

# Real world use of lenacapavir in France: a national, observational study

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## PURPOSE

French guidelines recommend lenacapavir (LEN) for persons with HIV (PWH) with multidrug-resistant virus who cannot achieve viral suppression with oral antiretroviral therapy (ART).

Since June 2023, the early access program (EAP) for LEN has ended, and the drug is now commercially available. However, to preserve resources, and due to limited indications, prescriptions must be validated locally in hospitals by a multidisciplinary committee.

The LENAddOn national study aims to:

1. Assess LEN continuation rates at M6 and M12,
2. Characterize PWH initiating LEN post-early access programme in France,
3. Describe reasons for LEN discontinuation.

## METHODS

We conducted an observational, retrospective study across 19 centres, including people with HIV-1 who initiated LEN injections between 20/06/2023 and 30/06/2024.

Socio-demographic, clinical, and laboratory data were extracted from medical records.

The primary outcome was the proportion of individuals receiving a second and third LEN series of injections 6 and 12 months after initiating LEN. We collected reasons for switching to LEN. Safety and virological efficacy of LEN and optimized background regimens (OBRs) were evaluated.

Study was approved by the Sud-Est II Ethics Committee (ref. number: 24.05319.000402).

## CONCLUSIONS

During the first year of LEN routine availability in France, clinicians extended its use beyond strict salvage indications, incorporating it into regimen simplification strategies and fully injectable combinations designed for individuals characterized by extensive treatment exposure, social vulnerability, and facing major adherence barriers.

**Continuation of LEN injections was high at M6 (94.8%) and remained substantial at M12 (81.8%). Importantly, most discontinuations were not driven by virological failure but by loss to follow-up, death, injection-site reactions, or reassessment of clinical indication.**

These real-world data complement long-term CAPELLA findings and support further prospective evaluation of LEN-based injectable strategies in populations currently underserved by existing long-acting regimens.

## RESULTS

**77 participants were included out of 80 eligible PWH in 19 centres spread across France (Table 1).**

- They had frequent histories consistent with adherence issues and vulnerability factors. Main reasons for LEN initiation were multidrug resistance (63.6%), adherence challenges (35.1%), person-requested treatment simplification (27.3%), poor tolerability of oral ART (19.5%) and avoidance of drug-drug interactions (19.5%).
- Based on cumulative genotypes, 42 participants (54.6%) had viral resistance to  $\geq 2$  drugs in  $\geq 3$  of the 4 major antiretroviral classes.

These baseline data have been described previously (EACS Conference, Paris, 2025, Abs. eP101).

At LEN initiation, 34 participants (28.6%) had a pVL  $\geq 50$  copies/mL, and 43 (55.8%) a pVL  $< 50$  copies/mL (Table 1).

