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BACKGROUND

- Low-level viremia (LLV) is commonly observed among people with HIV (PWH) receiving long-acting (LA) cabotegravir/rilpivirine (CAB/RPV) in real-world clinical settings.
- Real-world CAB and RPV drug concentrations appear more variable than those reported in clinical trials, with unclear implications for virologic outcomes.
- In a large clinic-based cohort, the Ward 86 Special Program on LA ART to Stop HIV (SPLASH), we measured CAB/RPV drug levels and examined their association with subsequent virologic outcomes

METHODS

- Residual plasma samples were collected from participants in the Ward 86 SPLASH program 8/2024–2/2025 under research protocols (UCSF IRB# 10-03640)
- CAB and RPV plasma concentrations were measured using liquid chromatography–tandem mass spectrometry at the UCSF Hair Analytical Laboratory using validated methods
- Samples from late injections were excluded; drug levels categorized per PAIC90 and 4×PAIC90 thresholds
- Tobit regression evaluated predictors of viral load ≥30 copies/mL, adjusting for age, sex, BMI, viremia at initiation, and time since injection

RESULTS

- 114 PWH contributed 193 plasma samples.
- Median age 51 years (IQR 38–59); 22% women.; 26% Black, 47% White, 29% Hispanic
- One-third of participants initiated LA ART with viremia ≥50 copies/mL
- At most recent measurement, 8% had viral load 30–200 copies/mL, 4% had viral load >200 copies/mL

Drug Concentrations

- For every 8-week dosing: CAB mean = 1422, SD = 802; RPV mean = 75, SD = 116
- For every 4-week dosing: CAB mean = 2263, SD = 1420; RPV mean = 290, SD = 1436

With real-world use of long-acting ART, lower cabotegravir concentrations were associated with detectable viral load, highlighting the potential importance of pharmacokinetically informed dosing strategies.

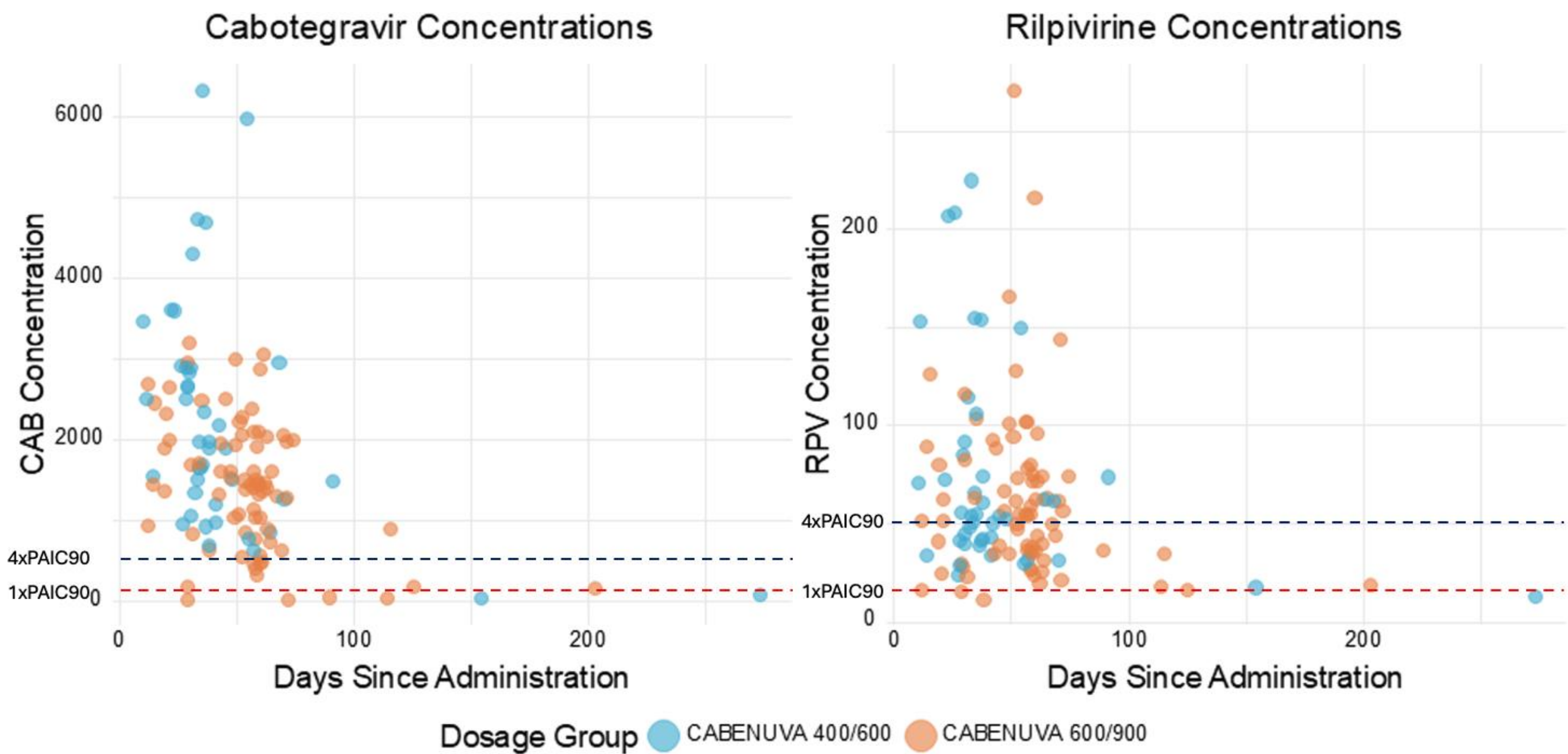
RESULTS CONTINUED

- For RPV: 41% (80/193) of samples had levels below 4×PAIC90; 8% < PAIC90
- For CAB: 17.1% (33/193) of samples were below 4×PAIC90; 4.2% < PAIC90

Drug Concentrations and HIV Viral Load

- For bimonthly 600/900 mg dosing, 15% had viral load >30 copies/mL vs, 7.5% with monthly dosing; difference still statistically significant (p=0.03) after controlling for viremia at initiation and time since injection
- Lower CAB levels were associated with increased risk of detectable viremia.**
- Participants with CAB concentrations <4×PAIC90 had a two-fold higher risk of viral load >30 cps/mL (20% vs. 11%; p=0.04)
- No association between RPV concentrations and viral load >30 cp/mL (10% vs. 13%; p=0.22)
- After adjustment for age, sex, and BMI, both CAB and RPV concentrations demonstrated high inter-individual variability (**Figure**)

Figure: Cabotegravir and Rilpivirine Concentrations by Dosing Interval and Time Since Administration



CONCLUSIONS

- CAB and RPV levels during LA ART are highly variable in a real-world clinic population
- Lower cabotegravir concentrations—but not rilpivirine concentrations—were associated with elevated viral load
- These findings suggest that pharmacokinetic variability, potentially related to population characteristics or injection practices, may influence treatment success
- Concentration-dependent or individualized dosing strategies may optimize outcomes on LA ART

ADDITIONAL KEY INFORMATION

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PLAIN LANGUAGE SUMMARY

In a real-world HIV clinic, blood levels of long-acting HIV medications (cabotegravir and rilpivirine) varied widely between patients and were often lower than what was seen in clinical trials. People with lower cabotegravir levels were more likely to have detectable virus, suggesting that drug exposure matters for keeping HIV fully suppressed on long-acting treatment. In the future, we may dose long-acting treatment based on drug levels

