stopping NA treatment. Nobody had HBsAg loss. Of the patients with undetectable HBcAg, 39% had HBsAg level of <100 IU/ml. Of the patients with HBsAg level of <100 IU/ml, 63% had undetectable HBcAg. Only 7.6% of all patients had undetectable HBV DNA, HBcAg, and HBsAg level of <100 IU/ml after NA treatment. Patients with undetectable HBcAg were older, and tended to be treated longer by NA, and had significantly lower HBV DNA level at baseline. All patients with undetectable HBcAg were HBeAg negative and anti-HBe positive at baseline. Patients with HBsAg level of <100 IU/ml had no significant difference of background at baseline, however, HBcAg level during NA treatment was significantly lower (3.1±0.3 vs. 4.3±1.0 log U/ml).

**Conclusions:** Despite HBV DNA suppression, decline of HBcAg and/or HBsAg after NA treatment was rare in Japanese patients with chronic genotype C HBV infection. HBcAg and HBsAg provide a viral marker which is independent of HBV DNA, but not same way for monitoring NA treatment.

### 485 PREVALENCE AND CLINICAL SIGNIFICANCE OF OCCULT HEPATITIS B INFECTION IN PATIENTS WITH CHRONIC HEPATITIS C INFECTION

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**Background and Aims:** Occult HBV infection is reported to be more frequent in HCV-positive subjects than in healthy subjects, but there are quite contradictory data about its clinical significance. The aim of this study is to determine frequency and clinical significance of occult HBV infection in subjects with chronic HCV infection.

**Methods:** From March 2004 to December 2010 the study prospectively included 188 subjects with chronic HCV infection (112 chronic hepatitis C, 50 liver cirrhosis, 26 HCC), all HbsAg-negative (mean age 58.5±12.02 years) and 106 healthy adults, all anti HCV Ab- and HbsAg-negative (mean age 39±24.04 years). Sera of all subjects were tested for the presence of HBV DNA by realtime PCR Cobas TaqMan® Test with detection limit of 6 IU/ml (35 copies/ml) (Roche Molecular Systems, Inc.). Two consecutive liver biopsies were performed in 52 subjects with chronic hepatitis C and the rate of fibrosis progression was calculated. 83 HCV-positive subjects received antiviral treatment.

**Results:** Occult HBV infection, defined in this study as positive serum HBV DNA, was found in 21.3% of subjects with chronic HCV infection and in 3.8% of healthy adults (P<0.0001). Positive HBV DNA significantly associates with positive antiHbc Ab (P<0.0001).

Positive HBV DNA was found in 15, 2% of subjects with chronic hepatitis C, in 28% of subjects with cirrhosis and in 34.6% of subjects with HCC (P=0.005). In subjects with chronic hepatitis C positive HBV DNA associates with more severe necro-inflammation (P=0.001), no association was found with liver fibrosis (P=0.545).

Positive HBV DNA was found in 29.4% of subjects with progression of fibrosis and in 5.7% of the patients without fibrosis progression (P=0.0004). Occult HBV infection didn't affect efficacy of antiviral treatment (P=1.000). In subjects with HCC positive HBV DNA was associated with HCC development at earlier age (41±9.89 years), compared with subjects with negative HBV DNA (66±12.12 years) (P=0.0018).

**Conclusion:** Occult HBV infection is more frequently found in subjects with chronic HCV infection than in healthy adults and associates with more advances liver disease and development of HCC at earlier age.

### 486 QUANTIFICATION OF HEPATITIS B SURFACE ANTIGEN AS A PREDICTOR OF OFF-TREATMENT SUSTAINED VIROLOGICAL RESPONSE IN CHRONIC HEPATITIS B PATIENTS TREATED WITH ORAL NUCLEOS(T)IDE ANALOGUE

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**Background and Aims:** The absolute value or reduction of hepatitis B surface antigen (HBsAg) level can be a useful marker for on-treatment response or durability of off-treatment response. We examined the appropriate cutoff value of serum HBsAg level that predict off-treatment sustained virological response in patients with chronic hepatitis B (CHB) treated with oral nucleos(t)ide analogues (NAs).

**Methods:** From June 1998 to Dec 2010, 81 patients with CHB who discontinued NAs were enrolled [HBsAg (+), n=50(62%)]. Oral NAs were lamivudine (n=53), adefovir (n=15), lamivudine combined with adefovir (n=4), entecavir (n=9). The mean duration of antiviral treatment and the follow-up period after discontinuation of treatment were 31±16 and 32±24 months respectively. The sustained virological response after treatment discontinuation (SVR) was defined as follows; complete (cSVR, HBV DNA undetectable) or partial (pSVR, normal ALT and detectable HBV DNA <20,000 IU/ml in HBeAg positive and HBV DNA <2,000 IU/ml in HBeAg negative). Serum HBsAg levels were determined by the ARCHITECT i2000 HBsAg (Abbott, USA, 0.09–250 IU/ml).

**Results:** Thirty-three of 81 (40%) patients had complete or partial SVR [cSVR, 11/81 (14%); pSVR 22/81 (27%)]. The relapse rate were 37/81 (46%), 5/81 (6%) at 6 months, 12 months after discontinuation of treatment. Baseline HBV DNA, ALT, presence of HBeAg were not different in patients with or without cSVR. The mean treatment duration, the reduction of HBsAg level at 6 month on-treatment, and HBsAg level at the end of treatment were significantly different in patients with or without cSVR (47 vs. 28 months, P=0.011; -0.9 vs. +0.2 log IU/ml, P<0.05; 0.2 vs. 3.5 log IU/ml, P<0.05). In multivariate analysis, only HBsAg level at the end of treatment was significant (P=0.007). Serum HBsAg level <2 log IU/ml at the end of treatment were predictive of SVR [AUROC, 0.991; 95% confidence interval (CI), 0.900–1.000; P<0.05]; sensitivity, 100%; specificity, 93%; positive predictive value, 69%; negative predictive value, 100%.

**Conclusions:** In CHB patients with long term nucleos(t)ide analogue therapy, absolute value of HBsAg off-treatment can be a predictive of SVR, and treatment discontinuation can be considered.

### 487 KEY PATTERNS OF HBX AND PRE-S1/S2 MUTATIONS ARE INVOLVED IN MECHANISMS UNDERLYING HBV-INDUCED HEPATOCELLULAR CARCINOMA IN VIVO

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**Background:** HBx and Pre-S1/2 play a critical role in mediating HBV-induced tumorigenesis. However, little information is available...