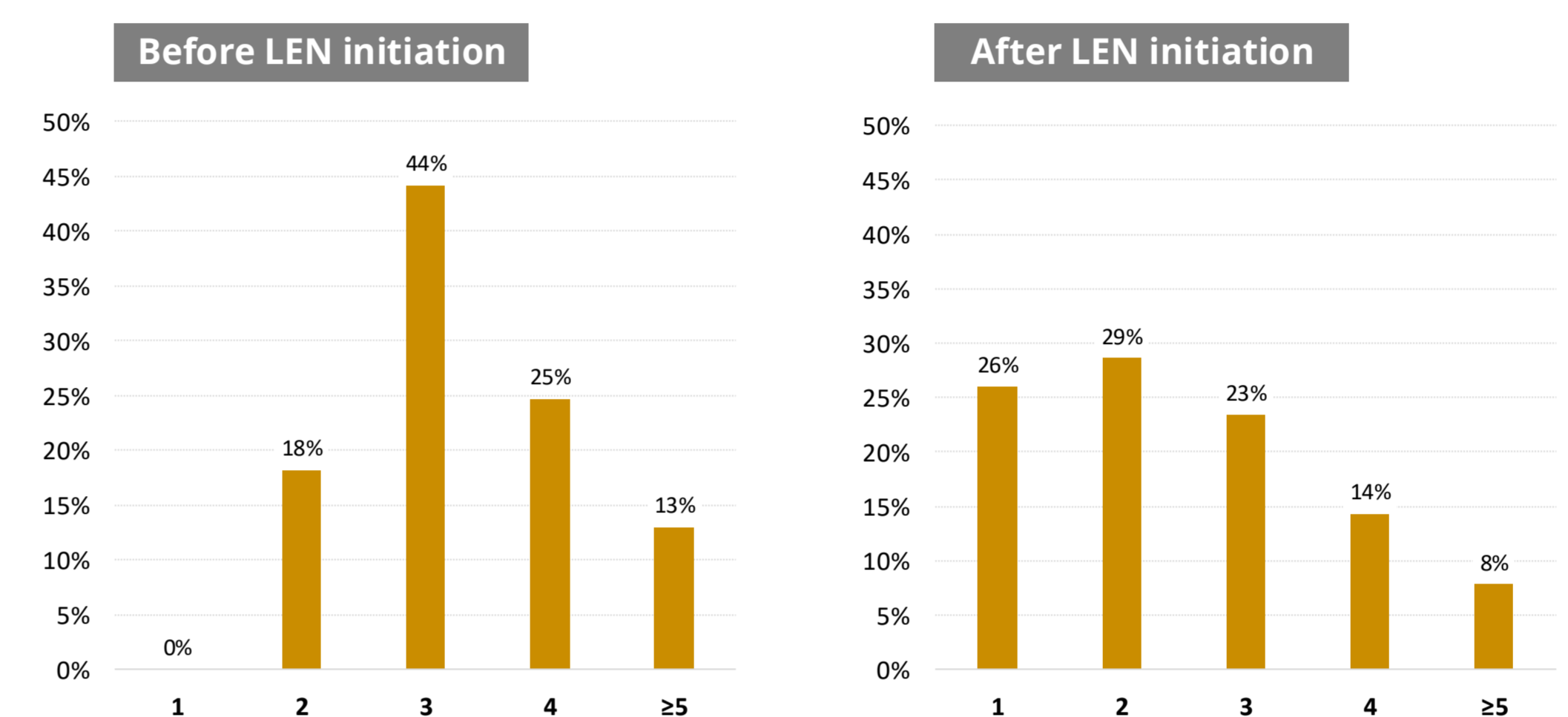
**Table 1. Baseline patient characteristics.**

<b>Age, years, median (IQR)</b>	57 (44-63)
<b>Gender, n (%)</b>	
- Cis-men	52 (67.5)
- Cis-women	24 (31.2)
- Trans-woman	1 (1.3)
<b>Birth country, n (%)</b>	
- France	49 (63.6)
- Other	28 (36.4)
<b>Transmission route, n (%)</b>	
- MSM	28 (36.4)
- Heterosexual	32 (41.5)
- Other	17 (22.1)
<b>Time from HIV diagnosis, years, median (IQR)</b>	30 (21-34)
<b>CD4 nadir, cells/<math>\mu</math>L, median (IQR)</b>	58 (10-142)
<b>AIDS-defining event, n (%)</b>	47 (61.0)
<b>HBV coinfection, n (%)</b>	5 (6.5)
<b>Time from ART initiation, years, median (IQR)</b>	25 (17-29)
<b>Vulnerability factors, n (%)</b>	
- No stable employment	33 (42.9)
- Insufficient financial resources to cover basic needs	16 (20.8)
- Irregular administrative status	7 (9.1)
- Homeless	6 (7.8)
- Poor level of French	3 (3.9)
<b>Psychiatric issues, n (%)</b>	17 (22.1)
<b>Problems with HIV / ART, n (%)</b>	
- Previous unplanned ART discontinuations	30 (39.0)
- Difficulties in adhering to oral ART	35 (45.5)
- Non-acceptance of HIV	17 (22.1)
- Poor understanding of HIV and/or ART	14 (18.2)
- Stigmatisation from friends and relatives	6 (7.8)
<b>Plasma viral load (pVL) at LEN initiation, n (%)</b>	
- $< 50$ cp/mL	43 (55.8)
- 50-199 cp/mL	12 (15.6)
- $\geq 200$ cp/mL	22 (28.6)
<b>CD4 count at LEN initiation, cells/<math>\mu</math>L, median (IQR)</b>	418 (174-700)

