

# HEPATOLOGY INTERNATIONAL

Official Journal of the Asian Pacific Association for the Study of the Liver (APASL)

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# HEPATOLOGY INTERNATIONAL

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## ABSTRACTS

**Abstracts—APASL 2013 S1**

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# HEPATOLOGY INTERNATIONAL

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*Hepatology International* is the official journal of the Asian Pacific Association for the Study of the Liver (APASL). This is a peer-reviewed journal featuring articles written by clinicians, clinical researchers and basic scientists dedicated to research and patient care issues in hepatology. This journal will focus mainly on new and emerging technologies, cutting-edge science and advances in liver and biliary disorders.

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## Topic: 13.b Clinical

Absno: 2579

### Hepatocellular carcinoma presenting with heart metastases: case series

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**Introduction:** Hepatocellular carcinoma (HCC) is one of the most common types of malignant liver tumor, which is the third leading cause of cancer mortality worldwide. Advanced HCC with invasion into the heart through the hepatic vein is a rare occurrence with an extremely poor prognosis. Patients who present with right heart tumor have generally been considered inoperable.

#### Case illustration:

Case 1 A 53-year old man came with increased swelling of abdomen 3 months before admission. He had been infected with Hepatitis B 20 years ago without any treatment. On abdominal examination there is palpable mass in the upper abdomen, the surface was uneven, firm and immobile, ascites and venecation was present. He was diagnosed hepatic cirrhosis with Child Pugh B. Serum alpha-fetoprotein was 8753 µg/L. A tri phase CT of the abdomen showed a hepatic solid tumor that has infiltrated diaphragm, the right atrium of the heart and the inferior cava vein. The tumor located in the left lobe and in the segment 5th, 7th, 8th of the right lobe. The size of the tumor is 18.96 cm × 25.44 cm × 20.96 cm.

Case 2 A 61-year old man came with dyspepsia since 3 months before admission. He felt nausea, loss of his appetite and significant loss of his weight. There was abdominal tenderness. Serum Alpha-fetoprotein result was > 484000 µg/L. Chest x-ray showed multiple nodules in both lungs. Abdominal ultrasound showed hepatic solid tumor with enlargement of spleen. The abdominal CT scan revealed HCC with ascites, thrombosis of portal vein and inferior cava vein with the size of tumor 11.1 cm × 7.0 cm × 5.3 cm. He was diagnosed as hepatic cirrhosis Child Pugh B and HCC. The thorax MSCT showed continuous thrombus from right atrium to inferior cava vein. From trans-esophageal echocardiography revealed hyper-echoic mass infiltrating right atrium wall.

## Topic: 13.b Clinical

Absno: 2595

### Demographic profile and outcome of 126 consecutive HCC cirrhotic patients treated with Nexavar. A 5 year Greek multicentrer study

**Dimitrios Dimitroulopoulos<sup>1</sup>, Andreas Protopappas<sup>2</sup>, Stylianos Karatapanis<sup>3</sup>, Ioannis Elefsiniotis<sup>4</sup>, Aikaterini Fotopoulou<sup>5</sup>, Dimitrios Kyreos<sup>1</sup>, Maria Nikaki<sup>1</sup>, Apostolos Malalias<sup>1</sup>, Klisthenis Tsamakidis<sup>1</sup>, Dimitrios Xinopoulos<sup>1</sup>**

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**Aim:** The aim of the study was to estimate if and to what extent Sorafenib (Nexavar) improves survival and quality of life in cirrhotic patients with advanced hepatocellular carcinoma (HCC).

**Methods:** The data of a total of 126 (Group A - 69.4 ± 6.3 years, 78 males) consecutive cirrhotics, stages A-B (stage B 66), due to chronic viral infections and with advanced stage HCC (BCLC stage C 106) treated with Nexavar (400 gr twice daily) were reviewed retrospectively and were compared with that of a similar historic group of 66 (69.4 ± 5.6 years, 36 males) non-treated HCC patients that were followed up in the same manner (Group B, stage B cirrhosis 32, BCLC stage C 56). Follow-up was worked out in both groups monthly as well as the estimation of quality of life (QLQ-C30 questionnaire).

