Lenacapavir Adherence and Effectiveness Over 2 Years of Use in the OPERA Cohort

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Epividian

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Lenacapavir (LEN) for HIV treatment

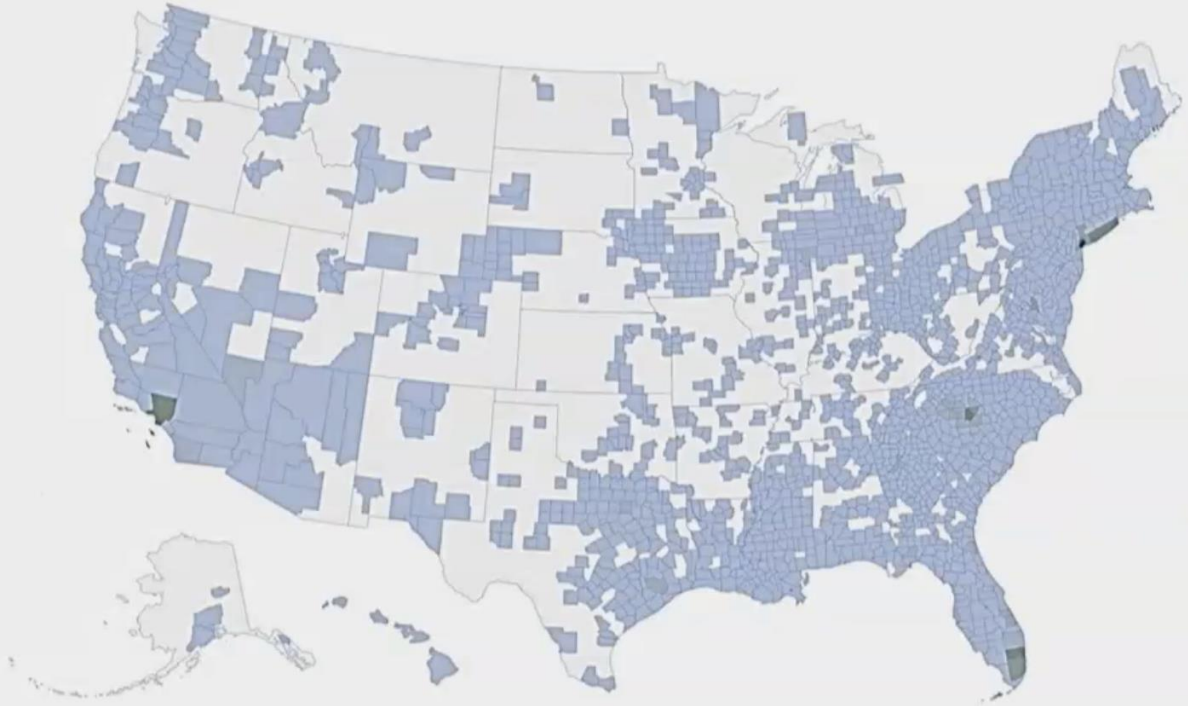
- 1st capsid inhibitor
- Indicated for the treatment of HIV-1 infection in heavily treatment-experienced (HTE) adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations
- 2 subcutaneous injections, every 6 months ± 2 weeks, in combination with an optimized background regimen (OBR)
- Approved based on efficacy evidence from 72 HTE participants in the CAPELLA trial
- Limited real-world evidence to date

Study Objectives

- Characterize people with HIV receiving LEN in routine clinical care in the US
- Describe antiretroviral use before, at the start, and during LEN use
- Assess the virologic effectiveness of LEN-containing ART
- Describe real-world LEN injection adherence

OPERA®

The Longitudinal Cohort



Observational **P**harmaco-**E**pidemiology **R**esearch & **A**nalysis

101 clinics in 23 US states/territories

>157K people with HIV

~14% of people with HIV in the US

Study Population
(N=116)

Inclusion Criteria

- Adults with HIV (aged 18+ years)
- ART-experienced
- Received ≥1 set of LEN injections between 22DEC2022 and 30SEP2024

