286. Hepatitis B Vaccine Compliance: Comparing 2-Dose and 3-Dose Vaccines

Katia Bruxvoort, PhD, MPH[1]; Jeff Slezak, MS[1]; Runxin Huang, MS[1]; Lina S. Sy, MPH[1]; William Towner, MD[1]; Bradley Ackerson, MD[2]; Kristi Reynolds, PhD[1]; Lei Qian, PhD[1]; Cheryl M. Carlson, MPH[3]; Zendi Solano, BS[1]; Randall N. Hyer, MD, PhD, MPH[4]; Robert Janssen, MD[5] and Steven J. Jacobsen, MD, PhD[1]; [1]Kaiser Permanente Southern California, Pasadena, California; [2]Kaiser Permanente, South Bay Medical Center, Harbor City, California; [3]Southern California Kaiser Permanente Medical Group, Pasadena, California; [4]Dynavax Technologies, Berkeley, California; [5]Dynavax Technologies Corporation, Berkeley, California

Session: 41. Hepatitis

Thursday, October 3, 2019: 12:15 PM

Background. Less than 1 in 3 US adults who initiated the 3-dose (0, 1, 6 months) hepatitis B vaccine series have completed it. HepB-CpG (Heplisav-B; Dynavax) is a new licensed adjuvanted vaccine that requires only 2 doses (0, 1 month). As part of a cluster study performed at Kaiser Permanente Southern California, we compared compliance with second dose and series completion for HepB-CpG vs. comparator vaccine (Engerix-B; GlaxoSmithKline) recipients.

Methods. The cohort included adults not on dialysis who received their first dose of hepatitis B vaccine in family or internal medicine departments from 8/7/2018 to 2/1/2019. Second dose compliance was assessed for the full cohort, but series completion was assessed for a subset vaccinated from August 7, 2018 to September 30, 2018 to allow at least 6 months' follow-up. Compliance rates were estimated using the Kaplan Meier method. Adjusted hazard ratios (aHR) were estimated using Cox proportional hazard regression with robust variance to account for within medical center correlation, adjusting for age, race/ethnicity, census block income and education, prior healthcare utilization, and factors that trigger alerts for hepatitis B vaccination (diabetes and testing for sexually transmitted infections).

Results. There were 6500 HepB-CpG and 7733 comparator vaccine recipients (1,442 and 2,604 prior to September 30, 2018). Rates of second dose compliance at 60 days were 32.9% for HepB-CpG and 29.1% for comparator vaccine, and rates of series completion at 210 days were 56.9% and 20.6%. There was no significant difference in second dose compliance (aHR 1.14, 95% CI: 0.91, 1.47), but HepB-CpG recipients were 5 times more likely to complete the series (aHR 5.17; 95% CI: 3.84, 6.98). Second dose compliance and series completion were significantly less likely among Blacks compared with Whites and significantly more likely among Asians, adults ≥60 years compared with those < 30 years, and adults living in census blocks with a median annual income of $40,000–69,000 compared with < $40,000.

Conclusion. Overall, second dose compliance was similar, but series completion was better for HepB-CpG recipients than comparator vaccine recipients, suggesting that the 2-dose vaccine could lead to improvements in coverage and protection against hepatitis B virus.

Disclosures. **All authors:** No reported disclosures.

287. Exploring the Natural History and Clinical Outcomes of Hepatitis B Core Antibody Positive Hemodialysis Patients in a Large Metropolitan Tertiary Care Hospital System with a Focus on Occult Hepatitis B

Amit T. Vahia, MD, MPH[1]; Chandrika Chitturi, MD[1]; Olivia Rizzo[2]; Nihn Lwin, MD[1]; Sandeep Soman, MD[1]; Jerry Yee, MD[1]; Vivek Soi, MD[1]; Junior Uduman, MD[1] and George J. Alangaden, MD[3]; [1]Henry Ford Health System, Livonia, Michigan; [2]Wayne State University School of Medicine, Detroit, Michigan; [3]Henry Ford Hospital, Detroit, Michigan

Session: 41. Hepatitis

Thursday, October 3, 2019: 12:15 PM

Background. Occult Hepatitis B (OHB) is defined as hepatitis B core antibody (HBcAb) positivity in the absence of surface antibody (HBsAb) or surface antigen (HBsAg) positivity. The reported incidence ranges from 0.3% to 58% in the hemodialysis (HD) population. Our study is among the first in the United States to examine the natural history of OHB patients (patients). This work is of interest in HD patients to estimate Hepatitis B transmission risk.

