P027

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Common Adverse Events in Clinical Studies of People Using Lenacapavir for HIV Treatment

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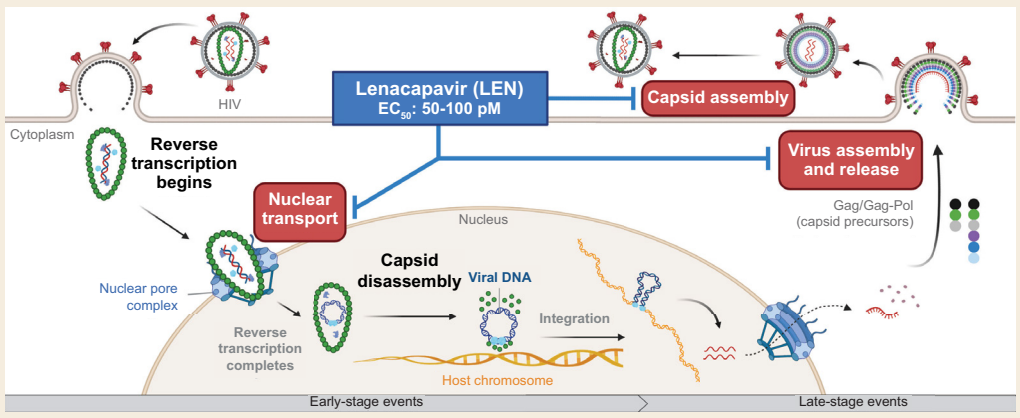
Introduction

Lenacapavir (GS-6207) Targets Multiple Stages of HIV Replication Cycle[1,2]



EC_{50} = half-maximal effective concentration; Gag = group-specific antigen; Pol = polymerase.

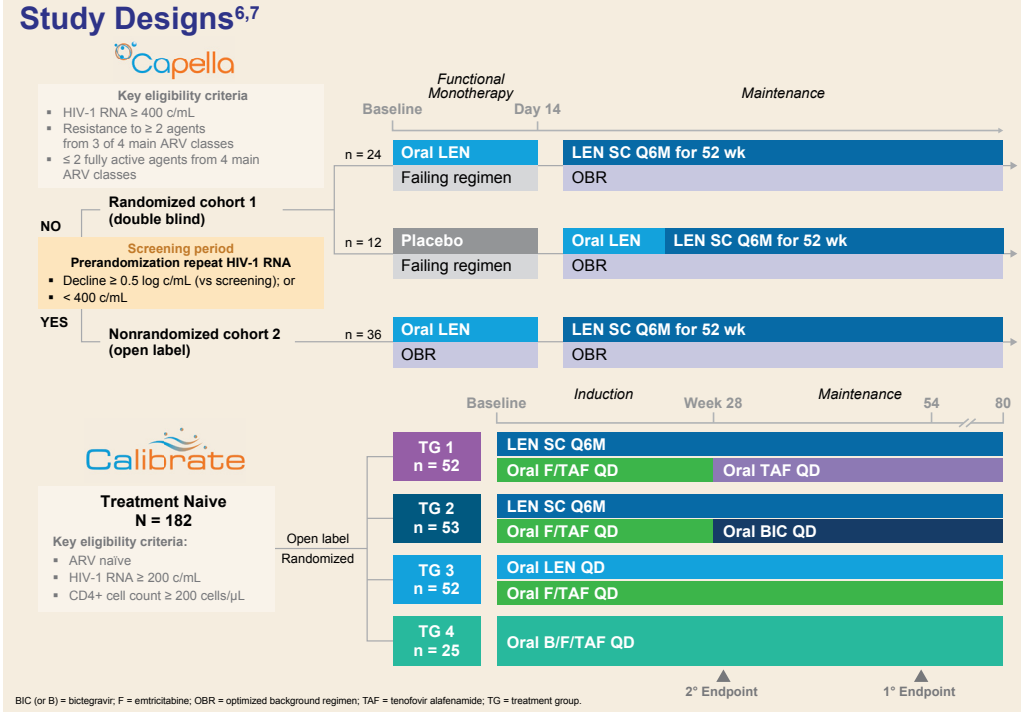
- LEN is a long-acting, first-in-class inhibitor of HIV-1 capsid protein
  - Can be administered subcutaneously (2 x 1.5 mL [927 mg] in abdomen Q6M)[3-5] or orally (daily or weekly)
  - Approved by the European Commission for the treatment of HIV-1 infection, in combination with other antiretrovirals (ARVs), in adults with multidrug resistance for whom it is otherwise not possible to construct a suppressive antiviral regimen
  - In development as a long-acting agent for treatment and prevention of HIV
- In people with HIV (PWH) who are heavily treatment experienced or treatment naïve, LEN in combination with other ARVs was well tolerated and led to high rates of virologic suppression through 1 year[6-8]
- LEN-related injection-site reactions (ISRs) were previously characterized[9]

Objective

- To characterize adverse events (AEs) other than ISRs in participants who received ≥ 1 dose of oral or SC LEN in clinical studies in PWH who were heavily treatment experienced (CAPELLA [ClinicalTrials.gov NCT04150068]) or treatment naïve (CALIBRATE [NCT04143594])

Methods

Study Designs[6,7]



BIC (or B) = bictegravir; F = emtricitabine; OBR = optimized background regimen; TAF = tenofovir alafenamide; TG = treatment group.

