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BACKGROUND

- Low plasma cabotegravir (CAB) and rilpivirine (RPV) concentrations are associated with increased risk of virologic failure
- Clinically, therapeutic drug monitoring is being performed with single trough concentrations to evaluate therapy
- High interindividual (CAB 31%, RPV 35%) and intraindividual (CAB 52%, RPV 29%) variability are reported during first 12 months of long-acting (LA) CAB/RPV use

METHODS

- **Prospective, observational cohort study**
 - Trough concentrations prior to each dose x 3 visits per patient
- **Inclusion Criteria:**
 - People with HIV who received > 12 months of continuous LA CAB/RPV (600 mg/900 mg) given IM every 2 months
 - No missed or off-schedule doses in 12 months prior to enrollment or during the study period
- **Primary Outcome:**
 - Inter- and intraindividual CAB and RPV trough concentrations (% coefficient of variation [CV]; Fleiss Kappa; intraclass correlation coefficient [ICC])
- **Secondary Outcomes:**
 - Proportion of participants with CAB or RPV concentrations below 4x PA-IC₉₀ (CAB = 664 ng/mL; RPV = 48 ng/mL)
 - Laboratory or clinical characteristics associated with CAB or RPV below 4x PA-IC₉₀

RESULTS

Table 1: Participant Demographics at Entry

n=30 participants	
Age, years	45 (33, 59)
Male	24 (80%)
Race	
White	21 (70%)
Black	8 (26.7%)
Alaska Native	1 (3.3%)
Body mass index, kg/m ²	30 (26, 34)
Duration on LA CAB/RPV, weeks	71 (55, 97)

Data reported as median (IQR) or n (%)

After 1 year of continuous use, high inter- and moderate intraindividual variability were observed. This variability should be considered when performing therapeutic drug monitoring to guide and evaluate therapy.