Methods. We performed a retrospective analysis of 352 Hep B cAb positive HD patients between 2010 and 2017 in the Henry Ford Health System and Greenfield Dialysis Centers in SE Michigan. This system contains 5 hospitals including a 900-bed tertiary referral center in Detroit, serving a high-risk, medically complex population. Our primary outcomes were the development of HBsAb positivity, considered protective, or development of HBsAg positivity or new Hepatitis B viremia, considered adverse events. Univariate and multivariate logistic regression analysis was performed to study pertinent risk factors for the clinical outcomes comparing OHB and Non-OHB patients. Statistical analysis was performed using SAS 9.4.

Results. Of the 352 HBcAb patients studied, 98 (27%) were OHB patients. Each group shared similar baseline demographics apart from OHB patients having higher ALT and a greater proportion of drug use and Hepatitis C (Hep C) compared with non-OHB patients (Table 1). There were 15 adverse events in the non-OHB group, including 10 viremias. Only 1 adverse event was seen in the OHB group, a patient who developed viremia of 19 copies/mL (Table 2). Conversely, OHB status was a statistically significant predictor of protective HBsAb development in follow-up ($P < 0.01$), occurring at a 7-fold increased rate compared with non-OHB patients. Univariate analysis showed that a history of liver disease, Hep C, and drug use predicted HBsAb development (Table 3). When studying adverse outcomes, history of liver disease raises the risk of adverse events in unadjusted models ($P < 0.05$) (Table 4).

Conclusion. OHB patients in our center tend to develop protective HBsAb titers over time rather than develop viremia or antigenemia in contrast to non-OHB patients. Our study finds that OHB confers minimal risk of potential transmission of Hepatitis B among HD patients.

Table 1: Hepatitis B Core Antibody Positive Patients at HFHS and Greenfield Dialysis Centers, SE Michigan. 2011-2018. Total N = 352

Demographics	Non-Occult Hepatitis B (N = 254)		Occult Hepatitis B (N=98)		P Value
Age in Years (Mean, SD)	68.57	12.8	68.65	10.10	0.9472
Gender (N Male, %)	152.00	59.8	63.00	64.30	0.4435
Baseline AST (Mean, SD)	25.45	18.11	33.82	43.59	0.0689
Baseline ALT (Mean, SD)	19.21	15.21	30.72	48.10	**0.0236**
Baseline Bilirubin (Mean, SD)	0.50	0.34	0.53	0.39	0.6246
Baseline INR (Mean, SD)	1.29	0.55	1.22	0.28	0.2167
Baseline Albumin (Mean, SD)	3.42	0.62	3.57	2.37	0.556
History of Liver Disease (N, %)	66.00	26.0	29.00	29.6	0.3989
History of Hepatitis C (N, %)	81.00	31.9	48.00	49.0	**0.0017**
Diabetes (N,%)	140.00	55.1	52.00	53.1	0.8262
HIV (N,%)	12.00	4.7	5.00	5.1	0.7878
IVDU (N,%)	29.00	11.4	24.00	24.5	**0.0014**
Organ Transplant (N, %)	34.00	13.4	7.00	7.1	0.0972

Table 2: Outcomes Examined - Clinical Endpoints

Endpoint	Non Occult Hepatitis B Patients N=254		Occult Hepatitis B patients N=98		P-Value
Acute Viremic Patients, N, %	10	3.9	1	1.0	0.3026
Total Conversions of Serum Antibody - N, %	13	5.1	32	32.7	**<.0001**
Total Conversions of Serum Antigen - N, %	11	4.3	1	1.0	0.191
Maximum Viremia level (Mean, SD)	4002748	62750171.0	0.1939	1.9	0.3103
Received Hep B Treatment - N, %	11	4.3	0	0.0	0.0677
Adverse Outcome (Ag Conversion or Viremia) N,%	15	5.91	1	1.0	0.1295
Protective Outcome (Ab Conversion Alone) N,%	11.00	4.3	31.00	31.6	**<.0001**

