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HBV-HIV Co-Infection & Tenofovir Interruption in the United States:

Monitoring Practices and Incidence of Hepatitis B Reactivation or Hepatitis Flare

Douglas T. Dieterich
Icahn School of Medicine at Mount Sinai

Laurence Brunet, Ricky K Hsu, Gerald Pierone Jr, Karam Mounzer, Rachel Palmieri Weber, Megan S Dunbar, Joshua Gruber, Leland J Yee, Catherine Frenette, Gregory P Fusco

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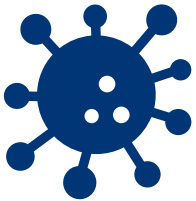
Background

- People with HBV and HIV are at risk of HBV reactivation in the absence of a suppressive HBV treatment
- An ART regimen including tenofovir (TDF or TAF) is recommended to maintain HBV viral suppression
  - Lamivudine (3TC) or emtricitabine (FTC) without tenofovir: high risk of HBV resistance
  - Entecavir (ETV) without tenofovir: high risk of HIV resistance



Background

- Most people with HIV and HBV have undetectable HBV DNA because of the therapeutic overlap between HIV and HBV. Therefore, HBV may be forgotten by primary and HIV care providers
- The rise in popularity of 2-drug regimens for HIV treatment could lead to preventable HBV reactivations and hepatitis flares in people with HIV and HBV for whom HBV has previously been well controlled with standard tenofovir-containing ART regimens

Study Objectives

Among people with HIV and HBV in routine clinical care:

Describe TDF and TAF interruptions

Describe HBV monitoring practices before and during each interruption

Assess the incidence of HBV reactivation and hepatitis flare

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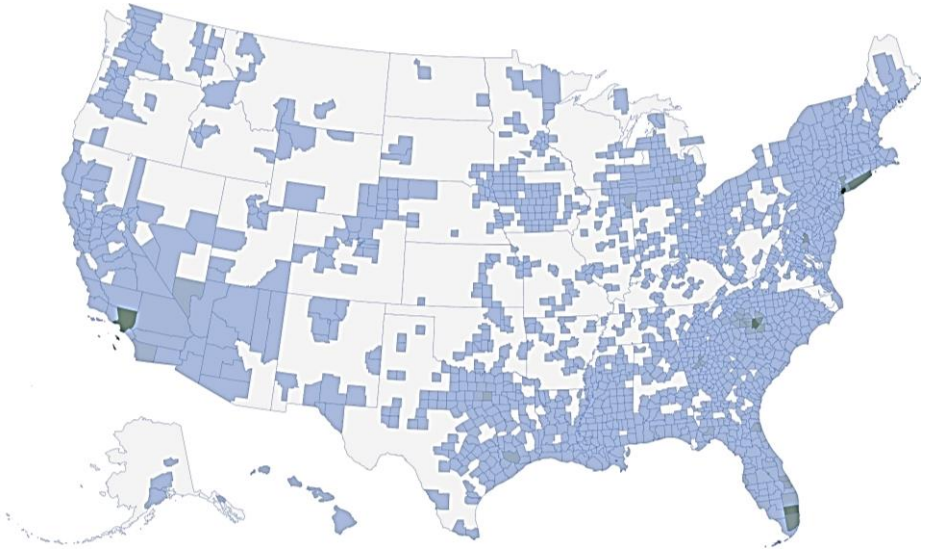
The Longitudinal Cohort



- Database of EHR
- > 150K people with HIV
  - ~ 14% of people with HIV in the US
  - > 8K people with HBV (6%)
  - 17% women
  - 42% Black
  - ~ 40% on Medicare, Medicaid or ADAP/Ryan White

Study Population

- HIV and HBV (HBsAg+ and/or HBcAb+)
- Tenofovir interruption: stopped TDF or TAF for ≥45 days between 3 Oct 2001 and 20 Apr 2023
- ≥1 ALT, HBsAg, or HBV DNA measurement during the interruption

5343 individuals
14% had ≥2 interruptions

6252 tenofovir interruptions
Median duration: 23 months (IQR: 7, 53)
79% lasting ≥6 months

HIV Characteristics at Start of First Interruption

	People with ≥1 tenofovir interruption N = 5343
HIV viral load[a]	
<50 copies/mL	3,391 (54%)
≥50 to <200 copies/mL	714 (11%)
≥200 copies/mL	1,692 (32%)
CD4 cell count >500 cells/μL[a]	2850 (46%)