Figure 1: Individual CAB Trough Concentrations

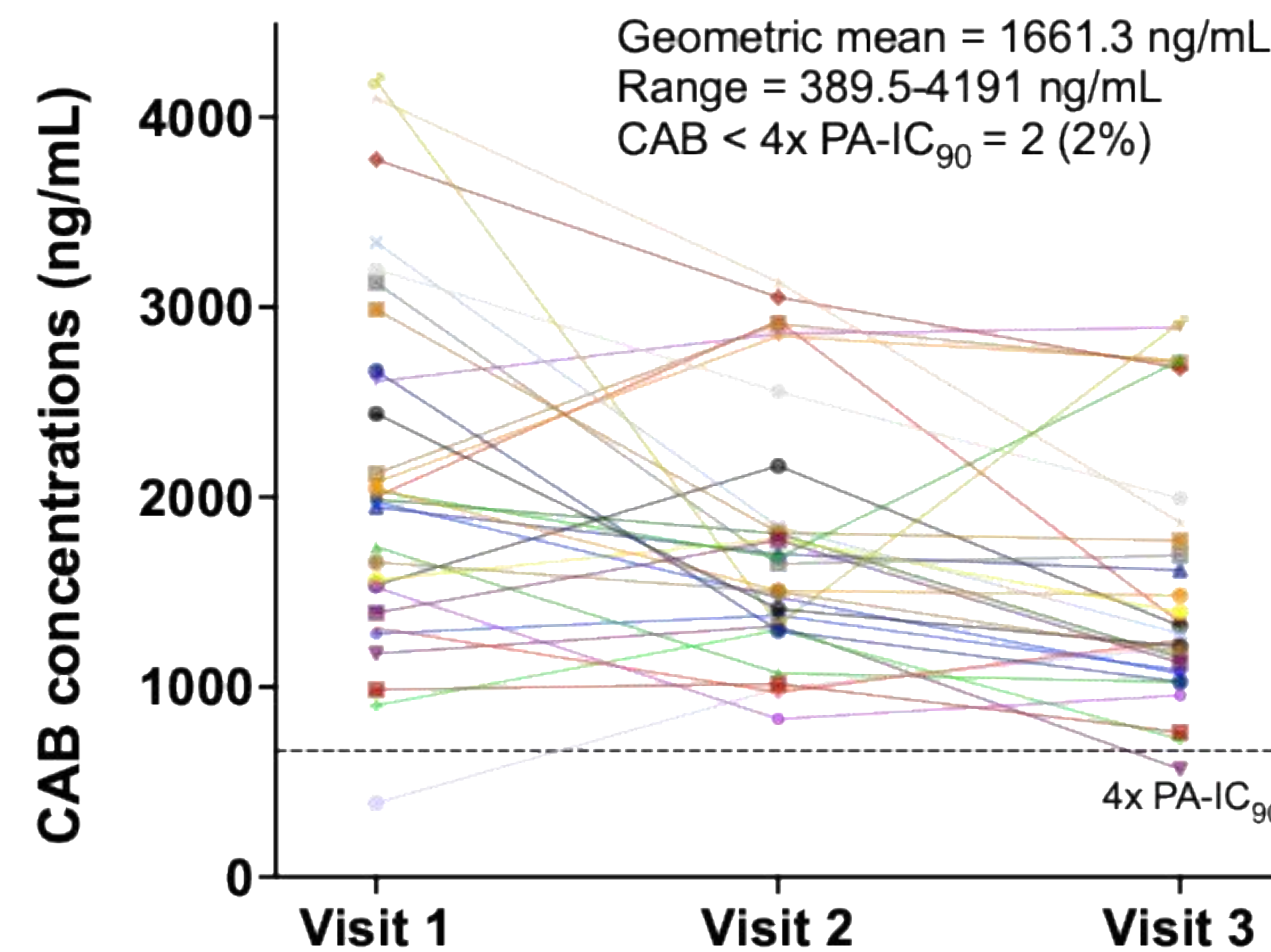
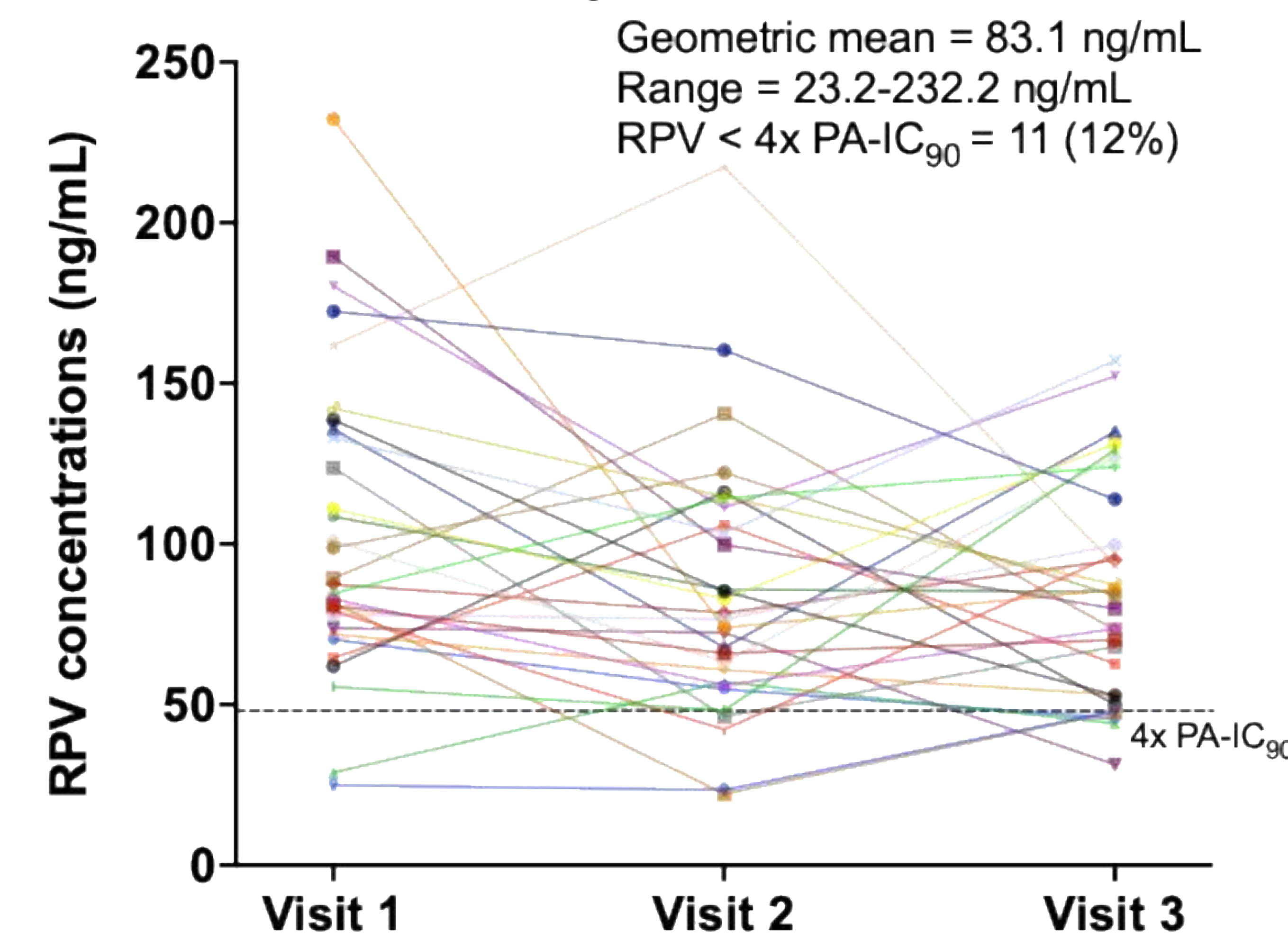