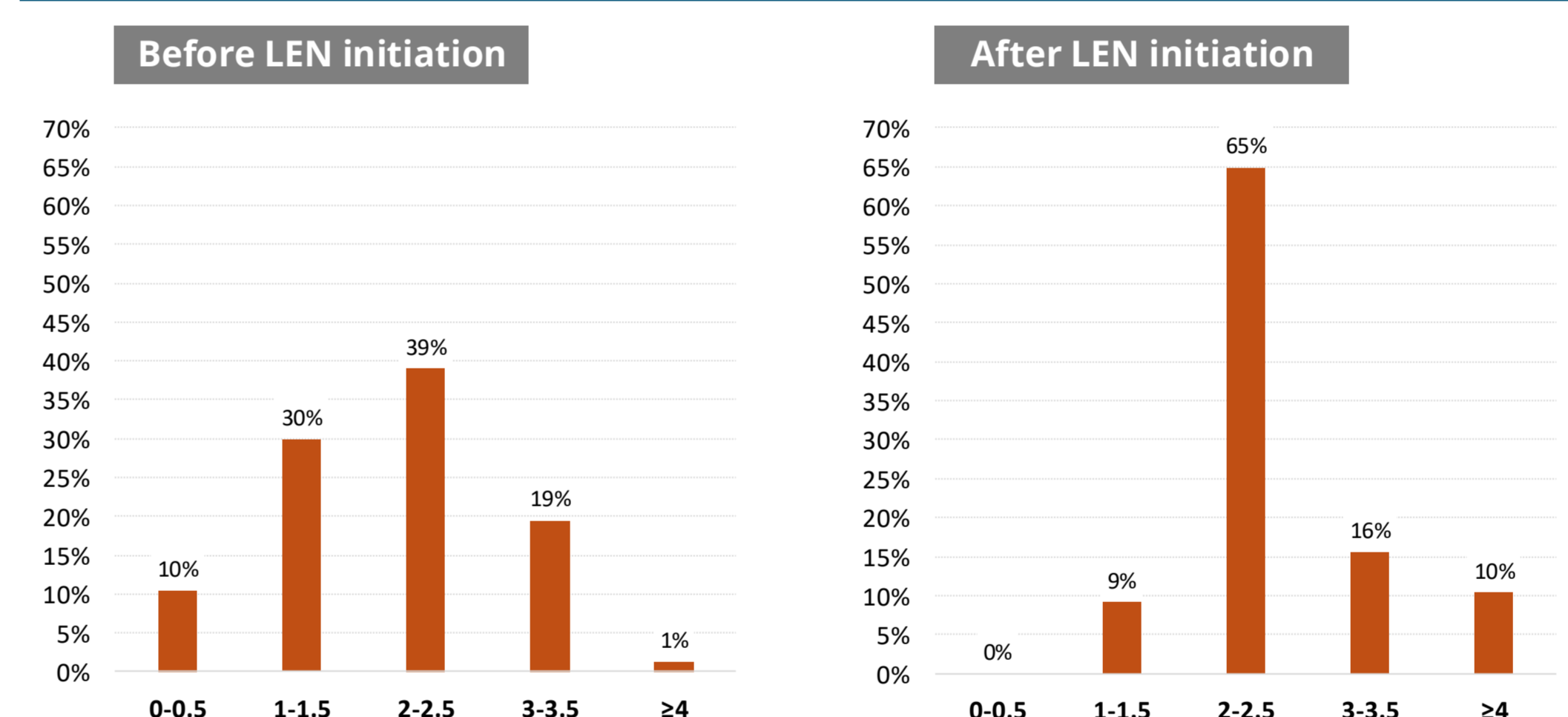
\* Psychiatry issues included depressive syndrome, severe psychological symptoms, and other psychiatric diseases

