

Chronic Hepatitis B and HIV

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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)

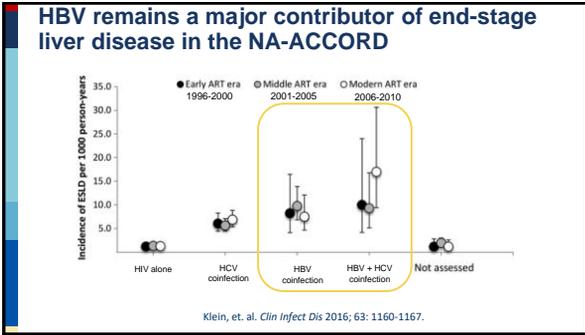
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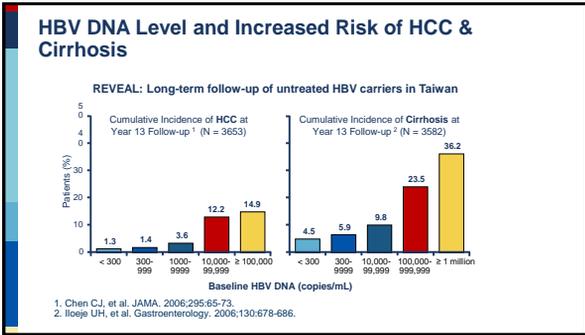
Learning Objectives

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**.

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- ### 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 ^c	No
Tenofovir ^d	High	High	Yes	Yes

^a = Anti-HIV activity at higher doses; more potent against HBV
^b = In patients without lamivudine resistance
^c = No in vitro activity observed against HIV, but HIV RNA decline reported
^d = Either TDF or TAF

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Treatment of HIV and Chronic HBV

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 regimen
APASL HBV 2015	All HIV-HBV patients, "irrespective of immunological, virological or histological considerations"	Two HBV-active agents: Tenofovir with lamivudine or emtricitabine

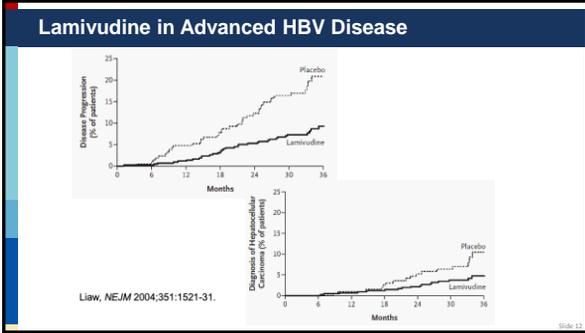
AASLD, American Association for the Study of Liver Diseases; HBV, hepatitis B; DHHS, US Department of Health & Human Services; OI, opportunistic infections; EASL, European Association for the Study of Liver; APASL, Asian Pacific Association for the Study of the Liver.

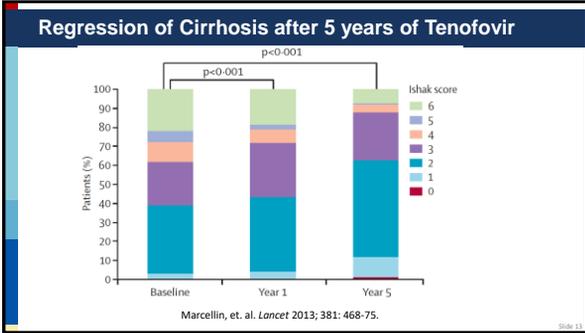
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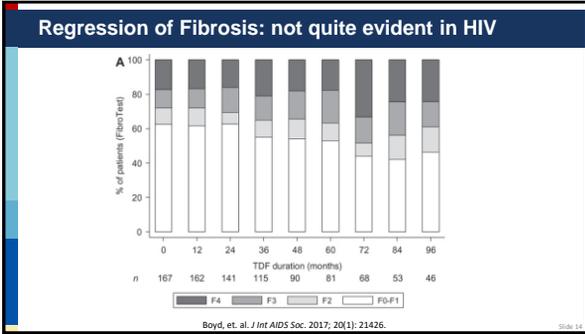
Probability of HBV Virologic Failure