Censoring Criteria

- Study end (31DEC2024)
- Loss to follow-up (12 months after last contact)
- LEN discontinuation
- Death

Demographic Characteristics
at 1st set of injections (N=116)

		Individuals on LEN
Age	Median years (IQR)	54 (42, 61)
Female sex	n (%)	26 (22)
Black race	n (%)	57 (49)
Hispanic ethnicity	n (%)	15 (13)

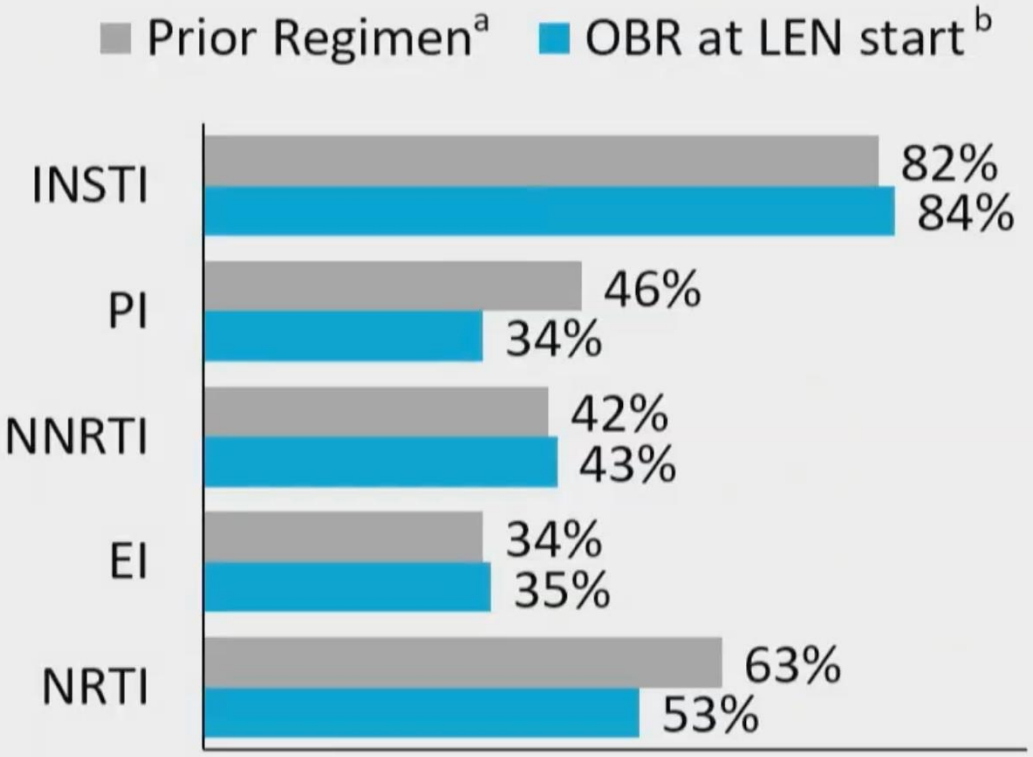
Clinical Characteristics
at 1st set of injections (N=116)

		Individuals on LEN
Years since HIV diagnosis	Median (IQR)	16 (5, 25)
History of AIDS-defining events	n (%)	60 (52)
HIV viral load (copies/mL)	<200, n (%)	74 (64)
	≥200 to <1,000, n (%)	10 (9)
	≥1,000, n (%)	32 (28)
CD4 cell count (cells/µL)	Median (IQR)	406 (215, 695)
	<200, n (%)	27 (23%)

