Plasma concentrations of Lenacapavir in people living with multidrug-resistant HIV : a real-life study

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BACKGROUND

- **Lenacapavir** (LEN) is a potent first-in-class, long acting, capsid inhibitor recently approved for the treatment of multidrug-resistant HIV-1, in combination with other antiretroviral agents, in heavily treatment-experienced (HTE) people living with HIV (PWH).
- PWH initiated usual or simplified regimen combining oral loading tablets and subcutaneous (SC) dose then SC maintenance dose (927 mg) every 6 months.
- The objective of this analysis was to describe the plasma concentrations (Cpl) of LEN in THE PWH.

METHODS

- A multicenter, cross-sectional, cohort was conducted from 2020 to 2023. PWH who were receiving LEN containing regimen were enrolled.
- Basic demographic data were recorded using DAT'AIDS database (NCT#02898987).
- Blood samples were collected during the routine clinic visits between week 2, every each 6 months, and month 12 if available.
- LEN Cpl were determined by UPLC-MSMS (Waters Acquity) with LOQ<5 ng/mL and interpreted using a cutoff of 15 ng/mL corresponding to 4-fold protein-adjusted 95% effective concentration on WT HIV-1.

Table 1. PWH characteristics at baseline

	N (%) or median (IQR)
Number of patients	61
Gender	
- **Male**	35 (57%)
- **Female**	25 (43%)
Age, years	56 (43-60)
Ethnicity	
- **Caucasian**	27 (44%)
- **Black African/Carribean**	24 (39%)
- **Latin Hispanic**	5 (8%)
- **North African**	5 (8%)
Concomitant ARV regimen (+/- NRTI)	
- **Cabotegravir +/- Rilpivirine**	28 (46%)
- **IP/r +/- oral INSTI**	16 (26%)
- **Oral INSTI**	4 (7%)
- **Fostemsavir**	4 (7%)
- **Oral NNRTI**	1 (2%)
- **Unknown regimen**	8 (13%)

Heavily treatment-experienced (HTE) PWH had **adequate** LEN plasma concentrations, **without** any reported **drug-drug interaction** nor **tolerance issues**

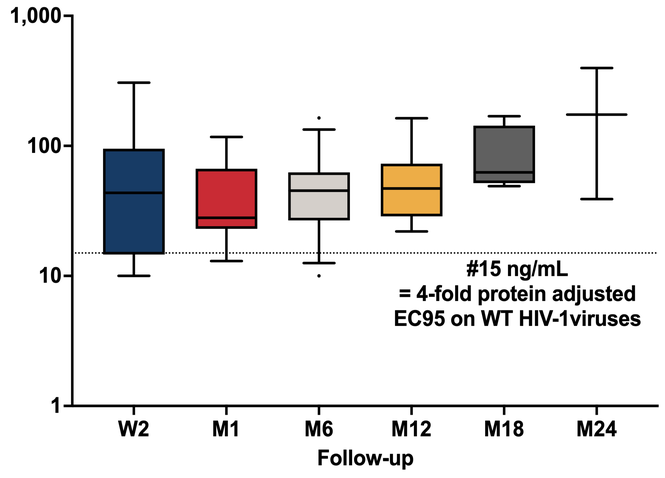


Figure 1. Plasma concentrations (ng/mL) of lenacapavir during the follow up (median, IQR)

RESULTS

- A total of 61 PWH (57% male; age 56 (43-60) years old) were enrolled (**Table 1**). All were receiving LEN as an add-on to their antiretroviral regimen. Among them, 28 received both CAB long-acting intramuscular injection q8w with an associated daily oral antiretroviral backbone.
- Over all PWH, median (IQR) LEN Cpl were 50 (28-74) ng/mL with a number of samples per PWH of 2 (1-5) (**Figure 1** & **Table 2**).
- Among our PWH, only one presented a LEN Cpl below the cutoff of 15 ng/mL.
- Of note, 5 patients presented LEN Cpl above 150 ng/mL, corresponding to PWH with acute or chronic kidney disease and/or receiving ritonavir-boosted atazanavir containing regimens.
- To date, no specific adverse events have been reported in these PWH, except some injection site reactions.

Table 2. Plasma concentrations of lenacapavir during the follow up

Patients (n=61)	W2	M1	M6	M12	M18	M24	Other periods	Overall
Samples, n	10	18	36	16	4	3	104	191
Samples/patient, median (IQR)	/	/	/	/	/	/		2 (1-5)
LEN Cpl (ng/mL), median (IQR)	**44 (15-95)**	**28 (23-67)**	**45 (27-63)**	**47 (29-73)**	**63 (52-143)**	**174 (39-397)**	**58 (34-92)**	**50 (28-74)**
CV(%)	124%	66%	63%	65%	65%	89%	83%	69%
Intra-patient CV(%)	/	/	/	/	/	/	/	30%

CONCLUSIONS

- In our population of HTE PWH, people living with HIV had adequate LEN Cpl.
- Kidney disease might cause accumulation of LEN in plasma.
- No drug-drug interaction was reported except with Atazanavir already described and tolerance of antiretroviral multitherapy was acceptable.

ADDITIONAL KEY INFORMATION

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