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Background

- CAB+RPV LA is a complete injectable 2-drug ART regimen with potential for improved adherence but no anti-HBV activity
- People with HIV-HBV co-infection should receive ART regimens that include ARVs with anti-HBV activity (full anti-HBV activity: TDF, TAF, ETV; high risk of resistance: 3TC, FTC)
- In the absence of anti-HBV medications:
 - High risk of HBV reactivation during active HIV-HBV co-infection (HBsAg+ and/or detectable HBV DNA)
 - Evidence is mixed for prior HBV (HBsAg- & HbCAb+)

Objective

- To assess the prevalence of HIV-HBV co-infection among CAB+RPV LA users in the US OPERA Cohort
- To describe HBV and HIV outcomes during CAB+RPV LA use with HIV-HBV coinfection

Methods

Study population

- OPERA cohort: Prospectively captured, routine clinical data from EHRs in the US (101 clinics, 23 US states/territories), representing ~14% of people with HIV in the US
- Inclusion criteria: People with HIV, aged 18+, started CAB+RPV LA injections between 21JAN2021 and 31DEC2024
 - Objective 2 only: Prevalent HBV co-infection (Table 1)
- Censoring criteria: CAB+RPV LA discontinuation, 12 months without clinical contact, death, or study end (30JUN2025)

Table 1. Serology-based HBV classification

	Prior HBV with immunity	Prior HBV without immunity	Active HBV
HBsAg	Unreactive or missing	Unreactive	Reactive
	AND	AND	
HbCAb	Reactive	Reactive	OR
	AND	AND	
HBsAb	Reactive	Unreactive	
	AND	AND	
HBV DNA	Undetectable or missing	Undetectable or missing	Detectable

HBV reactivation

- Assessed among individuals with follow-up HBsAg or HBV DNA
- Among those with prior HBV with/without immunity: Detectable HBV DNA and/or reactive HBsAg during follow up
- Among those with active HBV: ≥100-fold HBV DNA increase (if detectable baseline DNA), any HBV DNA ≥1,000 IU/mL (if undetectable baseline DNA), or any HBV DNA ≥10,000 IU/mL (if no baseline DNA)

HIV virologic suppression

- Assessed among individuals with a baseline HIV RNA <200 copies/mL (within 12 months before/at CAB+RPV LA start) and follow-up HIV RNA
- All or last follow-up HIV RNA <200 copies/mL; last follow-up HIV RNA <50 copies/mL

Results

Figure 1. HBV prevalence among people with HIV starting CAB+RPV LA injections in OPERA (N = 5,275)

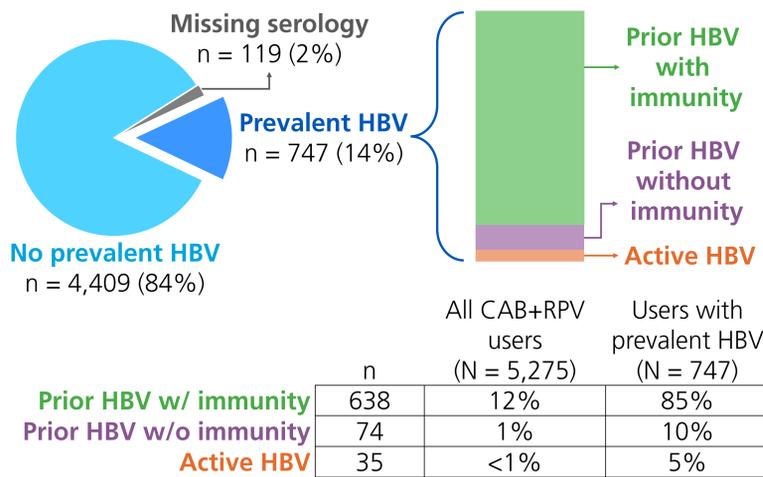


Table 2. Characteristics of people with prevalent HBV at CAB+RPV LA start

	Prior HBV with immunity N = 638	Prior HBV without immunity N = 74	Active HBV N = 35
Age, median (IQR)	50 (40, 58)	50 (41, 58)	51 (41, 58)
Women, n (%)	75 (12)	11 (15)	6 (17)
Black race	278 (44)	35 (47)	16 (46)
≥1 HBV vaccine dose, n (%)	179 (28)	42 (57)	11 (31)
Anti-HBV agent(s) prior to CAB+RPV LA start, n (%)	559 (88)	69 (93)	30 (86)
Concurrent anti-HBV agent at CAB+RPV LA start, n (%)	1 (<1)	0 (0)	3 (9)

Table 3. HBV and HIV measurements among people with prevalent HBV

	Prior HBV with immunity N = 638	Prior HBV without immunity N = 74	Active HBV N = 35
HBV measurements			
Baseline HBV DNA ^a , n (%)	31 (5)	6 (8)	13 (37)
Detectable, n (%)	---	---	6 (46)
Follow-up measurements ^b , n (%)	199 (31)	31 (42)	21 (60)
HIV measurements			
Baseline HIV RNA ^a , n (%)	634 (99)	74 (100)	35 (100)
<200 copies/mL, n (%)	610 (96)	70 (94)	34 (97)
Follow-up HIV RNA, n (%)	566 (93)	65 (93)	31 (91)

^a Within 12 months before/at first CAB+RPV injection
^b Include HBsAg or HBV DNA (prior HBV with/without immunity) or HBV DNA (active HBV), collected between CAB+RPV LA start and censoring