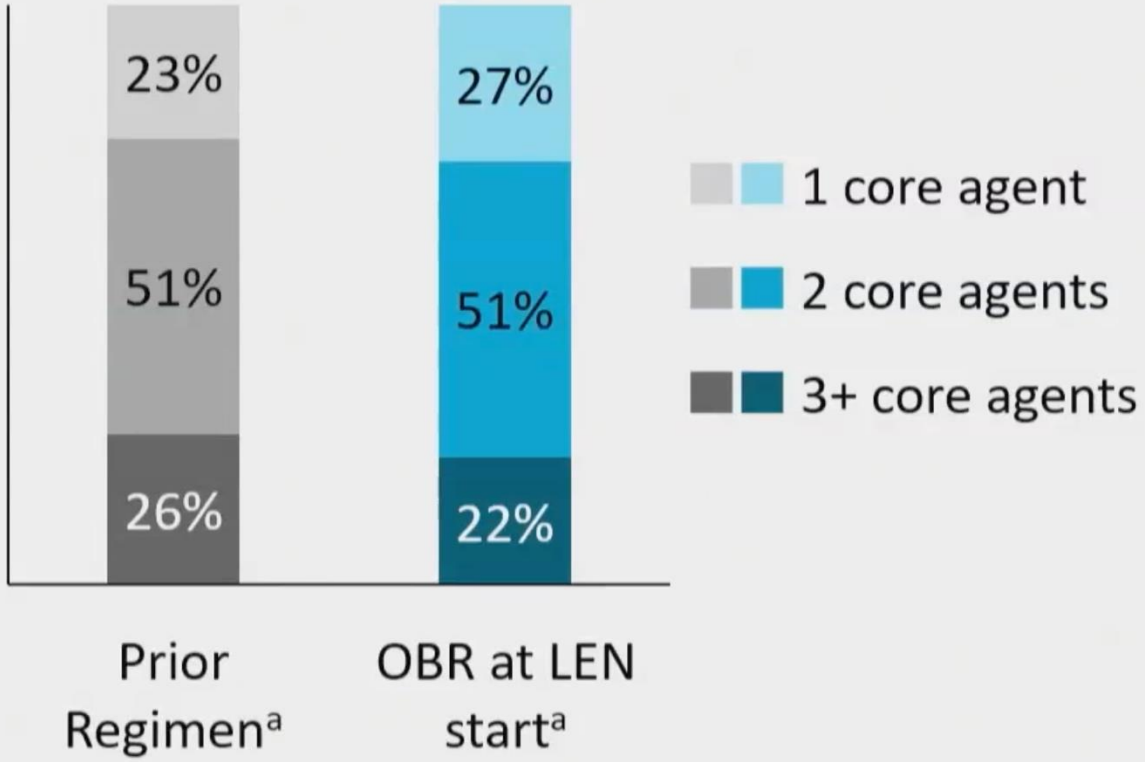
ART Regimen

before/at 1st set of injections (N=116 individuals)

ARV class (excluding LEN)



core[c] agents (excluding LEN)



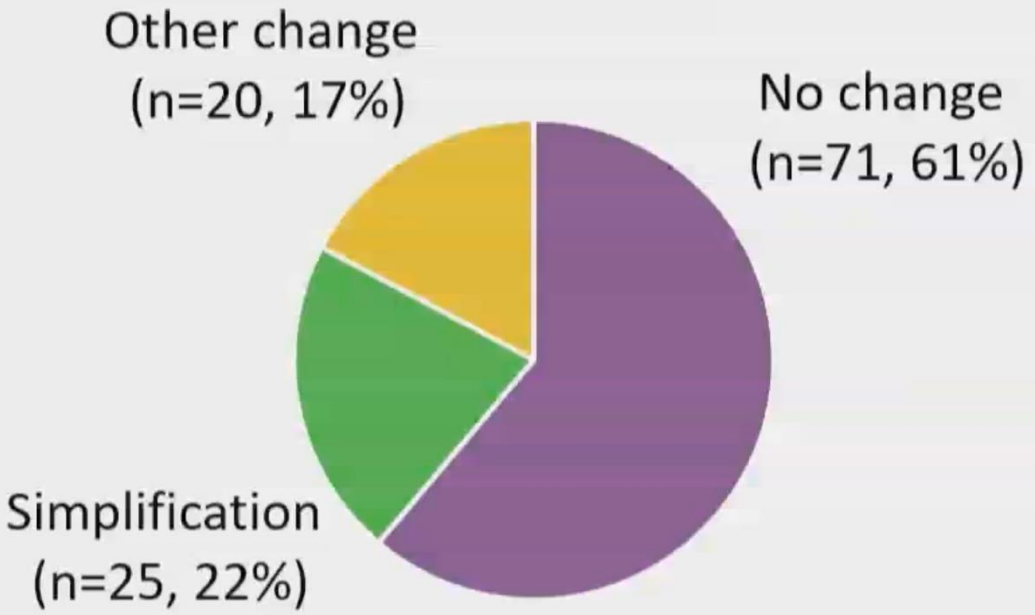
[a] Prior regimen: combination of ARVs 16 days prior to 1st set of injections (i.e., before the start of either LEN initiation options)