**Results:** The etiology of tumour was HBV 58, HCV 62, HBV + HCV 6 in group A and HBV 38, HCV 26, HBV + HCV 2 in group B. The morphology was multinodular in 26 and 13, massive in 86 and 45 and diffuse in 14 and 8 patients from group A and B respectively. Metastatic disease was observed in 19 and 8 patients and AFP values were 2714 ± 5049 and 3208 ± 4500 respectively in each group. A significantly higher survival time was observed for group A (49 ± 6 wk) as compared to group B (28 ± 2 wk) LR = 20.39, df = 2, P < 0.01. Group A presented 68.5% lower hazard ratio [95% CI (47.4%-81.2%)]. During the first year, a 22% and 43% decrease in the QLQ-C30 score was observed in each group respectively.

**Conclusion:** Nexavar administration has shown to improve the survival and quality of life in cirrhotic, stage A-B, Greek patients with advanced HCC.

## Topic: 13.b Clinical

Absno: 2617

### Relationship between vitamin B12 levels and survival of HCC

**Ali Riza Koksal, Salih Boga, Mehmet Bayram, Osman Ozdogan, Engin Altinkaya, Meltem Ergun, Canan Alatas Alkim**

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**Aim:** Although elevated blood vitamin B12 level has been identified as a prognostic indicator for advanced cancer patients; the predictive value of vitamin B12 for survival of patients with hepatocellular carcinoma remains unclear. The aim of our study is to evaluate relationship between vitamin B12 levels and survival rate in HCC cases.

**Materials and methods:** We retrospectively studied thirty-one patients diagnosed with HCC in our clinic from January 2009 to July 2012. Factors determining survival were analysed by univariate and multivariate analysis using the Kaplan-Meier method and Cox proportional hazard regression models.

**Results:** A total of 31 cases (26 male, 83.9%; mean age 58.2 ± 13.9) were enrolled the study. Most patients had cirrhosis (n = 29) and the most common etiology was HBV (18 cases, 58.1%). The mean survival time of 26 patients was 149.7 ± 172.7 days. The survival rate was decreasing with the increasing Child, MELD scores and the total lesion size, but this finding was not statistically significant (p > 0.05). According to AFP levels < 200 or > 200, median survival time difference was not statistically significant (183.1 days, 128 days respectively, p > 0.05). The median survival was 74.8 days in patients with vitamin B12 level > 663 (n = 11) and 204.6 days in patients with vitamin B12 levels < 663 group (n = 15) (p < 0.05). The survival time was significantly lower in patients who had vascular invasion (p < 0.05). The survival mean times according to treatment modalities were 342.2 days with RFA, 208.7 days with

TACE, 94.2 days with Sorafenib, and 85.5 days with palliative treatment.

**Conclusion:** Vitamin B12 levels were not elevated in all patients, but survival rates were dramatically lower in patients with high vitamin B12 levels.

### Topic: 13.b Clinical

Absno: 2622

#### Characteristics of hepatitis B virus related hepatocellular carcinoma in india: a comparative study of 142 patients from North India

**Ashish Kumar, Praveen Sharma, Pankaj Tyagi, Naresh Bansal, Vikas Singla, Jay Toshniwal, Anil Arora**

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**Background and aims:** The clinical profile of patients with hepatocellular carcinoma (HCC) may differ depending on the etiology of HCC. There is no study from India comparing the clinical profile of patients of HCC due to hepatitis B virus (HBV) infection with other etiologies.

**Methods:** We retrospectively reviewed the records of patients clinically diagnosed as HCC between Nov 2000 and Dec 2012 admitted under a single unit of Department of Gastroenterology at our hospital. We compared the clinical presentation of patients of Hepatitis B virus etiology (HBV group) with other etiologies (Non-HBV group).

