminotransferase (ALT), serum albumin (ALB) and HBV-DNA load ($P > 0.05$). 3. The liver inflammation grades (G) was positively correlated with the expression of $CD4^+$, $CD8^+$T lymphocytes, $CD20^+$B lymphocytes and $CD57^+$NK cells in liver tissues (the correlation coefficient was positive, $P < 0.05$).