[b] OBR at LEN start: combination of ARVs on day of 1st set of injections

[c] Core agent: INSTI, PI, NNRTI, EI

ARV Changes at LEN Initiation
(N=116)

OBR at 1st injection[a] vs. ARVs in prior regimen[b]



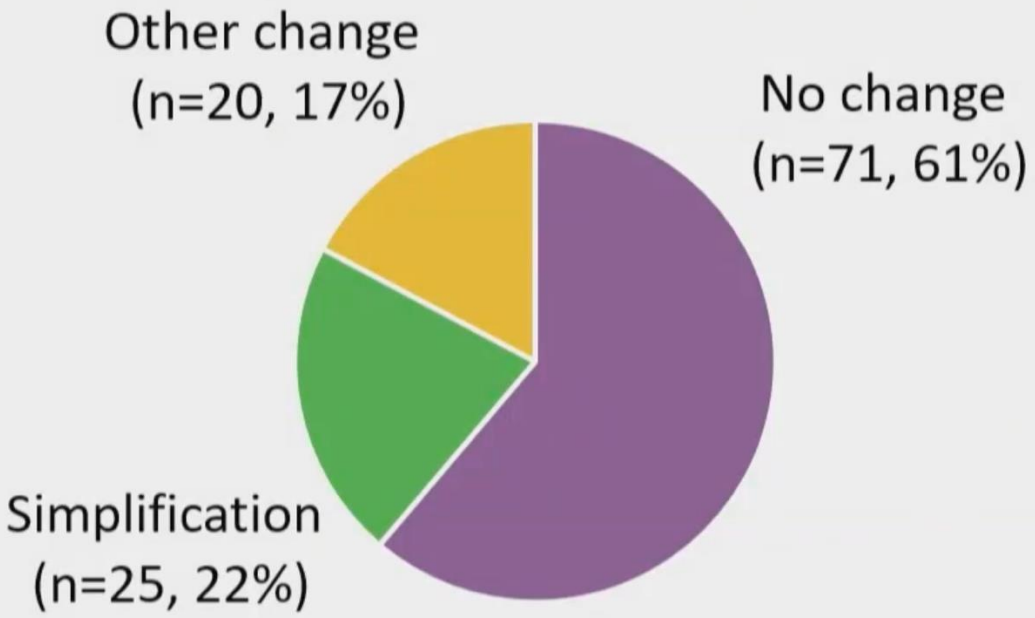
- **No change:** all ARVs remained the same
- **Simplification:** ARV changes resulting in fewer agents, fewer classes and/or fewer pills/days
- **Other change:** ARV changes resulting in the same or a larger number of agents, classes and pills/day

