Clinical Update on Lenacapavir:
First-in-class Long acting Capsid inhibitor

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Clinical Development in HIV Virology
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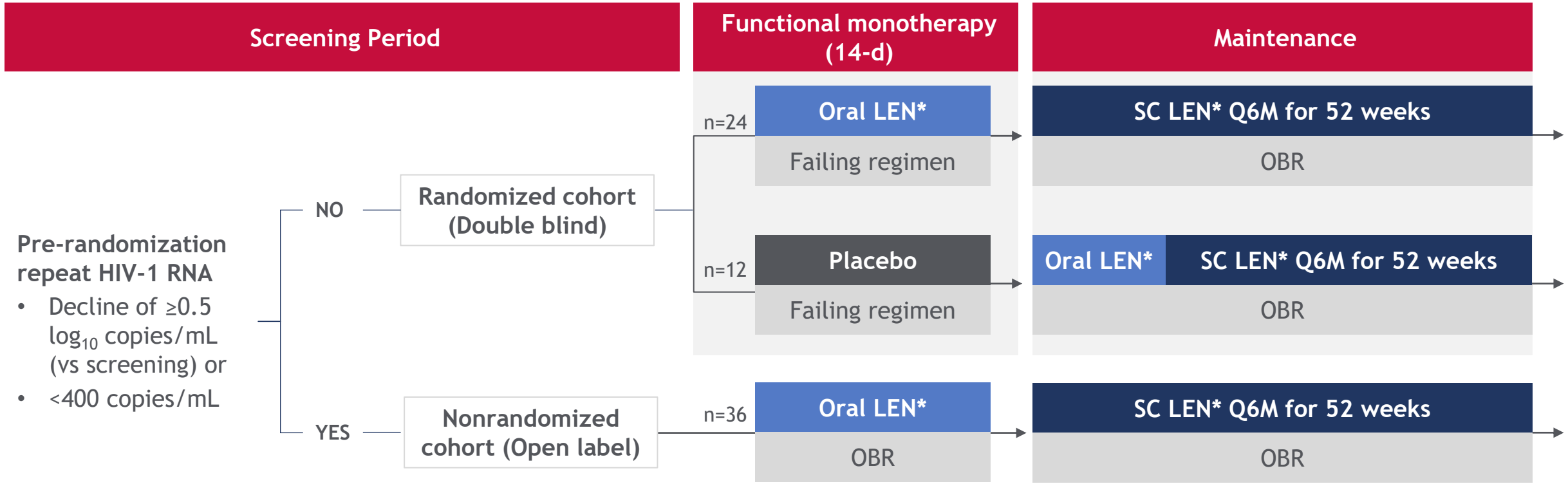
Phase 2/3 Study of LEN in combination with Optimized Background Regimen in Heavily Treatment-Experienced PWH: -Week 52 results (CAPELLA)-

Study Design



Key eligibility criteria:

- HIV-1 RNA ≥400 copies/mL
- Resistance to ≥2 agents from 3 of 4 main ARV classes
- ≤2 fully active agents from 4 main ARV classes

- Efficacy summarized only for randomized cohort (n=36), as most in nonrandomized cohort have not reached Wk 26 yet
- Safety summarized for both the randomized and nonrandomized cohort (n=72)

*Oral LEN administered as 600 mg on Days 1 and 2, 300 mg on Day 8; SC LEN administered as 927 mg (2 x 1.5 mL) in the abdomen on Day 15. OBR, optimized background regimen