Figure 2: Individual RPV Trough Concentrations



RESULTS

Table 2: Interindividual and Intraindividual Variability

n=30 participants; 90 trough samples	% CV Median (IQR)
Interindividual CAB ^{a,b}	44 (38, 54)
Interindividual RPV ^{a,b}	46 (40, 49)
Intraindividual CAB ^{c,d}	26 (6, 53)
Intraindividual RPV ^{c,d}	21 (10, 68)

^a CAB and RPV Fleiss Kappa = -0.01

^b Fleiss Kappa result < 0.4 indicates poor interindividual agreement

^c CAB ICC = 0.75; RPV ICC = 0.63

^d ICC 0.5-0.75 indicates moderate intraindividual agreement

- After 1 year of continuous use, over three doses:
 - High interindividual variability observed
 - Moderate intraindividual variability observed

Table 3: Assessment of Characteristics Associated with CAB or RPV Trough < 4x PA-IC₉₀ (n=30 participants) ^a

	Trough < 4x PA-IC ₉₀		P-value ^b
	Yes (n=8)	No (n=22)	
BMI	28 (18, 49)	30 (21, 46)	0.41
AST	20 (15, 28)	26 (17, 44)	0.07
ALT	21 (9, 34)	28 (13, 63)	0.18
Total bilirubin	0.5 (0.2, 0.8)	0.6 (0.2, 2.1)	0.45
ALP	68 (36, 91)	70 (33, 111)	0.57
HIV Viral Load > 20 copies/mL			
Visit 1	1 (33.3%)	2 (7.4%)	0.28
Visit 2	0 (0%)	1 (3.8%)	1
Visit 3	0 (0%)	5 (20%)	0.56

^a Sex, race, and SCr were also explored and not associated, all p = 1

^b Fisher's exact and Wilcoxon rank sum test

Data reported as median (IQR) or n (%)

- 7% and 23% of individuals had a CAB or RPV, respectively, concentration < 4x PA-IC₉₀
- No patient or laboratory characteristics correlated with trough concentrations < 4x PA-IC₉₀
- Small sample size may limit the ability to evaluate associations in this cohort