[a] OBR at LEN start: combination of ARVs on day of 1st set of injections

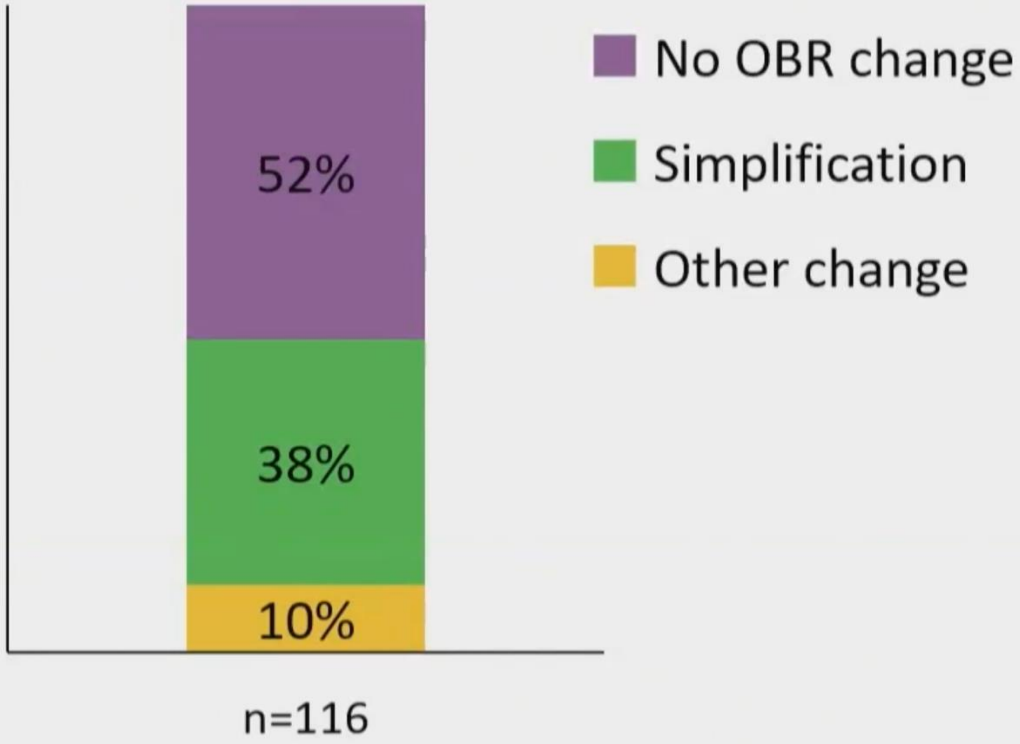
[b] Prior regimen: combination of ARVs 16 days prior to 1st set of injections (i.e., before the start of either LEN initiation options)

OBR Changes After LEN Initiation
(N=116)

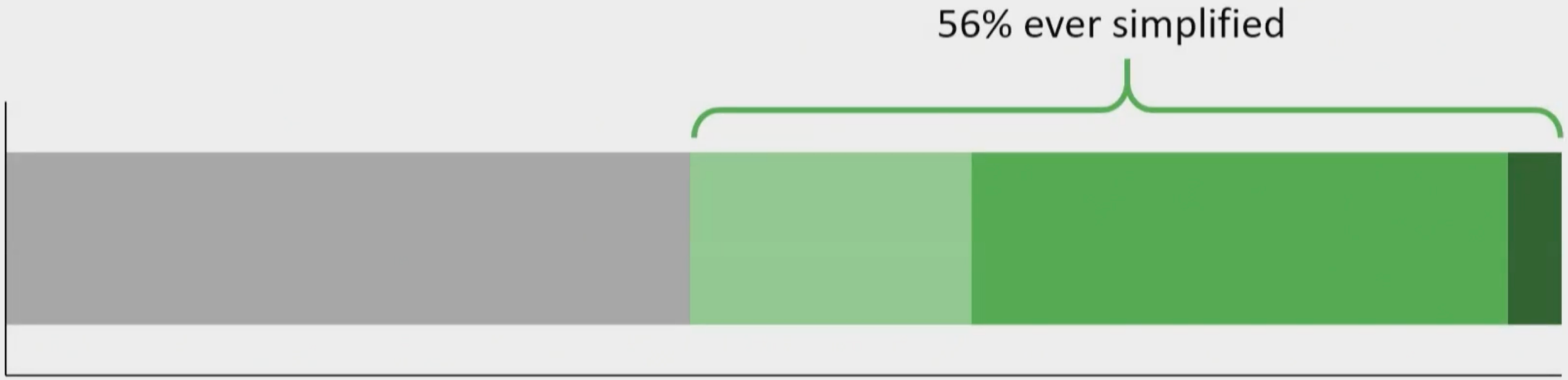
OBR at 1st injection vs. ARVs in prior regimen