Segal-Maurer et al., CROI 2021; Molina et al., IAS 2021

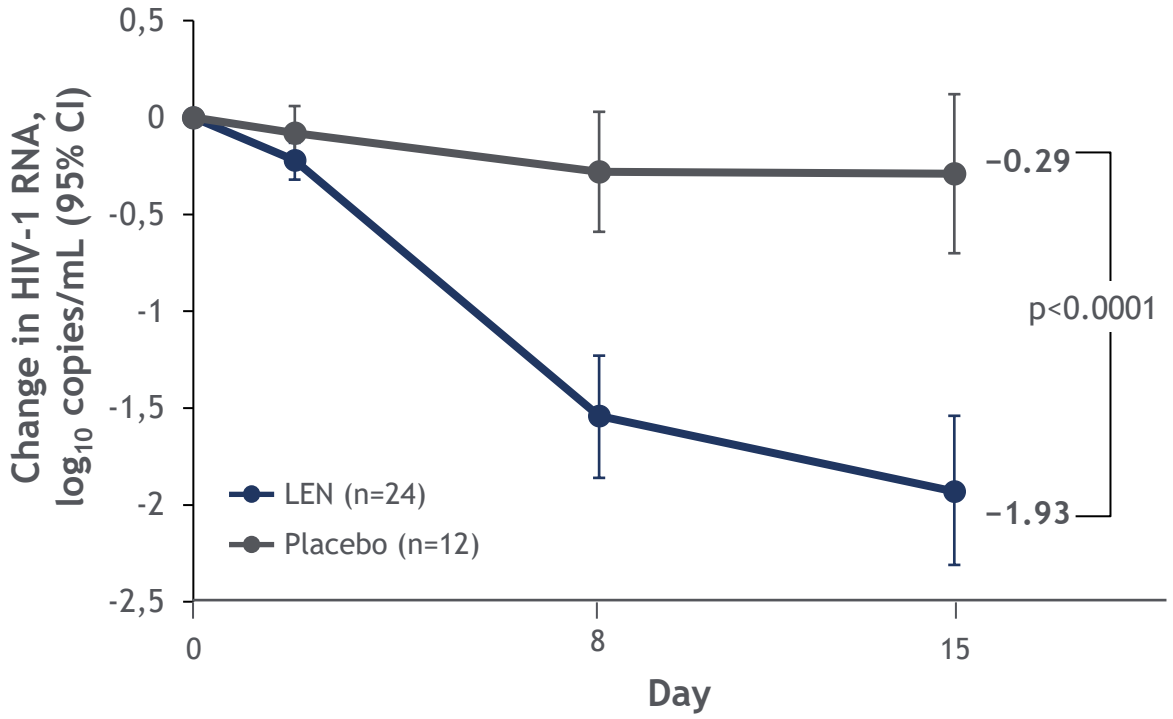
Baseline Characteristics

	Randomized		Nonrandomized	Total N=72
	LEN n=24	Placebo n=12	LEN n=36	
Age, median (range), years	55 (24 - 71)	54 (27 - 59)	49 (23 - 78)	52 (23 - 78)
Sex, % female at birth	29	25	22	25
Race, % Black	42	55	31	38
Ethnicity, % Hispanic/Latinx	25	36	14	21
HIV-1 RNA, median (range), $\log_{10}$ copies/mL	4.2 (2.3 - 5.4)	4.9 (4.3 - 5.3)	4.5 (1.3 - 5.7)	4.5 (1.3 - 5.7)
>75,000 copies/mL, %	17	50	28	28
CD4 count, median (range), cells/µL	172 (16 - 827)	85 (6 - 237)	195 (3 - 1296)	150 (3 - 1296)
≤200 cells/µL, %	67	92	53	64
Years since HIV diagnosis, median (range)	27 (13 - 39)	26 (14 - 35)	23 (9 - 44)	24 (9 - 44)
Number of prior ARV agents, median (range)	9 (2 - 24)	9 (3 - 22)	13 (3 - 25)	11 (2 - 25)
Number of ARV agents in failing regimen, median (range)	3 (1 - 7)	3 (2 - 6)	4 (2 - 7)	3 (1 - 7)
Known resistance to ≥2 drugs in class, %				
NRTI	96	100	100	99
NNRTI	92	100	100	97
PI	83	67	83	81
INSTI	83	58	64	69

