Disclosures:

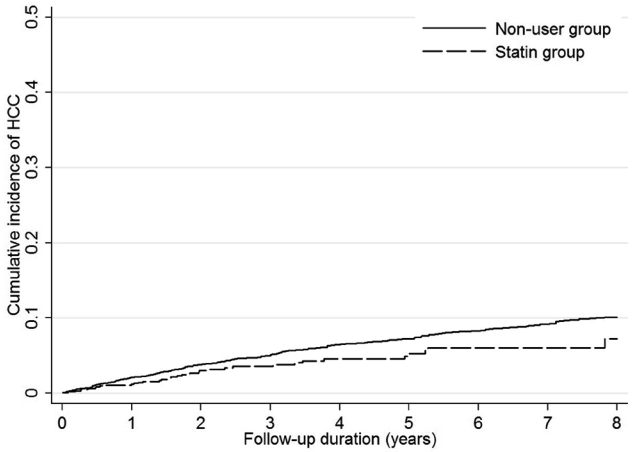
The following authors have nothing to disclose: ZhuJun Cao, Hui Wang, Xiaogang Xiang, FengDI Li, KeHui Liu, Weiliang Tang, Yuhan Liu, Lanyi Lin, Qing Guo, Qing Xie

1612
Statin and the risk of hepatocellular carcinoma and death in a hospital-based hepatitis B-infected population: a propensity-score landmark analysis

John C Hsiang, Grace LH Wong, Vincent W. Wong, Henry Lik-Yuen Chan; Chinese University of Hong Kong, Hong Kong, Hong Kong

BACKGROUND & AIMS The use of statin in hepatocellular carcinoma (HCC) and death prevention is still uncertain among hepatitis B-infected (HBV) patients. This study aimed to examine the effect of statin on HCC and death in a hospital-based HBV population **METHODS** We conducted a population study of HBV patients using the Hospital Authority registry database containing data of patients attending 43 public hospitals in Hong Kong. We defined statin use by landmark analysis to abrogate "immortal time bias" and propensity score (PS) weighting to minimise baseline confounders and "indication bias". Multiple imputation analysis were performed for missing laboratory data. The weighted Cox regression analyses was performed for the risk of HCC (adjusting for competing mortality) and death. **RESULTS** A total of 73,499 patients, with a crude HCC incidence of 1.75 per 100 patient-years, were entered into the 2-year landmark analysis. After landmark analysis and PS weighting of baseline covariates, statin users had 32% risk reduction in HCC (weighted sub-hazard ratio (SHR) 0.68; 95% CI 0.48-0.97, p=0.033). In a PS weighted cohort of statin users and non-users, there was no difference in mortality compared statin users to non-users (weighted HR 0.92; 0.76-1.11, p=0.386). In subgroup analysis, concurrent statin and nucleos(t)ide analogue (NA) use was associated with 59% risk reduction in HCC (weighted SHR 0.41; 0.19-0.89, p=0.023) compared to NA use alone. **CONCLUSION** In this HBV cohort adjusted for confounders and biases, statin use is associated with reduced HCC risk by 32%. Additive HCC chemopreventive effect was seen with the concomitant use of NA and statin. Further prospective studies are warranted to investigate the potential use of statin in HBV-infected NA users.

Weighted cumulative incidence of hepatocellular carcinoma (2-year landmark analysis, for a single multiple imputation dataset); p=0.033



Disclosures:

Grace LH Wong - Advisory Committees or Review Panels: Otsuka, Gilead; Speaking and Teaching: Echosens, Furui, Gilead, Janssen, Bristol-Myers Squibb, Otsuka, Abbvie

Vincent W. Wong - Advisory Committees or Review Panels: AbbVie, Gilead, Janssen; Consulting: Merck, NovaMedica; Speaking and Teaching: Gilead, Echosens

Henry Lik-Yuen Chan - Advisory Committees or Review Panels: Gilead, MSD, Bristol-Myers Squibb, Roche, Novartis Pharmaceutical, Abbvie; Speaking and Teaching: Echosens

The following authors have nothing to disclose: John C Hsiang

1613
Influence of the ethnic status in chronic hepatitis B patients: comparing the Netherlands, Belgium and Turkey

Özgür M. Koc[1], Sarah Konsten[1], Geraldine Jansen[1], Geert Robaeys[2,3], Beytullah Yildirim[4], Dirk Posthouwer[5], Ger H. Koek[6]; [1]Faculty of Health, Medicine and Life Sciences, University Maastricht, Maastricht, Netherlands; [2]Department of Gastroenterology and Hepatology, East Limburg Hospital, Genk, Belgium; [3]Faculty of Medicine and Life Sciences, Limburg Clinical Research Program, Hasselt, Belgium; [4]Department of Gastroenterology, Ondokuz Mayis University, School of Medicine, Samsun, Turkey; [5]Department of Internal Medicine, Infectious Diseases and Medical Microbiology, Maastricht University Medical Centre, Maastricht, Netherlands; [6]Department of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Centre, Maastricht, Netherlands