[a] Last measurement within 12 months before/at start of interruption; missing in 7% of the population

Risk of Reactivation by HBV Serology

	HBsAg	HBcAb	HBsAb	Interruptions
High Risk	+	Not Applicable		685 (11%)
Moderate Risk	— (or unknown)	+	— (or unknown)	1219 (19%)
Low Risk	— (or unknown)	+	+	4348 (70%)

Monitoring Within 12 Months Before the Interruption

	High Risk[a]	Moderate Risk[b]	Low Risk[c]
# interruptions	685	1219	4348
Any ALT test	622 (91%)	1115 (91%)	4055 (93%)
Last ALT ≤ ULN	456 (73%)	911 (82%)	3450 (85%)
Any HBV DNA test	302 (44%)	78 (6%)	354 (8%)

[a] HBsAg+
[b] HBsAg- or unknown, HBcAb+, HBsAb- or unknown
[c] HBsAg- or unknown, HBcAb+, HBsAb+

Monitoring During the Interruption

	High Risk[a]	Moderate Risk[b]	Low Risk[c]
# interruptions	685	1219	4348
Any ALT test	677 (99%)	1216 (100%)	4338 (100%)
Any HBV DNA test	359 (52%)	109 (9%)	236 (5%)
Median weeks to 1st test	19 (IQR: 8, 48)	48 (IQR: 16, 121)	65 (IQR: 15, 233)
Any HBsAg test	170 (25%)	373 (31%)	1207 (28%)
Both HBV DNA & HBsAg	116 (17%)	75 (6%)	131 (3%)

[a] HBsAg+
[b] HBsAg- or unknown, HBcAb+, HBsAb- or unknown
[c] HBsAg- or unknown, HBcAb+, HBsAb+

Anti-HBV Agents During TDF or TAF Interruptions

	High Risk[a]	Moderate Risk[b]	Low Risk[c]
# interruptions	685	1219	4348
Any anti-HBV agent[d]	300 (44%)	589 (48%)	2194 (50%)
3TC	258 (86%)	569 (97%)	2157 (98%)
FTC	15 (5%)	26 (4%)	57 (3%)
ETV	92 (31%)	3 (<1%)	3 (<1%)

[a] HBsAg+
[b] HBsAg- or unknown, HBcAb+, HBsAb- or unknown
[c] HBsAg- or unknown, HBcAb+, HBsAb+
[d] All anti-HBV agents used in any regimen throughout the interruption

HBV Reactivation Definition (AASLD Guidelines)

HBsAg+ (**high risk**)

- If detectable DNA at baseline: ≥100-fold DNA increase
- If undetectable DNA at baseline: DNA ≥1,000 IU/mL
- If DNA missing at baseline: DNA ≥10,000 IU/mL

HBsAg-/HBcAb+ (**moderate risk** or **low risk**)

- Any detectable HBV DNA

or

- Seroconversion to HBsAg+

Incidence of HBV Reactivation by Risk Group

High Risk
- 685 interruptions
- 117 reactivations (17%); 29% with flare

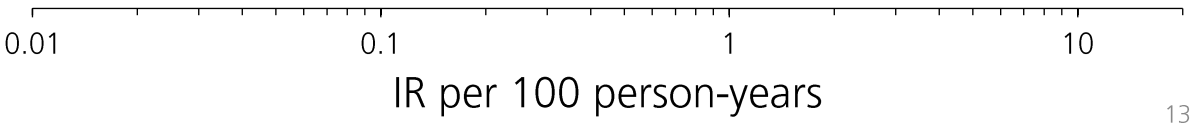
9.92 (8.28, 11.89)

Moderate Risk
- 1219 interruptions
- 24 reactivations (2%); 25% with flare

0.67 (0.45, 1.00)

Low Risk
- 4348 interruptions
- 10 reactivations (<1%); 10% with flare

0.08 (0.04, 0.15)



Hepatitis Flare Definition (AASLD Guidelines)

If ALT is available at baseline

- ALT >100 U/L

&

- ≥3-fold ALT increase

If ALT is missing at baseline

- ALT >5X ULN

Incidence of Hepatitis Flare by Risk Group

High Risk
- 685 interruptions
- 68 flares (10%); 50% with reactivation

5.53 (4.36, 7.01)