**Results:** One hundred and forty-two patients were included (median age 60 years [range 30–83], 92% males). The etiology was HBV in 56 (39%) and among the non-HBV group (n = 86, 61%) the etiological spectrum was following: alcohol 31 (22%), cryptogenic 26 (18%), HCV 27 (19%), and miscellaneous 2 (1%). The median age of presentation was significantly less for HBV group than in non-HBV [56 [30–77] vs. 62 [42–83] years, p < 0.01]. Clinical evidence of cirrhosis was significantly less common in the HBV group than non-HBV group (75% vs 98%, p < 0.01). HBV group had lower CTP score than non-HBV (median CTP score 7 vs 8, p < 0.05). Ascites was more common in non-HBV group than HBV group (65% vs 48%, p = 0.056). The BCLC staging was: A 13%, B 23%, C 35%, and D 29%, and there was no difference in tumor characteristics or BCLC staging between HBV or the non-HBV group.

**Conclusions:** HBV is a common cause of HCC in India, accounting for 39% of cases. The tumor characteristics of HCC due to HBV is similar to other etiologies, however, HBV causes HCC at an earlier age, and in less advanced or even absence of cirrhosis, thus confirming the directly carcinogenic potential of HBV.

### Topic: 13.b Clinical

Absno: 2646

#### Statins use and risk of hepatocellular carcinoma: a population-based case-control study in Taiwan

**Kuan-Fu Liao<sup>1,2</sup>, Shih-Wei Lai<sup>3,4</sup>, Pei-Chun Chen<sup>5</sup>, Wen-Chi Chen<sup>2</sup>, Chung-Yi Lin<sup>1,6</sup>**

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China Medical University, Taichung, <sup>5</sup>Graduate Institute of Epidemiology and Preventive Medicine, National Taiwan University, Taipei, <sup>6</sup>School of Medicine, Tzu Chi University, Hualien, Taiwan R.O.C.

**Objectives:** The objective of this study was to explore the association between statins use and risk of developing hepatocellular carcinoma (HCC).

**Methods:** We used the research database of the Taiwan National Health Insurance program to conduct a population-based case-control study. Cases were 3480 patients with newly diagnosed HCC identified during 2000 and 2009. Controls were 13920 subjects without HCC and frequency matched for age, sex and calendar year to cases. Six commercially available statins, including simvastatin, lovastatin, fluvastatin, atorvastatin, pravastatin, and rosuvastatin, were analyzed.

**Results:** The adjusted odds ratio [OR] of HCC was 0.62 (95% confidence interval [CI] 0.50–0.76) for the group with stains use, when compared to the group with non-use of statins. In sub-analysis, simvastatin (OR 0.54, 95% CI 0.39–0.75), lovastatin (OR 0.44, 95% CI 0.30–0.64), atorvastatin (OR 0.64, 95% CI 0.48–0.86), and pravastatin (OR 0.60, 95% CI 0.36–1.00) were associated with significant reduction in odds of HCC.

**Conclusions:** Statins use correlates with 38% decreased risk of HCC. The risk for HCC is not significantly different among each individual statins.

### Topic: 13.b Clinical

Absno: 2668

#### Effect and safety of interferon for hepatocellular carcinoma: a systematic review and meta-analysis

**Liping Zhuang, Zhiqiang Meng**

Fudan University Shanghai Cancer Center, Shanghai, China

**Objectives:** To evaluate the effect and safety of IFN for HCC.

**Methods:** PubMed, OvidSP, and Cochrane Library were searched from their establishment date until August 30, 2012. Studies that met the inclusion criteria were systematically evaluated and then subjected to meta-analysis.

**Results:** Thirteen randomized control trials (RCTs) involving 1344 patients were eligible for this study. Eight studies aimed to investigate the effect of adjuvant IFN therapy on HCC patients after curative therapy. Five studies evaluated the effect of IFN on intermediate and advanced HCC patients. When IFN was used as an adjuvant therapy for HCC patients after curative therapy, the meta-analysis showed that IFN reduced the 1-, 2-, 3-, 4-, and 5-year recurrence rates. Subgroup analysis showed that IFN reduced the 2-, 3-, 4-, and 5-year recurrence rates of hepatitis C viral (HCV)-related HCC. The effect of IFN for on hepatitis B virus (HBV)-related HCC patients could not be determined because of insufficient data. After surgical resection, adjuvant IFN therapy reduced the 4- and 5- recurrence rates. All studies reported the negative results about the overall survival rate of HCV-related HCC patients after curative therapies. Only one study reported positive result about the overall survival rate of HCC patients after curative therapy and subanalysis of HCC patients after surgical resection. Thus, meta-analysis was not performed. A varied setting of control was used to study the effect of IFN for intermediate and advanced HCC patients, thus meta-analysis was not appropriate. All included studies, except for one, reported that IFN treatment was well tolerated.

