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Durability of lenacapavir in viremic HTE PWH: real-world data from the PRESTIGIO Registry

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PURPOSE

- Lenacapavir (LEN), the first-in-class capsid inhibitor, is approved for use in people with HIV (PWH) who have limited treatment options [1,2].
- While its efficacy has been demonstrated in clinical trials [3,4], real-world data in individuals with extensive treatment experience remain scarce.
- Therefore, our aim was to explore outcomes of LEN-containing regimens in viremic individuals with 4-class drug-resistant (4DR) HIV strains.

METHODS

- Cohort study on PWH with resistance to NRTIs, NNRTIs, PIs and INSTIs from the PRESTIGIO Registry (NCT04098315; https://registroprestigio.org) [5], who initiated a LEN-containing regimen with viral load (VL) ≥50 copies/mL.
- The primary outcome was LEN durability (by Kaplan-Meier curve).
- Secondary outcomes included:
  - virological suppression [(VS) ≥1 VL <50 copies/mL] (by cumulative incidence function and FDA snapshots);
  - CD4+ and CD4+/CD8+ changes (by Wilcoxon signed-rank test).
- Follow-up accrued from LEN initiation [baseline (BL)] to its discontinuation or the last available VL.
- Descriptions by median (interquartile range, IQR) or frequency (%).

CONCLUSIONS

- Our real-life data on viremic 4DR-PWH support the high durability and effectiveness of LEN-containing regimens.
- The combination with FTR yielded encouraging results, even in individuals with extremely limited treatment options.
- LEN may represent a key component in treatment strategies for multidrug-resistant HIV.

REFERENCES

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2. **Panel on Antiretroviral Guidelines for Adults and Adolescents.** Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV.
3. **Segal-Maurer S et al.** *N Engl J Med* 2022; 386: 1793-803.
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RESULTS

- Overall, 15 viremic 4DR-PWH initiated a LEN-containing regimen (Table 1).
- During a median follow-up of 1.6 (0.5-2.7) years, 11 (73.3%) individuals maintained LEN, while 4 (26.7%) discontinued it (Figure 1): 1 for injection site reactions, 2 by individual decision, and 1 for a non-drug-related death.
- Eleven (73.3%) PWH achieved VS within 2.8 (0.5-5.6) months (Figures 2 and 3).
  - Nine of 11 (81.8%) maintained VS, whereas 2 (18.2%) experienced confirmed low-level viremia (LLV; 50-199 copies/mL).
- Of the remaining 4 viremic PWH, 3 (75%) had LLV at last measurement.
  - In the only individual with sustained viremia, new resistance-associated mutations to both LEN and optimized background therapy (OBT) were detected at DNA-based next-generation sequencing.
- During LEN-containing regimens, median $CD4^+$ count and $CD4^+/CD8^+$ tended to increase [$CD4^+$: from 190 (111-734) to 287 (159-664) cells/mm^3, p=0.073; $CD4^+/CD8^+$: from 0.28 (0.19-0.48) to 0.33 (0.23-0.79), p=0.067].
- Notably, 6 PWH initiated a LEN + fostemsavir (FTR)-containing regimen at BL and 2 started FTR later (Table 2).

Figure 1. Cumulative probabilities of LEN retention in viremic 4DR-PWH

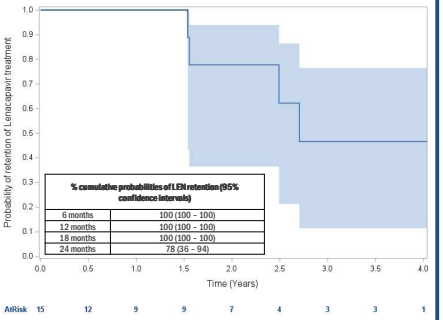

Table 1. BL characteristics of 4DR-PWH who initiated a LEN-containing regimen

BL characteristics	Viremic 4DR-PWH (n=15)
Age (years)	57.5 (46.8-62.9)
Male sex assigned at birth	14 (93.3%)
ART duration (years)	27.0 (22.6-28.7)
VL (copies/mL)	5460 (1800-23800)
LLV	3 (20.0%)
$CD4^+$ T-cell count (cells/mm3)	190 (111-734)
$CD4^+/CD8^+$	0.28 (0.19-0.48)
$CD4^+$ nadir (cells/mm3)	70 (5-137)
Number of drugs in the OBT	5 (3-6)
Drugs contained in the OBT	
≥1 NRTI	11 (73.3%)
NNRTI	10 (66.7%)
PI/b	8 (53.3%)
2nd generation INSTI	6 (40.0%)
MVC and/or T20	7 (46.7%)
IBA and/or FTR	7 (46.7%)
OBT GSS	2 (1-3)
Number of fully active agents in the OBT	
0	3 (20.0%)
1	5 (33.3%)
≥2	7 (46.7%)

Figure 3. FDA snapshot analysis at week 26 and week 52

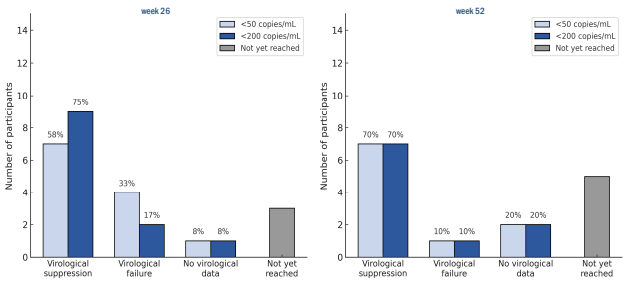

Figure 2. Cumulative probabilities of VS in viremic 4DR-PWH who started LEN

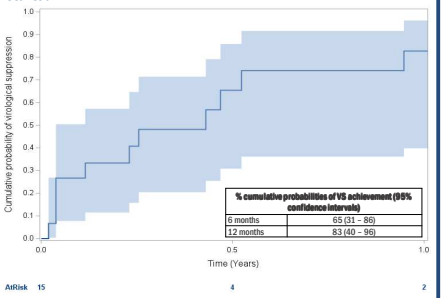

Table 2. Outcomes of LEN + FTR combination in the PRESTIGIO Registry

Cases	OBT accompanying LEN+FTR	Date of LEN+FTR initiation	Date of LEN+FTR discontinuation	OBT GSS	Previous FTR exposure	Previous LEN exposure	VL at LEN+FTR initiation (copies/mL)	Last VL (copies/mL)	CD4+ at LEN+FTR initiation (cells/mm³)	Last CD4+ (cells/mm³)
Case 1	DRV/r + DTG	27 May 2024	Ongoing	2	Yes	No	97600	134	410	440
Case 2	B/F/TAF + DOR + MVC	16 Jan 2024	Ongoing	2.5	Yes	No	20280	40	190	290
Case 3	DOR/3TC/TDF + MVC + IBA	18 Jan 2021	Ongoing1	2	Yes	No	2982	33	734	664
Case 4	F/TAF + DRV/r + DTG + IBA	12 Sep 2022	Ongoing	3	Yes	No	2400	19	296	315
Case 5	DOR + DTG	08 Aug 2024	Ongoing	1	Yes	No	113	108	942	1020
Case 6	F/TAF + AZT + T20 + IBA	01 Feb 2023	Ongoing2	2	No	No	5460	39	144	283
Case 7	DOR	30 Sep 2024	Ongoing	0.5	No	Yes	20	73	640	1120
Case 8	B/F/TAF + DRV/c	23 Jul 2024	Ongoing	2.5	No	Yes	98032	80571	64	96

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