Background & Aims Hepatitis B virus (HBV) is a global threat affecting different ethnic groups. In some diseases, ethnicity is an essential predictor of disease outcome. Therefore, this study aimed to understand the influence of ethnic status on the natural history of chronic hepatitis B (CHB) infections in the Netherlands, Belgium and Turkey. **Methods** In this multicentre retrospective cohort study, 269 CHB patients from the Hepatology Outpatient Departments of three hospitals one in the Netherlands, Belgium and Turkey were included. Variables as baseline characteristics, route of transmission, laboratory characteristics and HBV endpoints were collected. Ethnicity was defined as country of birth. Chi-square and ANOVA tests were used for categorical and continuous variables, respectively. **Results** The CHB population in the Netherlands, Belgium and Turkey consisted of respectively 98, 68 and 103 patients. In the Netherlands 32.7 and 16.3% were respectively of Dutch and Chinese origin. In Belgium mainly Belgian (36.8%) and Turkish (33.8%) patients were included, whereas the population in Turkey consisted in 99% of patients of Turkish origin. The CHB population in the Netherlands, Belgium and Turkey differed significantly in the number of vertical (40.8, 17.6 and 15.5% respectively, p= .000), sexual (16.3, 13.2 and 3.9% respectively, p= .013) and intra-familial transmission (1.0, 11.8 and 26.2% respectively, p= .000). In addition, the countries showed significant differences in HBV endpoints such as the number of cirrhosis (11.2, 17.6 and 38.8% respectively, p= .000) and hepatocellular carcinoma (2.0, 2.9 and 11.7% respectively, p= .008). Subsequently, patients from Belgium and the Netherlands were categorized as of Dutch / Belgian (n=46), Turkish (n=27) and Chinese (n=18) origin. There was a significant difference in the number of vertical transmission (12.1, 22.2 and 83.3% respectively, p= .000), sexual transmission (27.6, 7.4 and 0.0% respectively, p= .007) and cirrhosis (8.6, 22.2 and 0.0% respectively, p= .045). **Conclusions** The Netherlands, Belgium and Turkey differed regarding ethnicity, routes of transmission and disease progression. Chinese patients were characterized by vertical transmission and

absence of cirrhosis. In addition, Turkish and Dutch/Belgian patients had significantly more cirrhosis and acquired the disease by intra-familial and sexual transmission, respectively.This study therefore implies the importance of ethnicity as there is an association between ethnic groups, routes of transmission and disease progression.

Disclosures:

Geert Robaeys - Advisory Committees or Review Panels: Gilead; Speaking and Teaching: Merck, Janssens

The following authors have nothing to disclose: Özgür M. Koc, Sarah Konsten, Geraldine Jansen, Beytullah Yildirim, Dirk Posthouwer, Ger H. Koek

1614
High-throughput and ultrasensitive assay for the quantification of HBV precore and basal core promoter mutants and their clinical significance

Motokazu Mukaide, Kazumoto Murata, Masaya Sugiyama, Masashi Mizokami; National Center for Global Health and Medicine, Ichikawa, Japan

