

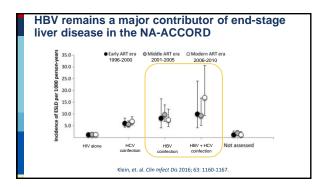
Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Kim has received funding paid to her institution from Gilead Sciences, Inc. (Updated 09/26/22)

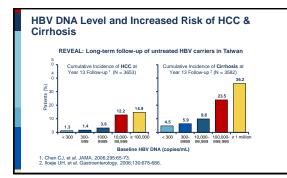
Learning Objectives

After attending this presentation, learners will be able to:

- Incorporate the key components of clinical management of HBV coinfection, including treatment, staging and liver cancer screening
- · Discuss why HBV suppression is a critical goal in therapy.
- Explain the importance of HBV immunization.







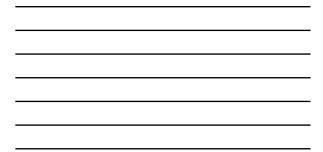


Goals of HBV Antiviral Therapy

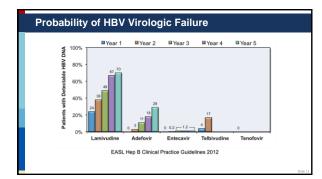
- Short-term Goals
 - Suppress HBV DNA levels
 - Normalize serum ALT levels
 - Loss of HBeAg (if positive at baseline) → loss of HBsAg
 - Reduce necroinflammation → fibrogenesis
- Long-term Goals
 - Delay development of end-stage liver disease
 - Reduce risk of HCC
 - Improve survival

Oral Antiviral Therapy for HBV

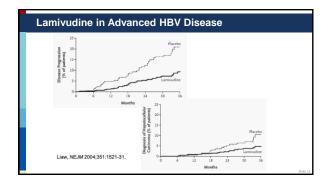
Medication	Potency against HBV	Barrier to HBV Resistance	HIV Activity	Selection of HIV Resistance
Lamivudine	Moderate	Low	Yes	Yes
Adefovir	Low	Moderate	No ^a	No
Entecavir	High	High ^b	Partial	Yes
Emtricitabine	Moderate	Low	Yes	Yes
Telbivudine	High	Low	Partial®	No
Tenofovir ^d	High	High	Yes	Yes
b = In patients wi	thout lamivudine	as; more potent again resistance jainst HIV, but HIV RI		d



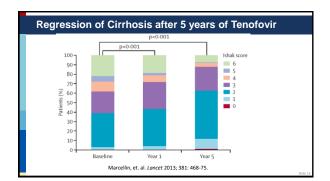
Guidelines	When to Initiate	What to Initiate
AASLD HBV 2018 update	All HIV-HBV patients, regardless of CD4 cell count	Two HBV-active agents: Tenofovir (TAF or TDF) with lamivudine or emtricitabine
DHHS OI, 2022	All HIV-HBV patients, regardless of CD4 cell count	Tenofovir (TAF or TDF) with emtricitabine; chronic administration of lamivudine or emtricitabine as the only HBV-active agent as part of ART should be avoided.
EASL HBV 2017	All HIV-HBV patients, regardless of CD4 cell count	Tenofovir (TAF or TDF) containing ART regimer
APASL HBV 2015	All HIV-HBV patients, "irrespective of immunological, virological or histological considerations"	Two HBV-active agents: Tenofovir with lamivudine or emtricitabine

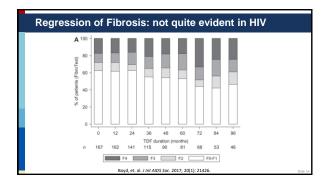


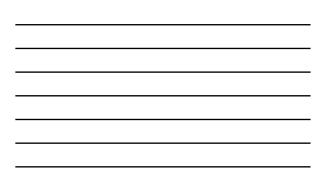












Antiviral Efficacy – Treatment-Naïve, Immune Active HBeAg (+)