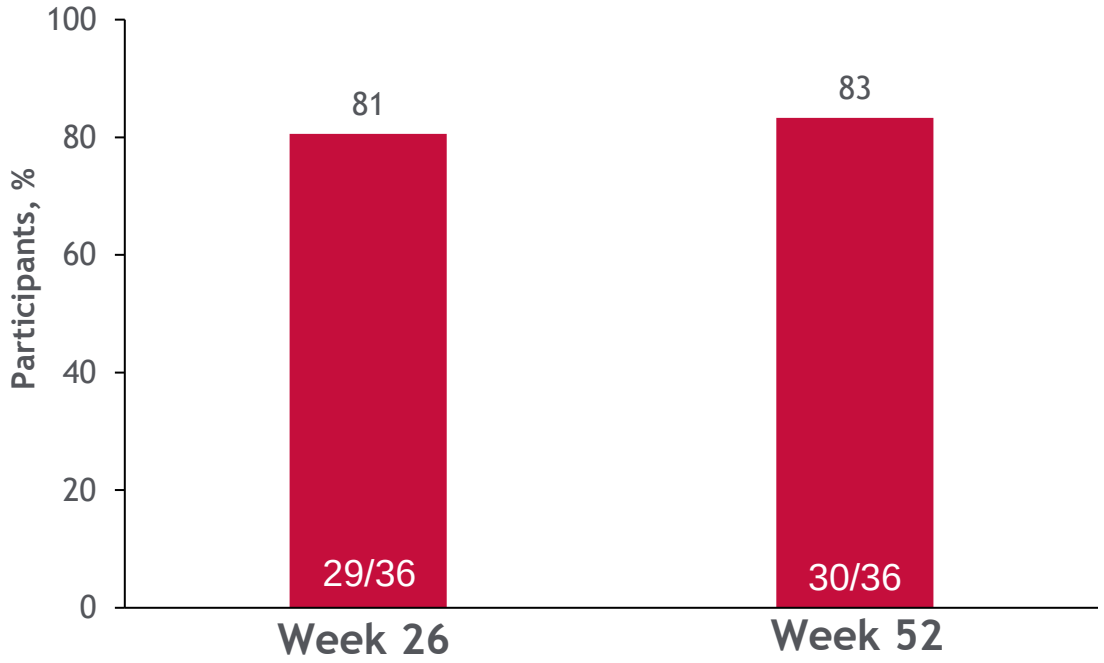
Molina et al., IAS 2021

Antiviral Activity and Efficacy
(Randomized Cohort; n=36)