Table 3: Odds of HepB Sab conversion As a Function of Various Risk Factors

Univariate Analysis

Variable	Odds Ratio Estimate	95% Confidence Limits		P Value
Age	0.987	0.961	1.013	0.3225
Gender Male	1.315	0.666	2.598	0.4298
Baseline AST	1.1487	0.9844	1.3405	0.0784
Baseline ALT	1.0291	0.8873	1.1936	0.7045
Baseline Bilirubin	0.7953	0.5242	1.2066	0.2815
Baseline INR	0.8349	0.5579	1.2493	0.3802
Baseline Albumin	0.899	0.583	1.387	0.6314
History of Liver Disease	**2.467**	**1.274**	**4.778**	**0.0074**
Hepatitis C Antibody Positive	**2.527**	**1.312**	**4.866**	**0.0056**
Diabetes	0.984	0.512	1.892	0.9617
HIV	0.965	0.213	4.378	0.9627
IVDU	**3.417**	**1.65**	**7.078**	**0.0009**
Organ Transplant	1.021	0.377	2.766	0.9672
Occult Hepatitis B Status Positive	**10.221**	**4.881**	**21.404**	**<.0001**

Multivariate Analysis

Variable	Odds Ratio Estimate	95% Confidence Limits		P Value
Age	0.987	0.952	1.023	0.4731
Gender Male	0.978	0.438	2.183	0.9573
History of Liver Disease	2.169	0.935	5.03	0.0713
Hepatitis C Antibody Positive	0.882	0.354	2.196	0.7874
Diabetes	1.003	0.467	2.155	0.9929
IVDU	2.243	0.846	5.947	0.1045
Occult Hepatitis B Status Positive	**11.887**	**5.335**	**26.484**	**<.0001**

Table 4: Odds of HepB SAg Conversion or Viremia As a Function of Various Risk Factors

Univariate Analysis

Variable	Odds Ratio Estimate	95% Confidence Limits		P Value
Age	0.974	0.937	1.013	0.1819
Gender Male	1.561	0.537	4.532	0.4132
Baseline AST	1.0579	0.8274	1.3526	0.6537
Baseline ALT	1.0885	0.9243	1.2818	0.3093
Baseline Bilirubin	0.97	0.206	4.568	0.969
Baseline INR	0.628	0.095	4.169	0.6298
Baseline Albumin	0.53	0.247	1.136	0.1025
History of Liver Disease	**2.782**	**1.013**	**7.639**	**0.0471**
Hepatitis C Antibody Positive	0.689	0.237	2.002	0.4938
Diabetes	1.245	0.442	3.51	0.6781
HIV	1.275	0.158	10.265	0.8192
IVDU	1.361	0.371	4.994	0.6426
Organ Transplant	1.798	0.49	6.596	0.3766
Occult Hepatitis B Status Positive	0.332	0.075	1.48	0.1482

Multivariate Analysis

Variable	Odds Ratio Estimate	95% Confidence Limits		P Value
Age	0.978	0.939	1.019	0.2899
Gender Male	1.415	0.451	4.438	0.5518
History of Liver Disease	3.259	0.994	10.69	0.0512
Hepatitis C Antibody Positive	0.3	0.074	1.218	0.0921
Diabetes	1.658	0.506	5.437	0.4037
IVDU	2.595	0.552	12.204	0.2272
Occult Hepatitis B Status Positive	0.185	0.023	1.491	0.113

Disclosures. **All authors:** No reported disclosures.

288. Hepatitis B Virus Reactivation in Patients with Hematologic Malignancies after Anticancer Therapy Which Included Ibrutinib

Alexandre Malek, MD[1]; Yago Nieto, MD, PhD[2]; Ariel D. Szvalb, MD[2]; Shaheer Siddiqui, MD [2]; Mehnaz A. Shafi, MD [2]; Jessica P. Hwang, MD, MPH [2]; Issam I. Raad, MD[2] and Harrys A. Torres, MD [2]; [1]University of Texas- McGovern Medical School/MD Anderson Cancer Center, Houston, Texas; [2]The University of Texas MD Anderson Cancer Center, Houston, Texas