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Liver Cancer in Numbers



3rd leading cause of cancer-related death



20% - median survival rate in 5 years in US



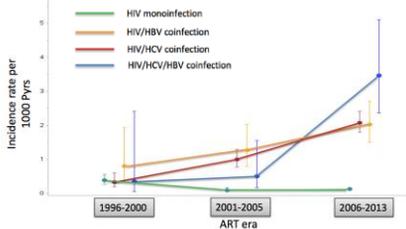
5-100-fold increased odds of HCC (if you have HBV)



70-90% HCC occurs in patients with cirrhosis

Globocan 2020: Sung et al, CA Cancer J Clin. 2020.
 NIH Cancer Stat Facts: <https://www.cancer.gov/statfacts/html/livbdt.html>
 El Serag et al, Gastroenterol. 2012;142:1264-73.

HCC in North American AIDS Cohort



Sun J et al, 21st IWHOD, Lisbon 2017.

Key Predictors of HIV-HBV associated HCC

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

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Risk of HCC by DNA Level in HIV/HBV

HBV DNA level (Time-Updated)	Adjusted HR ¹ (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)

¹ Hazard ratio after adjusting for age and year of start of follow-up

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

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Risk of HCC by Duration of HBV Suppression

Characteristic (Time-Updated)	Adjusted HR ¹ (95% CI)
Duration of HBV Suppression ²	
Detectable	Reference
Undetectable <1 year	1.12 (0.55-2.28)
Undetectable ≥1 year	0.42 (0.24-0.73)
Duration of HBV Suppression ³	
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)

¹ Adjusted for age, sex, race, diabetes, HIV RNA, CD4 %, heavy alcohol use, year of follow-up

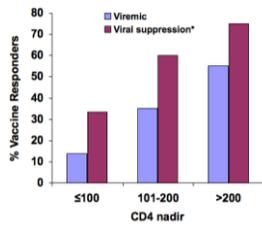
² p-value test for trend = 0.002

³ p-value test for trend = 0.001

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

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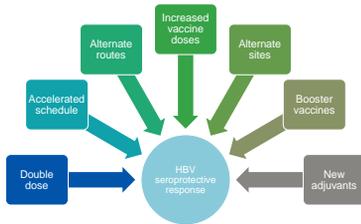
Suboptimal HBV Vaccine Response in HIV



Kim, *Int J STD AIDS* 2008;19:600-604.

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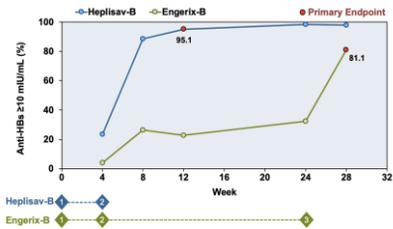
Optimizing HBV Vaccine Immunogenicity in HIV



Adapted from Farooq, Curr HIV/AIDS Rep. 2019 Oct;16(5):395-403.



Novel Adjuvanted HBV Vaccine – HepB-CpG

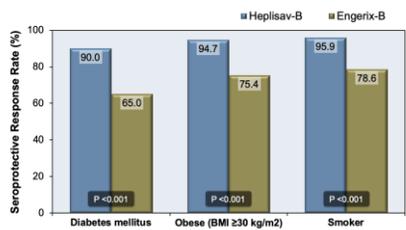


Source: Halperin SA, et al. Vaccine. 2012;30:2556-63.



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HepB-CpG (Heplisav-B) in Adults aged 18-70



Source: Jackson S, et al. Vaccine. 2018;36:668-74.



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Rate of HBV Immunization among People receiving Care for HIV, 2009-2012



Weiser, Ann Intern Med. 2018;168:245-254.

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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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