OBR changes during LEN use



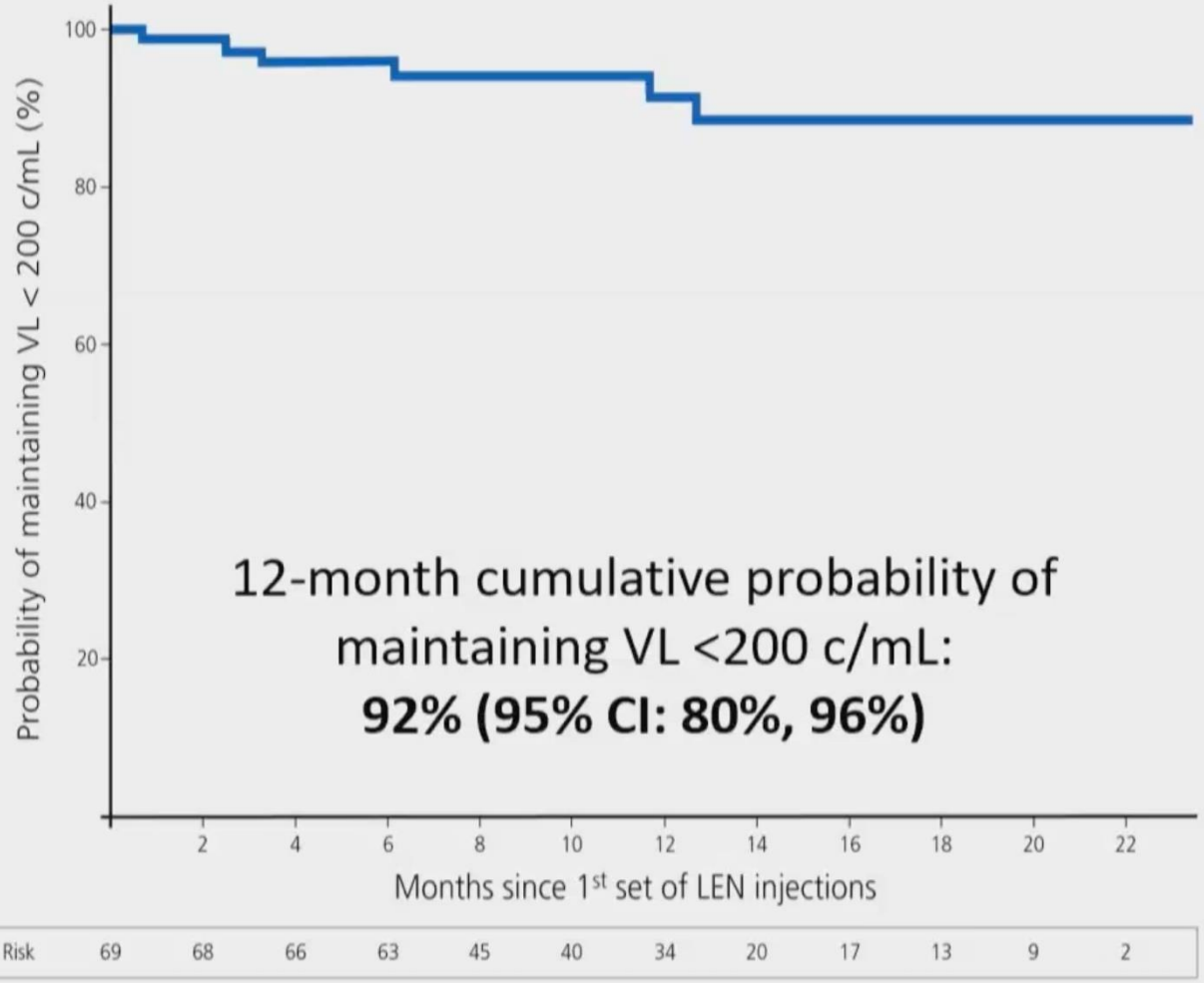
Regimen Simplification
(N=116)