Session: 41. Hepatitis

Thursday, October 3, 2019: 12:15 PM

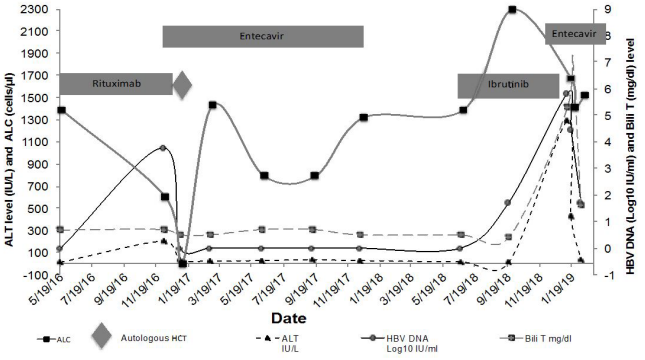
Background. Several cases of severe bacterial, fungal, and viral infections have been reported following ibrutinib therapy. Here, we report a case of a patient with non-Hodgkin lymphoma who developed hepatitis B virus (HBV)–associated liver failure after anti-cancer treatment most recently with ibrutinib. We also review reported cases of HBV reactivation (HBVr) after ibrutinib.

Methods. We searched the Medline and Embase databases and identified 5 patients with HBVr related to ibrutinib for a total of 6 study patients, including our case (figure). HBV-related outcomes were defined according to the 2018 AASLD HBV guidance document.

Results. All 6 patients were men and most (5 or 83%) had chronic lymphocytic leukemia and past HBV infection (table). Three patients (50%) developed HBV-related hepatitis and 2 of them progressed to liver failure. Four patients (67%) had a remote history (≥24 months) of other potential risk factors besides ibrutinib that could contribute to HBVr, including the use of direct-acting antivirals for hepatitis C co-infection (1 pt), hematopoietic cell transplant (HCT) (1 pt) and rituximab use (4 patients). HBVr occurred at least 6 months after initiation of ibrutinib in most patients (4 or 67%), with a median of 9.7 months (range, 1.5–42). In all 4 patients pretreated with rituximab, that treatment was completed at least 24 months before HBVr. Two of these patients received anti-HBV prophylaxis that was stopped 12 months after the completion of rituximab; the other 2 patients were only monitored without antivirals. The HCT recipient received anti-HBV prophylaxis per guidelines. None of the 6 patients treated with ibrutinib were receiving anti-HBV prophylaxis at the time of HBVr, but 5 patients were started on anti-HBV drugs at the first sign of HBVr. Four received entecavir and 1, tenofovir. All treated patients recovered from HBVr. No pt died of HBVr.

Conclusion. Life-threatening HBVr can occur following ibrutinib therapy in patients with past or chronic HBV infection. The temporal association between ibrutinib therapy and reactivation indicates that ibrutinib is the likely cause of the HBVr, and clinicians should be aware of the risk of HBVr in these patients. A provisional approach could be HBV monitoring at regular intervals with initiation of antiviral therapy at the earliest sign of HBV reactivation.

Figure. Changes in alanine aminotransferase, bilirubin, and hepatitis B viral load levels after cancer therapy in a patient with lymphoma and hepatitis B virus–associated liver failure. Labels on the x-axis indicate calendar dates in month, /date, or /year format. ALT, alanine aminotransferase; Bili T, total bilirubin; HBV, hepatitis B virus; HCT, hematopoietic cell transplant.



ALT: alanine aminotransferase; HBV: hepatitis B virus; Bili T: bilirubin total; HCT: hematopoietic cell transplantation

ALC: absolute lymphocyte count

Table. Cases of HBV reactivation in patients treated with ibrutinib

Age, yr	Sex	Cancer	Chemo[a]	Anti-CD20	Ibrutinib dose, mg/d	Months from initial ibrutinib dose to reactivation	Baseline				Post-ibrutinib			HBV-associated hepatitis[c]	HBV-associated liver failure	Rx[d]
							Anti-HBs	Anti-HBc	HBsAg	HBV DNA, log10 IU/mL	HBsAg	Anti-HBs	HBV DNA, log10 IU/mL			
79	M	CLL	No	No	420	13.5	+	+	–	–	N/A	–	6.27	Yes	Yes	TDF
80	M	CLL	Yes	No	280	5	+	+	–	2.62	+	+	7.36	Yes	No	ETV
57	M	CLL	No	Yes[b]	N/A	42	+	+	–	–	–	–	2.96	No	No	No
75	M	CLL	No	Yes[b]	N/A	31	+	+	–	–	+	N/A	8.23	No	No	ETV
59	M	CLL	No	Yes[b]	N/A	1.5	–	+	–	–	N/A	–	2.86	No	No	ETV
68	M	NHL	No	Yes[b]	560	6	–	+	–	–	+	–	5.83	Yes	Yes	ETV

Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; Chemo, chemotherapy; CLL, chronic lymphocytic leukemia; ETV, entecavir; F, female; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; M, male; N/A, not available; NHL, non-Hodgkin lymphoma; Rx, treatment; TDF, tenofovir disoproxil fumarate; +, positive; –, negative.