**Conclusions:** After curative therapies, adjuvant IFN reduced the recurrence of HCC. IFN did not improve the survival of HCV-related HCC patients after curative therapy. Whether IFN is effective for

node enlargement were found. Lymph node biopsy showed that granulomatous lymphadenitis of uncertain etiology with tubercloid-type granulomas. Treatment for HBV/HCV coinfection were completed total 48 weeks. Two weeks later antituberculous treatment was started. During the third month of treatment, acute hepatic flare due to HBV developed. Tenofovir was started for treatment of chronic hepatitis B. The outcome of antituberculosis therapy was favourable and completed after 9 months. Virological suppression was obtained for both viruses. At 6 months after pegylated interferon alfa-2a and ribavirin therapy, a sustained virological response was achieved for HCV. A maintained undetectable HBV DNA was achieved under tenofovir therapy. This is believed to be the first case report of virologic response from coinfection of HBV/HCV and tuberculosis treated concurrently with antiviral and antituberculous agents.

## Topic: 18 Case Report and Case Series

**Absno: 1120**

**A patient with cavernous transformation of portal vein and essential thrombocythemia**

**Fang Xu, Pujun Gao, Xiaolin Guo, Junjie Qin**

The First Hospital of Jilin University, Changchun, China

Cavernous transformation of portal vein (CTPV) is a uncommon disease which can cause extrahepatic portal hypertension. It can be classified as idiopathic and secondary the reasons of which consists of tumor, abdominal infection and chronic myeloproliferative diseases. Essential thrombocythemia(ET) is one of the most commonest myeloproliferative diseases. Embolus and bleeding are the common and lethal symptoms of ET. Here we reported a patient presenting as CTPV was finally diagnosed as ET. This patient was a 29 years old woman who had abdominal distension for 2 months and was initially suspected with liver cirrhosis before coming to our hospital. The liver CT showed she had normal liver, but splenomegaly and abnormal portal vein with thrombosis and collaterals. Gastroendoscopy showed severe esophageal and gastric varices. The platelet count was  $345 \times 10^9/L$ . The bone marrow biopsy and liver function test are normal. She underwent splenectomy and esophageal varices ligation. Seven months later, we found that the platelet count reached  $2706 \times 10^9/L$ . The bone marrow biopsy showed myeloproliferative disease. The JAK2 mutation test was positive. The results supported the diagnosis of ET. After treatment, the platelet count returned to normal level. When a patient has portal hypertension and CTPV without signs of liver cirrhosis, especially with a normal or slightly high level of platelet count, ET should not be ignored. Although the bone marrow biopsy is normal, JAK2 mutation test should be done.

## Topic: 18 Case Report and Case Series

**Absno: 1176**

**Acute liver failure related to the mobile phone battery material in china**

**Qinglong Jin, Yue Qi, Yanhang Gao, Yiping Li, Junqi Niu**

First Hospital of Jilin University, Changchun, China

A 26-year worker complained sever fatigue and jaundice for one week. He worked in the cell phone battery production line for several months. Physical exam showed deep jaundice. AST $\square 142U/L$ ,

ALT $\square 133U/L$ , GGT $\square 78U/L$ , ALB $\square 30.3 g/L$ , TBIL $\square 630.9\mu mol/L$ , DBIL $\square 254.2\mu mol/L$ , PT $\square 43.4 s$  and PTA 14%. Ultrasound screening showed the liver size reduced. And hepatic encephalopathy developed at the 2<sup>nd</sup> day of admission. The patient died in 3 days. The blood toxicological analysis showed the concentration of several heavy metal and compounds which were well known as battery materials were highly overproof. It is highly suspect that the acute liver failure was closely related to the environment of the factory. This case suggests the standard protocol of battery production is very important.