During Functional Monotherapy Period
Change in HIV-1 RNA

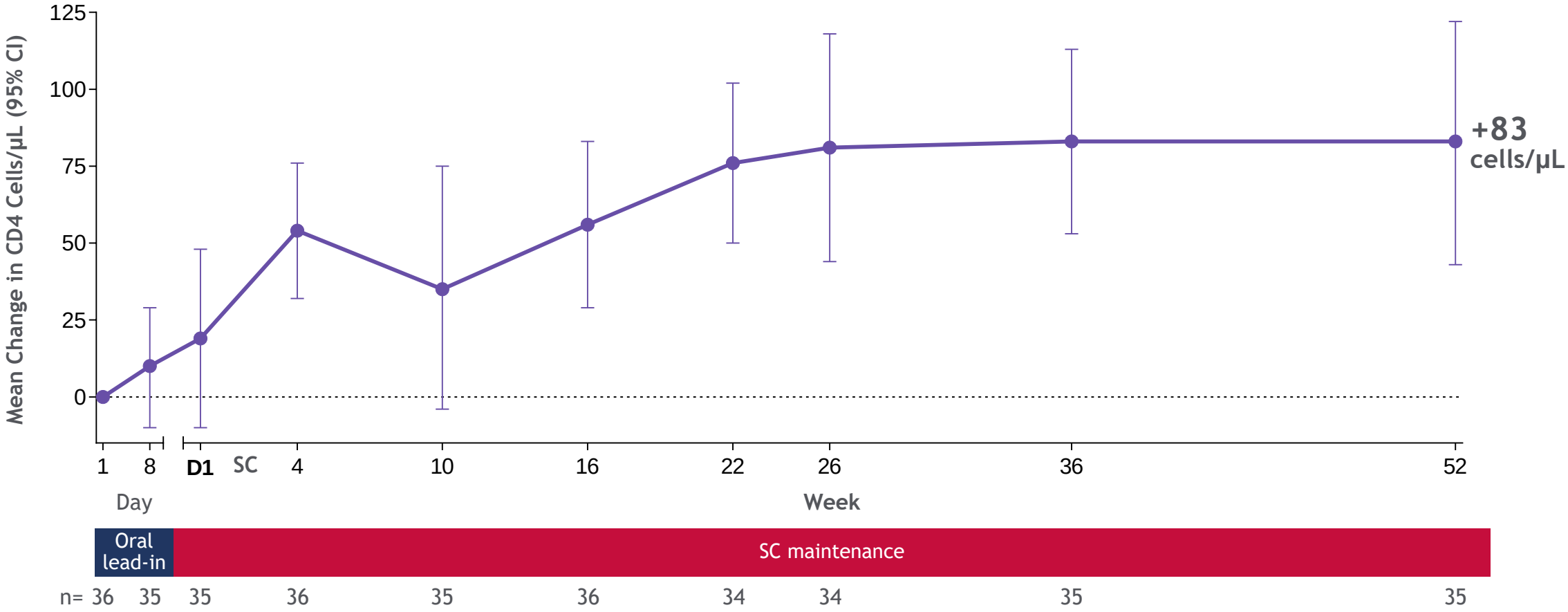


During Maintenance Period
HIV-1 RNA <50 c/mL



Segal-Maurer et al., CROI 2021

Changes in CD4 in Randomized Cohort (n=36)



- Randomized cohort: mean change in CD4, cells/µL (95% CI): 81 (44, 118) at Week 26; 83 (43, 122) at Week 52
- Nonrandomized cohort: mean change in CD4, cells/µL (95% CI): 98 (59, 136) at Week 26

D1 SC, 1st d LEN SC was administered. CI, confidence interval.
Ogbuagu et al., CROI 2022

Adverse Events (excluding ISRs)*

≥10% Total in Any Grade, % (n)	Total LEN N=72
Diarrhea	13 (9)
Nausea	13 (9)
COVID-19	11 (8)

- Duration of follow up: median 376 d (interquartile range: 306, 501)
- 70 participants with ≥197 d of follow-up and 36 participants with ≥379 d of follow-up
- No serious AEs were related to study drug
- 1 participant had a serious AE of malignant neoplasm with a fatal outcome and not related to study drug

*Serious adverse events (AEs) not related to study drug: malignant neoplasm and dizziness (n=1); abdominal pain, pancreatic mass, Clostridium difficile colitis, and angina pectoris (n=1); anal squamous cell carcinoma, proctalgia, impaired healing, and anal cancer (n=1); femoral neck fracture (n=1); COVID-19 (n=2); pneumonia (n=1); and septic shock, renal impairment, and shock (n=1). ISRs, injection-site reactions.

Ogbuagu et al., CROI 2022

Incidence of ISRs Related to SC LEN*

ISR Types, %	After 1st SC Dose at Week 1 N=72	After 2nd SC Dose at Week 26 n=70	Median Duration, d
Swelling	26	13	12
Erythema	24	11	6
Pain	22	21	3
Nodule	22	11	180
Induration	11	10	118

- Mostly Grade 1 or 2 ISRs
- No Grade 4 ISRs, but 2 participants had Grade 3: 1 participant with swelling and erythema, which resolved in 4 and 8 d, respectively, and 1 participant with pain, which resolved in 1 d
- All nodules were Grade 1, except in 1 participant (Grade 2) who had 2 AEs of Grade 2 nodules, each after the 2nd and 3rd injections (both resolved after 3 d)
- 1 participant discontinued study drug at Week 52 due to an ISR (nodule; Grade 1)