[a] Received within 12 months of HBVr.

[b] Anti-CD20 (rituximab) therapy was completed at least 24 months before HBVr in all cases.

[c] ALT with median 103 and range of 70-987 IU/l. We reported the peak values of ALT and HBV DNA.

[d] All patients recovered after treatment.

Disclosures. **All authors:** No reported disclosures.

289. Importance of Universal Screening for Hepatitis B in Cancer Patients: Quality Improvement Project in Japan

Nobuyoshi Mori, MD[1]; Tsutomu Motoki, HIM[1]; Takahiro Matsuo, MD[1] and Sachiko Ohde, PhD, EdM[2]; [1]St. Luke's International Hospital, Chuo-ku, Tokyo, Japan; [2]St. Luke's International University Graduate School of Public Health, Chuo-ku, Tokyo, Japan

Session: 41. Hepatitis
Thursday, October 3, 2019: 12:15 PM

Background. Hepatitis B virus (HBV) reactivation after immunosuppressive therapy in cancer patients is associated with significant morbidity and mortality. In the United States (US), infection rate of previous HBV infection and chronic HBV infection in cancer patients is 6.5% and 0.6%,, respectively. Universal screening of HBV including surface antigen (HBsAg) and core antibody (HBcAb) in cancer patients has not been recommended in the United States, but it may be warranted to prevent viral reactivation and adverse clinical outcomes in endemic countries such as Japan.

Methods. We conducted a retrospective chart review at a tertiary care hospital in Tokyo, Japan from July 2003 through March 2019 and collected the data of HBV screening tests in patients with cancer and without cancer. (1) We compared the positive results of HBsAg and HBcAb between patients with cancer and without cancer during the study period. (2) We started a quality improvement (QI) project in 2012 to raise the rate of HBV screening tests in cancer patients and analyzed the rate of HBV screening tests by comparing pre vs. post QI intervention.

Results. Overall, the positivity rate of HBsAg and HBcAb was 1.18% (10,979/929,024) and 20.2% (3,538/17,537), respectively. When we compared positive results of cancer patients with non-cancer patients, HBsAg was significantly higher (1.85% [424/22,934] vs. 1.16% [10,555/906,090], $P < 0.001$) (Figure 1), and HBcAb showed lower tendency (14.1% [701/4,981] vs. 22.6% [2,837/12,556], $P = 0.086$) (Figure 2). Annual trend of screening tests in cancer patients are shown at Figures 3 and 4. Through our QI project, the rate of both HBsAg and HBcAb tests significantly increased from 91.2% (5,064/5,551) to 99.4% (7,748/7,798) ($P < 0.001$) and from 3.9% (215/5,469) to 81.2% (6.304/7,767) ($P < 0.001$), respectively, from 2011 to 2018.

Conclusion. Prevalence of HBV is much higher in Japan than the United States. Universal screening tests of HBV in cancer patients is warranted especially in endemic countries to prevent reactivation and adverse clinical outcomes. The rate of screening tests dramatically increased through our QI project.

Fig 1

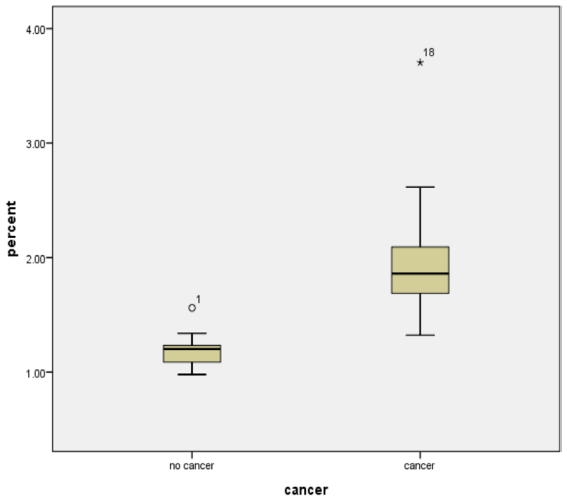


Fig 2