- Never simplified (44%)
- Simplified at LEN start only (18%)
- Simplified during LEN use only (34%)
- Simplified both at LEN start and during LEN use (4%)

Maintenance of Virologic Suppression

among individuals with baseline VL <200 c/mL and ≥1 follow-up VL (N=69[a])



12-month cumulative probability of maintaining VL <200 c/mL:
92% (95% CI: 80%, 96%)

n=6 (9%) had ≥1 follow-up VL ≥200 c/mL

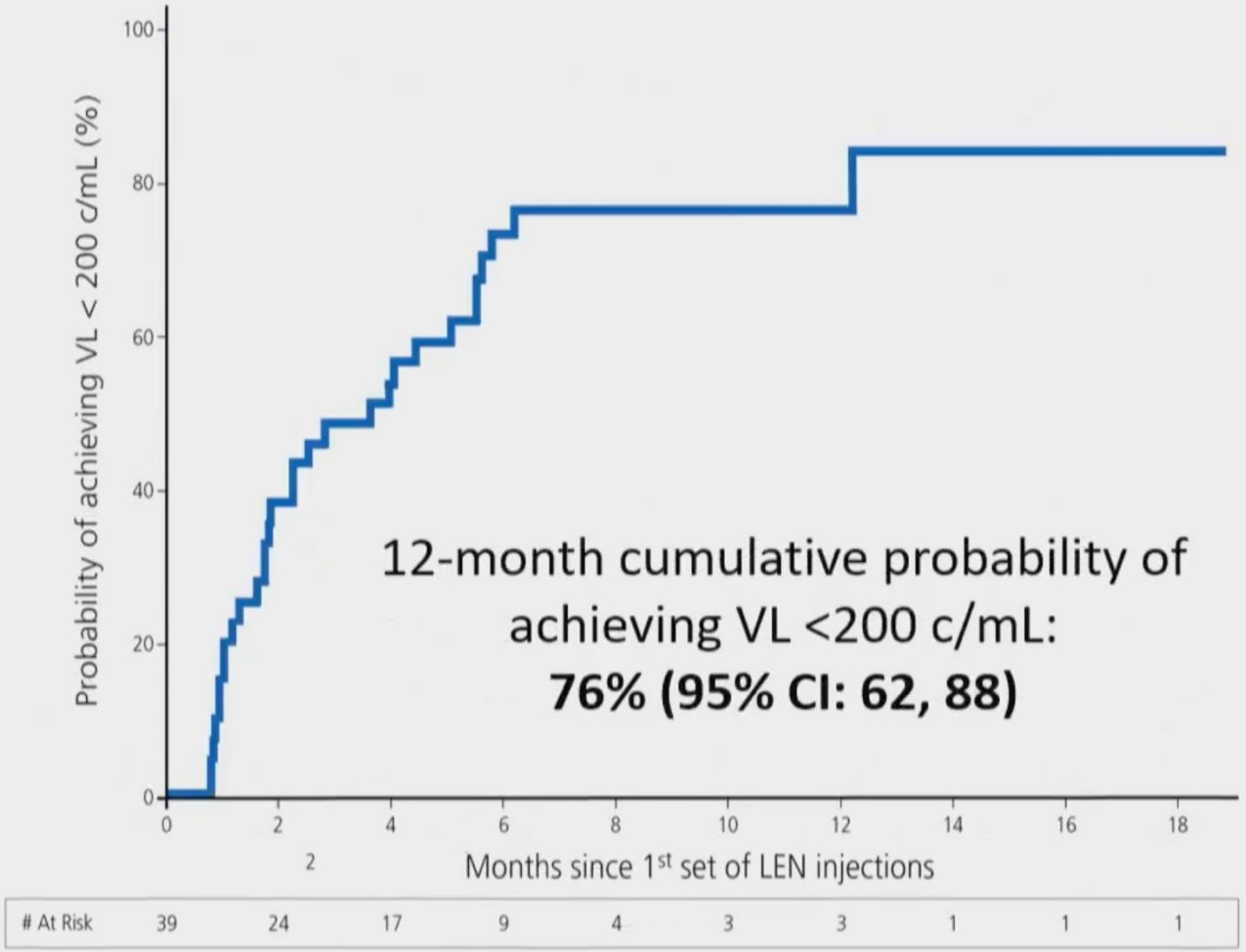
Median 5 months to 1st VL ≥200 c/mL (IQR: 2, 12)