Endpoint	Peginterferon	Entecavir [†]	Tenofovir DF [†]	Tenofovii AF [‡]	
% Viral Suppression	30-42%	61%	76%	73%	
% HBeAg loss +/- seroconversion	29-36%	21-25%	21%	22%	
% ALT normalization	34-52%	68-81%	68%		
% HBsAg loss	2-7%	4-5%	8%	1%	

Transient elastography

- Induces elastic shear wave
 propagated through liver tissue
- Pulse-echo ultrasound measures wave velocity, in kilopascals (kPa), as a measure of liver stiffness



Cirrhotic liver >12-14 kPa

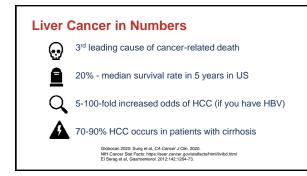
Rockey, et. al. *Gastroenterol*. 2008;134:8-14. Miailhes, et. al. *J Viral Hepat*. 2011;18:61-9.

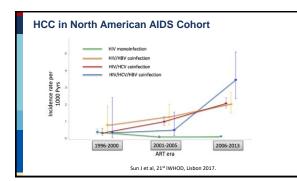
HCC Screening Indications in Patients with HBV

- All persons with cirrhosis
- The following, even in the absence of cirrhosis:
 - Asian or black/African males older than 40 years of age
 - Asian females older than 50 years of age
 - Persons with a family history of HCC
 - Persons with hepatitis D virus coinfection

Abdominal ultrasound every 6 months with or without serum alpha-fetoprotein.

HBV Primary Care Guidance (Feb 2020): https://www.hepatitisb.uw.edu.





Key Predictors of HIV-HBV associated HCC

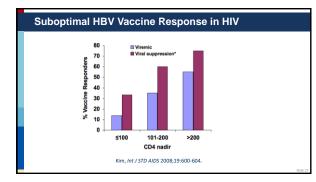
• Age

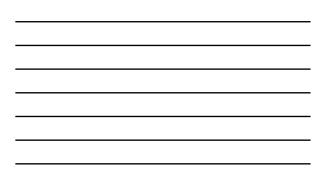
- · Alcohol use (hazardous)
- Chronic hepatitis C coinfection
- HBV DNA level

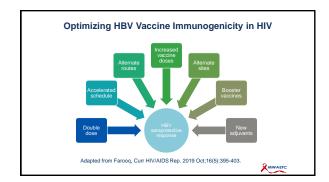
Ris	Risk of HCC by DNA Level in HIV/HBV				
	HBV DNA level (Time-Updated)	Adjusted HR [†] (95% CI)			
	HBV DNA, 200 IU/mL cut-off				
	≤200	Reference			
	>200	2.70 (1.23-5.93)			
	HBV DNA, 200,000 IU/ml cut-off				
	≤200	Reference			
	201-200,000	1.77 (0.63-4.94)			
	>200,000	4.34 (1.72-10.94)			
	$^{\dagger}\text{Hazard}$ ratio after adjusting for age and year of s	tart of follow-up			

Kim HN et al, Hepatology. 2021 Mar; doi/10.1002/hep.31839.

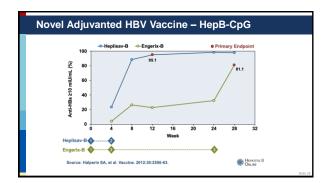
Risk of HCC by Duration of HBV Suppression				
	Characteristic (Time-Updated)	Adjusted HR [†] (95% CI)		
	Duration of HBV Suppression [‡]			
	Detectable	Reference		
	Undetectable <1 year	1.12 (0.55-2.28)		
	Undetectable ≥1 year	0.42 (0.24-0.73)		
	Duration of HBV Suppression§			
	Detectable	Reference		
	Undetectable <1 year	1.14 (0.56-2.31)		
	Undetectable 1-4 years	0.55 (0.28-1.07)		
	Undetectable ≥4 years	0.34 (0.17-0.67)		
	[†] Adjusted for age, sex, race, diabetes, HIV RNA, Cl [‡] p-value test for trend = 0.002 [§] p-value test for trend = 0.001	04 %, heavy alcohol use, year of follow-u		
	Kim HN et al, Hepatology. 2021	Mar; doi/10.1002/hep.31839.		