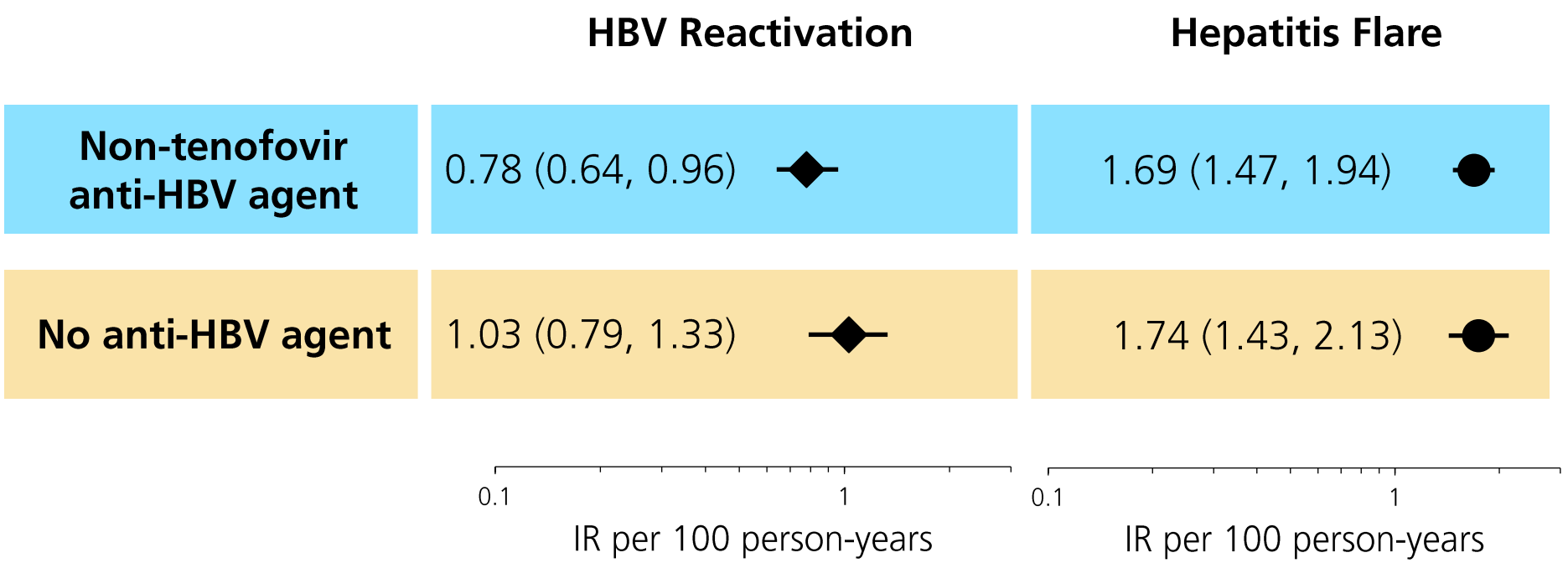
Moderate Risk
- 1219 interruptions
- 59 flares (5%); 10% with reactivation

1.74 (1.35, 2.24)

Low Risk
- 4348 interruptions
- 162 flares (4%); 1% with reactivation

1.31 (1.13, 1.53)

Incidence of Reactivation and Flares by Anti-HBV Agent (3TC, FTC, ETV) Use

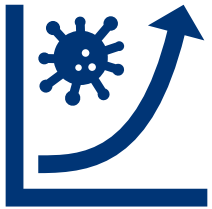


Discussion – Monitoring & Treatment

- In the presence of HIV infection, HBV monitoring and treatment is often overlooked by primary and HIV care providers:
  - High proportion of HIV virological suppression
  - Common and lengthy TDF and TAF interruptions
  - HBV DNA monitoring during only 52% of **high risk** interruptions and <10% of **moderate risk** or **low risk** interruptions

Discussion – Risk of Reactivation

- All were at risk for HBV reactivation
  - The risk was substantially higher in the **high risk** group (HBsAg+)
  - The risk was comparable whether or not non-tenofovir agents were used during the interruption
- Some reactivations were likely missed due to lack of testing
  - The very low levels of testing in the **moderate risk** and **low risk** groups limited our ability to draw definitive conclusions



Conclusions

- Awareness of HBV status and ongoing monitoring is necessary to avoid potential HBV reactivation or hepatitis flare and unnecessary morbidity and mortality from this highly treatable virus
- ART regimens treating HIV and HBV simultaneously should be a top consideration for people with HIV and HBV

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