## Topic: 18 Case Report and Case Series

**Absno: 1205**

**A case of fasciola hepatica presenting with neuropathy**

**Salih Boga, Ali Riza Koksal, Mehmet Bayram, Osman Ozdogan, Meltem Ergun, Canan Alatas Alkm**

Gastroenterology, Sisli Etfal Education and Research Hospital, Istanbul, Turkey

**Introduction:** Fasciola hepatica is an endemic parasite in Turkey. Chronic Fasciola hepatica infection may be asymptomatic or may cause biliary obstruction and inflammation.

**Case:** Seventy-year-old male patient complaining of weakness and difficulty in walking for 2 months had been investigated in a neurology clinic and determined as sensorimotor polyneuropathy by electromyography. During further investigations to detect any possible paraneoplastic etiology that may cause polyneuropathy, a few pieces of hypoechoic lesions with uneven borders in the liver parenchyma were detected by computed tomography, while biliary tracts were normal. The patient who lost 15 kg in two months and did not complain about abdominal pain, fever, nausea, vomiting, jaundice and did not describe dark urine or acholic stool. Physical examination revealed mild tenderness in epigastrium, global deficit of deep tendon reflexes, bilateral indifferent plantar reflexes, and 4/5 muscle strength in lower extremities. Except these, there was no additional finding. The patient whose cholestasis enzymes were in normal ranges in the arrival, developed fever and hyperbilirubinemia during the follow-up and cholestasis enzymes also increased. Dilatation of common bile duct was found in ultrasonography. The common bile duct was found to be dilated in the endoscopic retrograde cholangiopancreatography (ERCP) and there were also saccular dilatations in the intrahepatic bile ducts. After papillotomy, multiple sweeps of the common bile duct was done by balloon catheter and 2 leaf-shaped live *Fasciola Hepatica* each measuring nearly  $15 \times 25 mm$  were evacuated (Fig. 1).

Triclabendazole 10 mg / kg was prescribed as an oral single dose. In the clinic follow-up, the patient's complaint of difficulty in walking disappeared completely.



**Fig. 1** *Fasciola hepatica*

**Conclusion:** Although *Fasciola hepatica* is a parasite that resides in the bile ducts, neurological disorders can also be seen due to *fasciola hepatica* infestation.

## Topic: 18 Case Report and Case Series

**Absno: 1232**

**Acutehepatitis C virus infection following ozone autohaemotherapy**

**Elif Sahin Horasan, Ali Kaya**

Mersin University, Faculty of Medicine, Mersin, Turkey

**Introduction:** Acute hepatitis C is a serious infectious disease and leads chronic liver disease, cirrhosis and hepatocellular carcinoma. Transmission of hepatitis C virus (HCV) primarily occurs through parenteral exposure. Ozone autohaemotherapy (OAH) is a procedure in which 50–100 ml of blood is withdrawn from the patient and treated with a gaseous mixture of oxygen and ozone. Subsequently, the blood is promptly reinfused.

Here we report, one patient developed hepatitis C virus infection following OAH.

**Case description:** A 46-year-old woman was admitted to our hospital for weakness and anorexia starting 15 days previously. Vital signs were stable. Her exam is only remarkable for right upper quadrant tenderness to palpation. Laboratory tests showed that AST and ALT were elevated (607/1442 IU/L), direct bilirubine was 0.79 mg/dL (0–0.3 mg/dL), anti-HCV antibody was positive and HCV RNA titer was positive (3030 IU/mL, Genotip1b) (Cobas Taqman 48, Roche Diagnostics, Switzerland). Other laboratory investigations were normal. Her medical history revealed that she had attended a private practice because of immunomodulation, and her friend recommended ozone autohaemotherapy. She had received ozone autohaemotherapy 2 months ago.

Serologic tests, including other viral markers, showed nothing significant (HBsAg, AntiHbcIgM, AntiHAV-IgM were negative). Before OAH she had normal liver enzymes. She had no known risk factors for hepatitis C (such as intravenous drug abuse, tattoo nor transmission by sexual contact) and had not received any blood components before or after OAH. Health-care associated was suspected and she was diagnosed with acute HCV infection. At week 6, liver enzymes were normal, HCVRNA was nondetectable.