Twenty-two (28.6%) participants received a fully injectable regimen: LEN + cabotegravir (n=16) or LEN + cabotegravir + rilpivirine (n=5) or LEN + cabotegravir + enfuvirtide (n=1).

**Figure 1. Number of antiretrovirals included in regimen (except LEN), before and after LEN initiation.**



**Figure 2. Genotypic sensitivity score (including LEN) before and after LEN initiation.**



After LEN introduction, the proportion of participants who received four or more oral drugs decreased from 37.7% to 22.1% ( $p < 0.0001$ ) (Figure 1). The proportion of participants with a genotypic sensitivity score (GSS)  $\geq 2$  increased from 59.7% to 90.9% (Figure 2).

**Table 2. LEN discontinuations at M6 and M12.**

LEN discontinuations at M6	n (%)
Lost to follow-up	1 (1.3)
Death	1 (1.3)
Persistence of viral replication	2 (2.6)
LEN discontinuations at M12	n (%)
Persistence of viral replication	1 (1.3)
Loss to follow-up	2 (2.6)
Death	1 (1.3)
Grade 2 injection site reaction (painful nodules)	2 (2.6)
Neuropsychological and digestive adverse events	1 (1.3)
Insufficient clinical need*	3 (3.9)

\* P1: initial intensification with LEN added to bictegravir/emtricitabine/tenofovir because of resistance mutations with a theoretical impact on treatment efficacy, despite a baseline pVL  $< 50$  copies/mL. P2: lack of metabolic improvement after modification of the oral regimen enabled by LEN. P3: persistence of pre-existing low-level viremia despite LEN-based therapy.

**Continuation of LEN injections was 94.8% (95%CI 87.2-98.6) at M6, with 4 treatment discontinuations, and 81.8% (95% CI 71.4-89.7) at M12, with 10 additional treatment discontinuations (Table 2).**