67% re-suppressed on LEN

[a] 5 individuals had no follow-up VL

Achievement of Virologic Suppression

among individuals with baseline VL ≥200 c/mL and ≥1 follow-up VL (N=39[a])



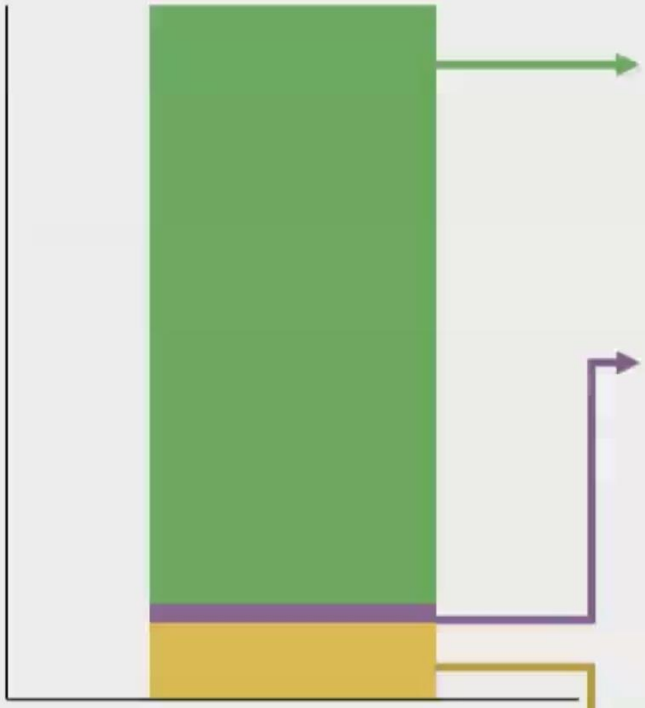
n=30 (77%) had ≥1 follow-up VL <200 c/mL

Median 2 months to 1st VL <200 c/mL (IQR: 1, 4)

[a] 3 individuals had no follow-up VL

Injection-Level Adherence

among sets of maintenance injections (N = 144)



N=144 sets of maintenance injection

86% on-time injections
(≥24 to ≤28 weeks after prior set)

3% early injections
(<24 weeks after prior set)

Median 10 days early
(IQR: 4, 14)

11% late injections
(>28 weeks after prior set)

Median 11 days late
(IQR: 4, 118)

81% with no Rx for oral LEN dosing

Persistence on LEN

among individuals with ≥2 sets of LEN injections (N=78)

Median 3 sets of injections per person (IQR: 2, 4)

N=78 individuals

91% remained on LEN at study end

(≤28 weeks between the last set of injections and study end)

9% discontinued LEN

(no further injections, with >28 weeks of follow-up left)

Key Findings

- 77% were on a complex regimen with ≥2 core agents before starting LEN
- 56% experienced regimen simplification either at initiation or during LEN use

Most individuals receiving LEN injections achieved or maintained viral suppression, regardless of baseline viral load

- 91% of users remained on LEN through study end
- Adherence to the injection schedule was very good
  - Most delays were short (median 11 days late)

Conclusion

In real-world settings, a high proportion of individuals started LEN while virologically suppressed, unlike participants in the CAPELLA trial.

This suggests that factors other than virologic control may be driving the decision to start LEN, such as concerns about safety, tolerability, underlying resistance, or regimen simplification.

In any case, when combined with other ARVs, LEN may serve as an effective long-acting injectable option.