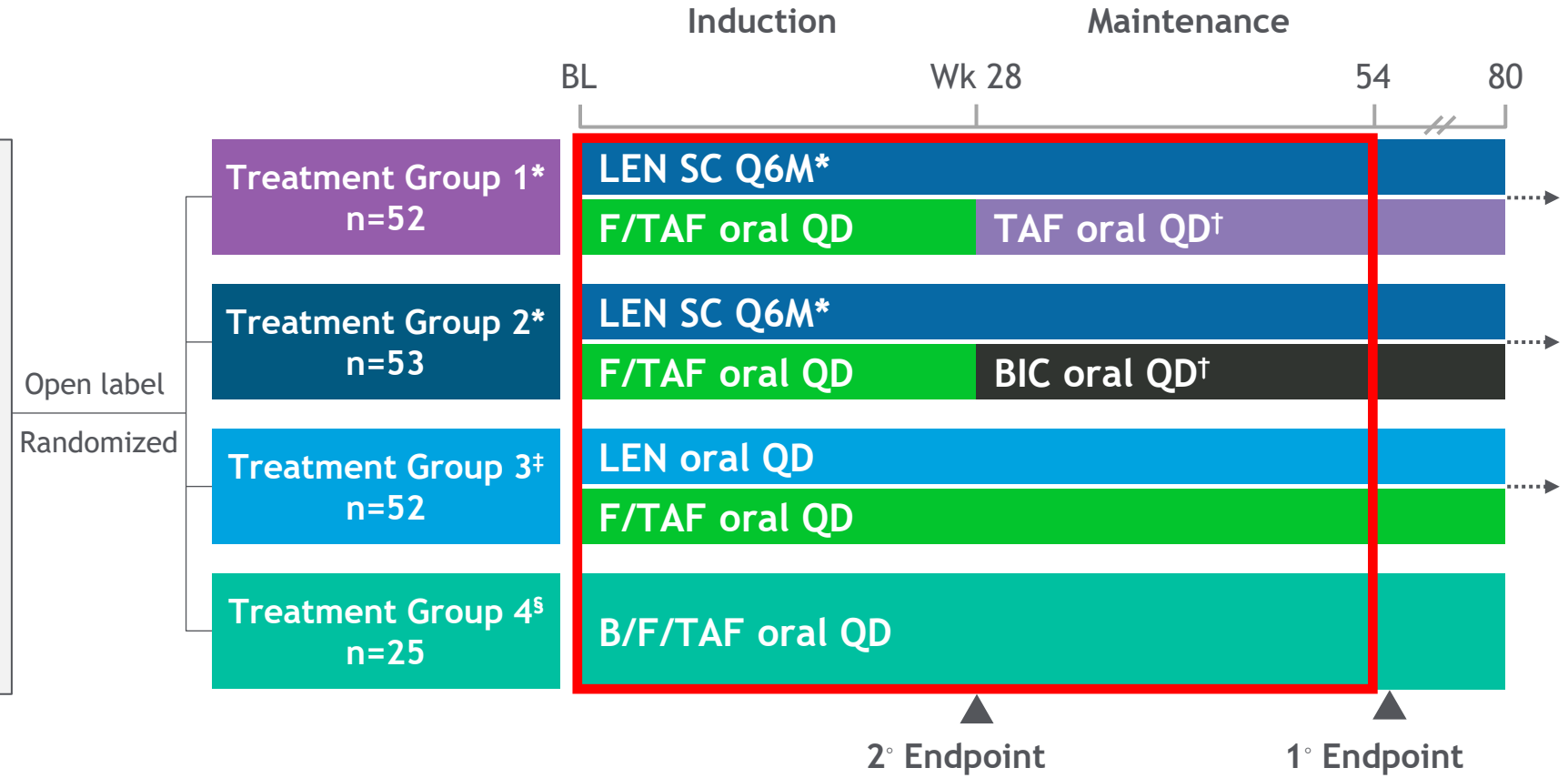
*Only includes AEs related to LEN and excludes those not related to it.
Ogbuagu et al., CROI 2022

Phase 2 Study of Lenacapavir as part of a Combination Regimen in Treatment-Naïve People with HIV: Week 54 Results (CALIBRATE)

Study Design

Treatment naïve
N=182
Key eligibility criteria:

- ARV naïve
- HIV-1 RNA ≥200 copies/mL
- CD4+ cell count ≥200 cells/µL



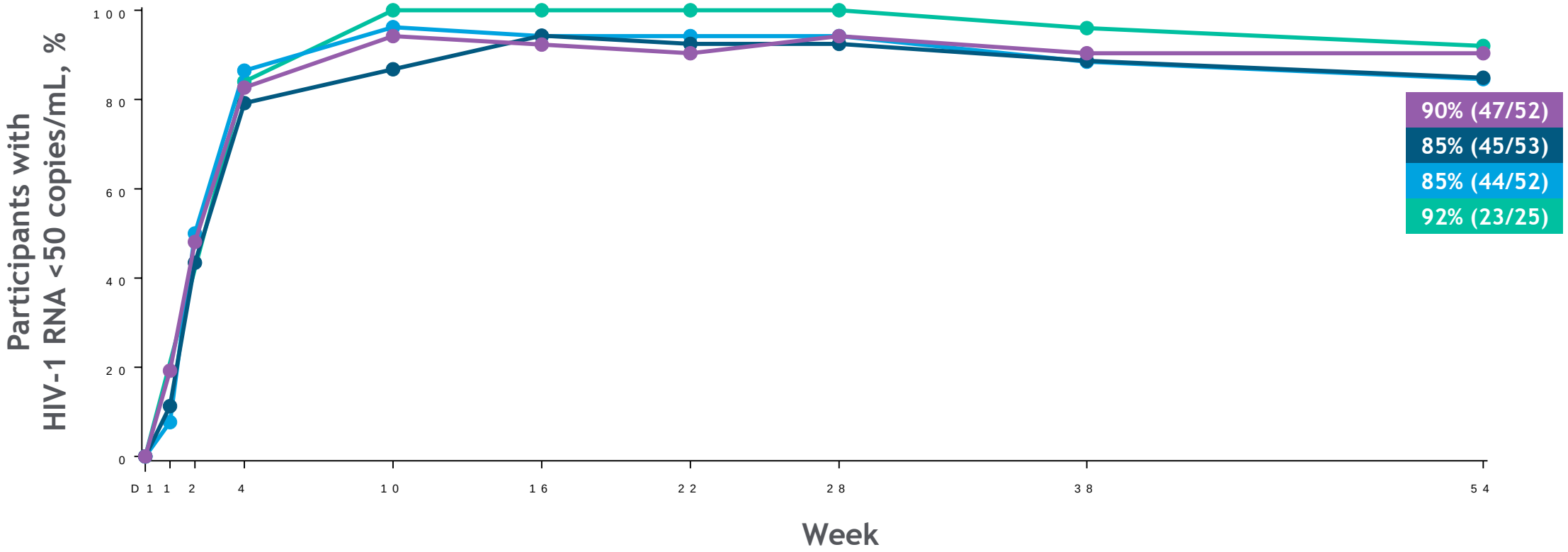
*LEN oral lead-in (600 mg on Days 1 and 2, 300 mg on Day 8) followed by LEN SC 927 mg on Day 15; F/TAF 200/25 mg; †Participants in TG 1 and 2 will need HIV-1 RNA results <50 copies/mL at Wks 16 and 22 to initiate either TAF 25 mg or BIC 75 mg at Wk 28; those with HIV-1 RNA ≥50 copies/mL will discontinue study at Wk 28; ‡LEN 600 mg on Days 1 and 2, followed by LEN 50 mg from Day 3; F/TAF 200/25 mg; §B/F/TAF 50/200/25 mg.
ARV, antiretroviral; BIC, B, bictegravir; BL, baseline; DMC, data monitoring committee; QD, once daily; Q6M, every 6 months; TG, treatment group; Wk, Week.
Gupta et al., CROI 2022

HIV-1 RNA <50 copies/mL by Visit

Missing = Failure (On Treatment)

Calibrate

TG 1: LEN SC + F/TAF to LEN SC + TAF
TG 2: LEN SC + F/TAF to LEN SC + BIC
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF



Gupta S et al., CROI 2022

Conclusions

LEN in combination with other agents led to high rates of virologic suppression

- In heavily treatment experienced PWH with multi-drug resistance
- In treatment naïve PWH

LEN was well tolerated

Two large Phase 3 HIV prevention studies are ongoing

These data support the ongoing evaluation of LEN for the treatment and prevention of HIV to address the diverse needs of PWH