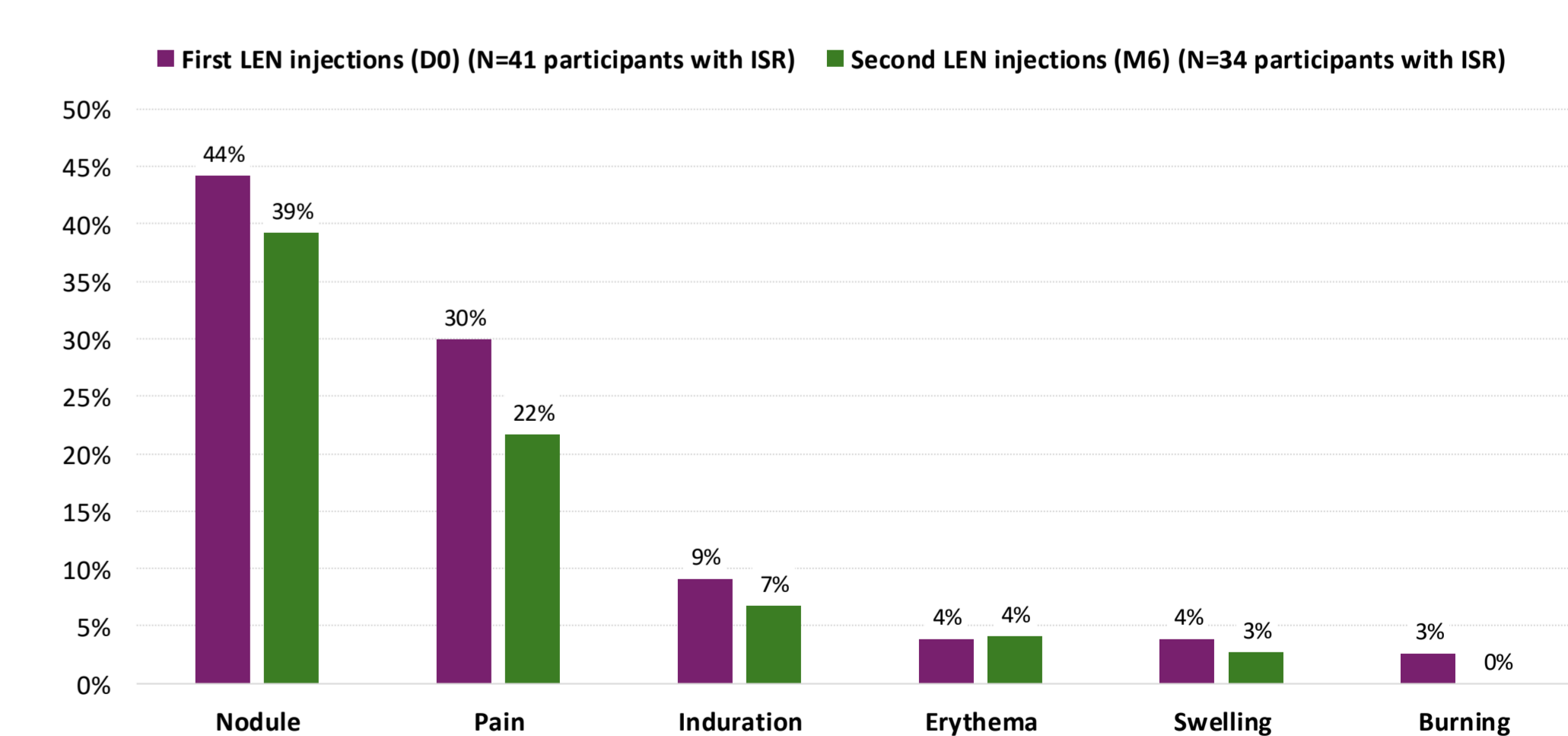
LEN was discontinued in 3 participants due to persistent viral replication:

- P1, with poor self-reported adherence and multidrug resistance, showed partial virological decline (52,000 to 2,300 copies/mL at M6) with emergence of an N74D capsid resistance-associated mutation.
- P2, switched to a fully injectable regimen (including enfuvirtide) due to oral adherence difficulties, experienced virological increase (1,770 to 16,300 copies/mL at M6) with failed capsid resistance assay.
- P3, who was viremic at LEN initiation (119,000 copies/mL), with no baseline INSTI resistance-associated mutation, achieved initial viral suppression at M3 under LEN + cabotegravir but experienced a viral rebound by M6-12 (250-1700 copies/mL), also with failed capsid resistance assay.

**At the end of the observation period, 62 participants (84.9%) had a pVL  $< 50$  copies/mL, and 71 (97.3%) had a pVL  $< 200$  copies/mL.**

CD4 cell counts significantly increased over follow-up in viremic participants at LEN initiation (median 265 to 486 cells/ $\mu$ L,  $p = 0.016$ ).

**Figure 3. Types of injection site reactions (ISRs) reported among participants who experienced ISRs.**



Injection site reactions (ISRs) were reported in 41/77 participants (53.2%) at time of first injections (D0), and 34/73 (46.6%) at time of second injections (M6).

Two participants experienced grade 3 ISRs at time of first injections (pain + nodule +/- erythema) that did not lead to LEN discontinuation, and two experienced grade 3 ISRs at time of second injections (pain + nodule +/- erythema as well) that did not lead to LEN discontinuation. ISR are detailed in Figure 3. No other grade  $\geq 3$  clinical or biological adverse events (AEs) were reported between first and second LEN injections.