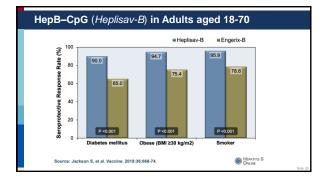














CPG 7909 Adjuvant plus Hepatitis B Virus Vaccination in HIV-Infected Adults Achieves Long-Term Seroprotection for Up to 5 Years

C. L. Cooper,' J. B. Angel,' I. Seguin,' H. L. Davis,¹³ and D. W. Camered' "Division of Intection Disease, University of Otaxes at the Otaxes Integrate, Otaxes Neutrin Research Institute, and "Caley Plannaceutical Group, Otaxes, Canada, and "Coley Plannaceutical Group, Welfeling, Monoschusetts

Unit, Units, Classi, and Units Productional Units, Weining Monachandi Background, Human Immunodedicisery (wiri) (HUV-infected persons are hyporesponsive to hepathin B vices (HBV) vaccination, CPG 7996 in an oligodeserpracelositic containing immunositumitatory CpG routifs that activate human B and planearies disolification. The HB line receiptor of the previously represent the addition of CPG Weinis B and planearies disolification. The control of the second sec

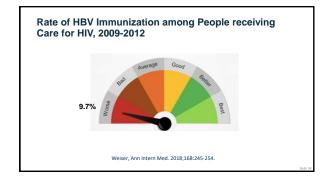
nginer in the CPG 1999 group main in the control group (without CPG 1999 adjuvant) at all measured nine points. *Conclusions*. The immunostimulatory properties of CPG 7909 present an important strategy in achieving longterm protection in HV-infected patients and other HBV vaccine-hyporesponsive populations.

Cooper et al, Clin Infect Dis 2008; 46:1310-4.

Time to Loss of HBV Seroprotection

Slide 32	

Hep B OI Guidelines – 2022 update			
Vá	ccination Schedule		
•	HepB vaccine IM (Engerix-B [®] 40 mcg or Recombivax HB [®] 20 mcg) at 0, 1, and 6 months (double dose, three-dose series) (AII); or		
•	Combined HepA and HepB vaccine (Twinrix [®]) 1 mL IM as a three-dose series (at 0, 1, and 6 months) (All); or		
•	Vaccine conjugated to CpG (Heplisav-B [®]) IM at 0 and 1 months (CIII)—a two-dose series can be used only when both doses given are Heplisav-B [®] .		
•	Anti-HBs should be obtained 1 to 2 months after completion of the vaccine series.		
Fo	r Vaccine Non-Responders		
•	Revaccinate with a second double-dose, three-dose recombinant HBV vaccine series (BIII). 4-dose series has not been demonstrated to be superior to the 3-dose; or		
•	Revaccinate with two-dose series of HepBCpG (Heplisav-B®) (BIII).		
•	For people with low CD4 count at the time of first vaccination series, some experts might delay revaccination until after a CD4 count ≥200 is achieved and sustained with ART (CIII).		
	Accessed at clinicalinfo.hiv.gov		



Summary

- HBV remains a big contributor to liver-related deaths.
- No functional cure for HBV but HBV suppression with antiviral therapy can reduce the risk of complications.
- Sustained HBV suppression is key in preventing HCC.
- Stage your patients with elastography if available; we can miss cirrhosis otherwise.
- HBV vaccination just do it! And don't forget to check for anti-HBs seroconversion...

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Hepatitis B Online		Course Modules
University of Washington National Hepatitis Training Center		Self Study with Progress Tracker
		Free CME and CNE/CE
funded by Centers for Disease Control and Prevention (CDC)		Start the Self-Study Medules +
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Hepatitis B Virus Modules		
	Quick Reference >	Self-Study CNUCHE
HBV Epidemiology Reserves United States and partial HTV incidence and prevalence, populations at mits for HTV acquisition, and the clinical and laboratory otheria for HTV case definitions.	Rapidly access into about Epidemiology	Track progress and receive CE credit
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