Abbreviations: 3TC, lamivudine; CAB, cabotegravir; EHR, electronic health records; ETV, entecavir; FTC, emtricitabine; HbCAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B; IQR, interquartile range; LA, long-acting; N, number; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; RPV, rilpivirine; US, United States; w/, with; w/o, without

Figure 2. HBV reactivation among people with prevalent HBV and any follow-up HBV measurements

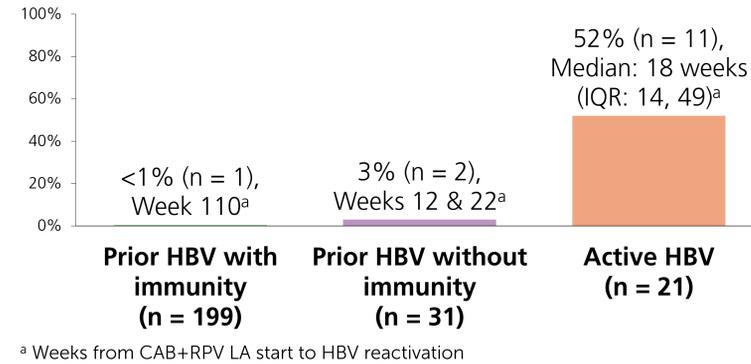
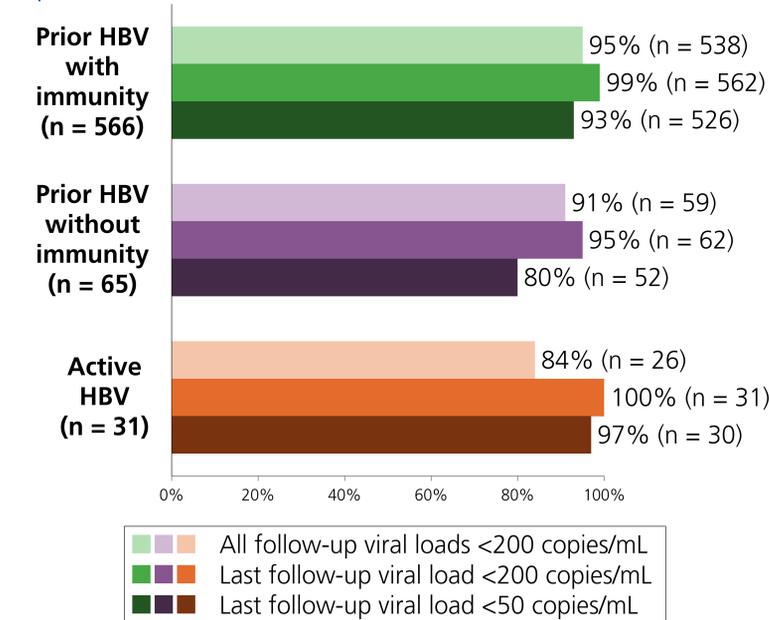


Table 4. Use of anti-HBV agent(s) among people with HBV reactivation

	Prior HBV with immunity N = 1	Prior HBV without immunity N = 2	Active HBV N = 11
Concurrent anti-HBV agent(s) before reactivation, n (%)	0 (0)	0 (0)	1 (9)
Switched to oral ART with anti-HBV activity after reactivation, n (%)	0 (0)	2 (100)	5 (46)
Continued CAB+RPV after reactivation, n (%)	1 (100)	0 (0)	6 (54)
Added anti-HBV agent(s) to CAB+RPV, n (%)	0 (0)	---	5 (83)

Figure 3. HIV virologic outcomes among people with prevalent HBV, baseline HIV RNA <200 copies/mL, and follow-up HIV RNA measurement(s)



Discussion

- Of 5,275 people with HIV starting CAB+RPV LA, 747 (14%) had prevalent HBV co-infection (Fig 1)
 - Most (85%) had prior HBV with immunity (HBsAb+)
 - Active HBV (HBsAg+ or detectable HBV DNA) was infrequent among CAB+RPV LA users (5%)
 - In the US, 3-8% of people with HIV are estimated to have HBsAg+ in systematic reviews
- Very few people with HBV co-infection received HBV treatment concurrently with CAB+RPV LA (Table 2)
- HBV serology and DNA measurements were often lacking before and during CAB+RPV LA use (Table 3)
- Incidence of reactivation varied greatly depending on baseline HBV serology (Fig 2)
 - Infrequent among people with prior HBV with/without immunity (<1% and 3%, respectively)
 - More than half of the people with active HBV (52%)
- Among people with active HBV who experienced a reactivation, 54% continued CAB+RPV LA injections, most of whom added an anti-HBV agent to CAB+RPV LA (Table 4)
- HIV virologic suppression was maintained at the end of follow-up by most (95-100% with last HIV RNA <200 copies/mL), regardless of baseline HBV serology (Fig 3)
- Limitations: Possible misclassification of HBV infection type or underestimation of HBV reactivation due to suboptimal HBV monitoring, and inability to distinguish between re-infection and reactivation

Key Findings

In people with HIV-HBV co-infection in routine clinical care in the US:

- CAB+RPV LA was highly effective for HIV control
- HBV reactivation was uncommon in people with prior HBV with (<1%) and without (3%) immunity, but frequent in people with active HBV (>50%)
- Concurrent HBV treatment and monitoring was insufficient

These results emphasize the importance of HBV screening, monitoring, and treatment among all people with HIV

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