**Conclusion:** Acute HCV infection is diagnosed rarely due to its asymptomatic course. Diagnosis of acute HCV infection can usually made in cases with history of exposure. In conclusion, universal precautions are very important to prevent risk of transmission of health care associated HCV.

## Topic: 18 Case Report and Case Series

**Absno: 1234**

**Carcinoid tumor of the minor duodenal papilla in an elderly patient: a rare case**

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Carcinoid tumors are neuroendocrine tumors result from enterochromaffine cells. Carcinoid tumor of minor papilla is very rare. We present a rare case of carcinoid tumor of the duodenal minor papilla in

an elderly patient. A 77- year- old male was admitted to our hospital with jaundice and abdominal pain lasting a week. Physical examination was normal except abdominal tenderness with palpation and conjunctival icterus. The blood tests revealed elevated bilirubin and transaminases levels. A dilatation of choledocus and a 1 cm in diameter stone in the distal choledocus was seen in abdominal ultrasound. We performed an endoscopic retrograde cholangiopancreatographical examination and removed the stone. While we were performing endoscopic retrograde cholangiopancreatographical examination we saw approximately 1 cm in diameter mass around minor papilla. We obtained biopsies from the lesion. Histological examination revealed that a submucosal well- differentiated neuroendocrin tumor. The tumor contained cells in small clusters which had small nuclei with fine uniform chromatin. The immunohistochemical study was positive for chromogranin and synaptophysin. Any mass or metastases were not seen in dynamic contrasted computed tomography series. By endoscopic ultrasound we found a small size mass which was located in the submucosal layer and muscularis propria was intact. Whipple operation was performed because of the patient's choice. Macroscopic examination displayed a tumor in the minor duodenal papilla measuring 1.2 cm in its largest diameter. Submucosal well- differentiated neuroendocrin tumor was confirmed and any Adjacent tissue and lymph node metastasizes were not revealed by pathological examination. Carcinoid tumor of minor papilla is difficult to diagnose in early stage because it is usually asymptomatic. Radiologic modalities usually are inadequate to show the tumor in early stage. ERCP is superior to radiologic examinations to show the tumor, and is used for taking biopsy and treatment approach such as local excision.

## Topic: 18 Case Report and Case Series

**Absno: 1250**

**Hepatocellular carcinoma in HBeAg negative compensated cirrhosis patients who received long term treatment of nucleotide analogs**

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Case 1, the patient was male, and 43 years old. The baseline clinical data was HBsAg +, anti-HBe +, anti-HBc +, HBV DNA  $1.26 \times 105$  copies/ml, ALT46U/L, AST 32 U/L, ALB 45.6 g/L, AFP 3.64 ng/ml. The patient received lamivudine treatment and the HBV DNA was undetectable from the 36<sup>th</sup> week. Hepatocellular carcinoma was found in the right lobe of liver after 3-year anti-HBV treatment, and the AFP was 399.4 ng/ml, HBVDNA<103 copies/ml at that time. TACE was performed several times and the sign of survival tumor during 1 year following up till now.

Case 2, the patient was male, and 56 years old. The baseline clinical data was HBsAg +, anti-HBe +, anti-HBc +, HBV DNA  $4.2 \times 104$  copies/ml. The patient received adefovir treatment and the HBV DNA was undetectable from the 24<sup>th</sup> week. HCC was diagnosed at the 3<sup>rd</sup> year of treatment and the patient died from the progressive cancer.

Case 3, the patient was male, and 56 years old. The baseline clinical data was HBsAg +, HBeAg +, anti-HBc +, HBV DNA  $7.59 \times 105$  copies/ml. After 14-week telbivudine treatment, HBV DNA was undetectable, and HBeAg -, AFP 3.98 ng/ml, HBV DNA<103 copies/ml after 2-year treatment, but the HCC was found. RFA was performed, and there was no recurring till now.

It is reported previously that the anti-HBV therapy reduce the HCC ratio in CHB patients. Our clinical data showed the hepatocellular carcinogenesis in the patients who received long term treatment