Background/Aim: Precore (PC) G1896A and basal core promoter (BCP) A1762T/G1764A mutations of HBV is associated with HBeAg seroconversion. However, in the previous studies, the percentage of PC and BCP mutant were examined by semi-quantitative assay, and lacked sufficient sensitivity, which make difficult for precise prediction for the response to therapies in each patient. Therefore, our aim of this study is to develop a novel quantitative assay for HBV, with special reference to PC and BCP, using new generation nanoliter-sized droplet technology paired with digital PCR (ddPCR), and to investigate its clinical significances. **Methods:** We collected serum samples from 95 HBV patients [mean: 54 years, sex male 69%, ALT 45U/L(range 14 to 333), DNA 3.6 logIU / mL, HBeAg positive 27.4%, HBV genotypes (B: 11, C: 84) . Serum samples were stored at -80°C until use. Among them, 57 patients were under treatment with nucleos(t)ide analogs and no patients were treated with IFN. ddPCR assays were performed using the QX100 ddPCRsystem. ddPCR primers and probes were designed on the basis of the conserved nature of these sequences using the Hepatitis Virus Database. **Results:** The assay using standard plasmid linearly detected HBV from 2.5 to 10^5copies, and the limit of detection was 0.005% of mutant (MT) in the presence of wild-type (WT). The total viral load (MT+WT) quantified by ddPCR showed a linear correlation with HBV DNA levels as measured by COBAS TaqMan HBV Test (range 2.1 to 9.1 $\log_{10}$IU/mL: PC: R^2=0:86, P<0.001 BCP: R^2=0:68, P<0.001), indicating that ddPCR assays accurately measured individual viral populations. In the HBeAg positive population (n=26), the PC-WT viral load was significantly higher than the PC-MT, and the BCP-MT viral load was higher than the BCP-WT, suggesting that PC-WT or BCP-MT could be stronger replicative viruses. In the HBeAg negative population (n=69), the PC-MT viral load was significantly higher than the PC-WT because of HBeAg seroconversion, but no differences were observed between BCP-WT and BCP-MT. In serum from 15 treatment-naïve patients (120samples), HBsAg, HBeAg, HBV-DNA, ALT, PC-WT, PC-MT, BCP-MT, BCP-WT was quantified before and during entecavir (ETV) therapy (0, week 1, 2, 3, 6, 12, 24 and 48 after ETV). Interestingly, in 58.3% patients (7/12), PC-MT was under detection limit 48 weeks after ETV treatment whereas PC-WT in all of patients (10/10) was still positive, suggesting PC-WT could be resistant clones against ETV. **Conclusions:** This is the first report that the MT and WT quantitative assay for PC and BCP, using ddPCR. This novel assay could be useful for prediction of the response to therapies such as nucleos(t)ide analogs.

Disclosures:

The following authors have nothing to disclose: Motokazu Mukaide, Kazumoto Murata, Masaya Sugiyama, Masashi Mizokami

1615
Changes of Hepatitis B surface antigen after allogenic hematopoietic stem cell transplantation

Do Seon Song, JinMo Yang, U Im Chang, Jeong Won Jang, Si Hyun Bae, Jong Young Choi, Seung Kew Yoon; Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea (the Republic of)

Background Changes in serologic markers of Hepatitis B virus (HBV) infection following allogenic hematopoietic stem cell transplantation (HSCT) in HBV endemic area are unknown. This study evaluated changes of hepatitis B surface antigen (HBsAg) and surface antibody (HBsAb) after HSCT. Material and method We reviewed the medical records of 19 HBsAg-positive acute leukemia patients who had available HBsAg data after allogenic HSCT between June 2009 and May 2014 in Seoul St. Mary Hospital. Recipients who received HSCT from HBsAg-positive donor were excluded. Patient information was retrospectively collected. Results A median age was 42 years old, and 11 patients (57.9%) were male. A median follow-up period was 13.6 months (0.3 - 59.2 months). Fifteen patients (78.9%) were acute myeloid leukemia (AML), and remained were acute lymphoid leukemia (ALL). Two patients had liver cirrhosis at the time of transplantation. Eighteen patients received antiviral prophylaxis (lamivudine in 2 patients, entecavir in 15 patients and tenofovir in 1 patient). HBsAg clearance occurred in five patients (26.3%). All the patients with HBsAg clearance were male patients and received entecavir or tenofovir prophylaxis. Only 2 donors had no hepatitis B surface antibody, and their recipients did not develop HBsAg clearance. HBsAg clearance was occurred in 0.7, 4.6, 12.2, 15.3, and 43.2 months after allogenic HSCT. Three patients out of 5 HBsAg clearance patients were positive for HBsAb after HSCT. One patient reverted to HBsAg positivity again after cessation of antiviral agent. Conclusion HBsAg clearance is frequently seen in the HBsAg-positive HSCT recipients. Further studies are necessary to identify the favorable factors for HBsAg clearance.

Disclosures:

JinMo Yang - Employment: catholic university

The following authors have nothing to disclose: Do Seon Song, U Im Chang, Jeong Won Jang, Si Hyun Bae, Jong Young Choi, Seung Kew Yoon

1616
Clinical scoring system for diagnosis of immune tolerant and reactive phases in chronic hepatitis B virus infection

Qing-Lei Zeng, Yan-Ling Fu, Jun Lv, Zu-Jiang Yu; Department of Infectious Diseases, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

Background Aims: Liver biopsy is frequently performed for separating the immune tolerant phase from immune reactive phase in HBeAg-seropositive chronic hepatitis B virus infection before antiviral therapy, and the non-invasive diagnostic tool for distinguishing these two phases is lacking. This study aims to develop a non-invasive scoring system to assess whether it may replace liver biopsy. **Methods:** We first evaluated 496 HBeAg-seropositive persons who performed liver biopsy and identified immune phases, and analyzed variables independently predicted immune reactive phase. These variables were used to construct a diagnosis score. The score was validated in another cohort of 240 HBeAg-seropositive persons whose immune phase was confirmed through liver biopsy. **Results:** The following three