Results

Baseline Characteristics

	CAPELLA n = 72	CALIBRATE LEN n = 157
Age, median (range), years	52 (23-78)	29 (19-72)
Sex, % female at birth	25	8
Race, % Black	38	50
Ethnicity, % Hispanic/Latinx	21	45
Weight, median (range), kg	70.5 (41.4-126)	77.1 (47.6-163.8)
Body mass index, median (range), kg/m^2	25.0 (14.9-42.6)	25.8 (17.3-51.1)
HIV-1 RNA, median (range), $\log_{10}$ c/mL	4.5 (1.3-5.7)	4.4 (2.3-5.8)
> 100,000 c/mL, %	19	15
CD4 count, median (range), cells/μL	150 (3-1296)	417 (175-1846)
< 200 cells/μL, %	64	3

Including Cohorts 1 and 2 in CAPELLA, and TG 1, 2, and 3 in CALIBRATE.

Exposure to LEN

	CAPELLA n = 72	CALIBRATE LEN n = 157
Exposure, median, wk	54	66
Q1, Q3	44, 72	57, 81
Min, Max	13, 92	8, 93

Including Cohorts 1 and 2 in CAPELLA, and TG 1, 2, and 3 in CALIBRATE; exposure during studies was calculated as last study day (last dose date + 60 days for TG 3 in CALIBRATE) minus 1st dose date of oral LEN + 1; for ongoing participants, last study day was imputed by data cut date. Max = maximum; Min = minimum; Q = quartile.

Safety Summary

%	CAPELLA n = 72	CALIBRATE LEN n = 157
Any AE	93	88
Grade ≥ 3	22	8
AEs related to study drug	67	44
Grade ≥ 3	6	1
Serious AEs	11	6
AEs leading to premature discontinuation of study drug	1[a]	2[b]
Death	1[c]	0

Including Cohorts 1 and 2 in CAPELLA, and TG 1, 2, and 3 in CALIBRATE; [a]Injection-site nodule; [b]2 participants with injection-site induration, and 1 with injection-site erythema and injection-site swelling; [c]1 participant had serious AE of malignant neoplasm with fatal outcome and not related to study drug.

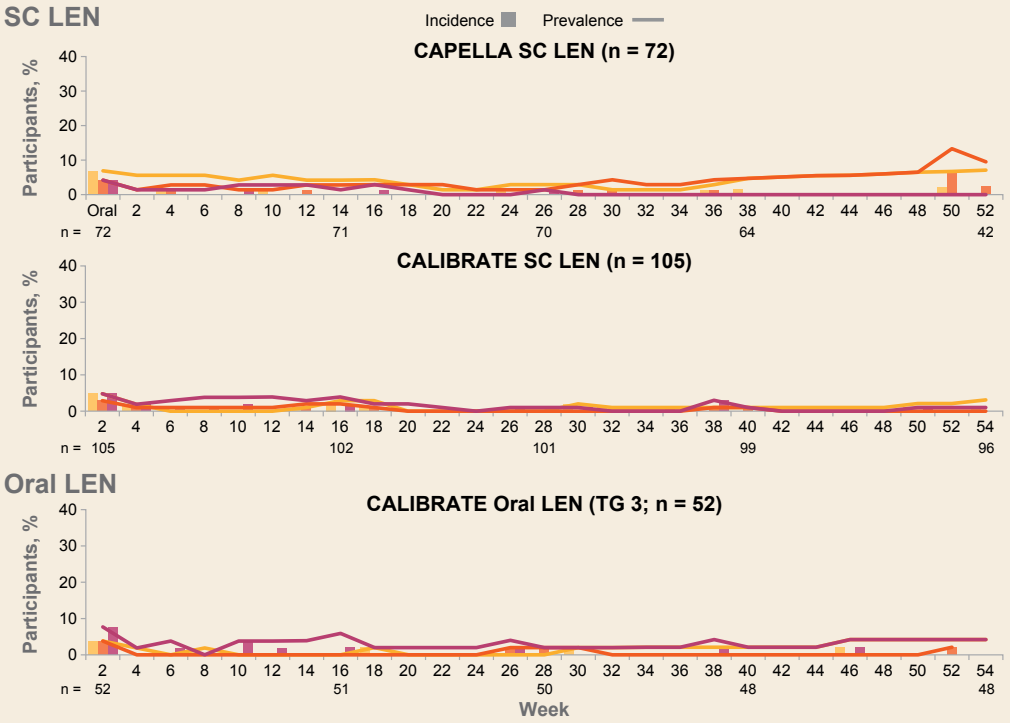
- There were no SAEs related to study drug
- Most non-ISR AEs were Grade 1 or 2 and resolved during ongoing treatment with LEN
- No participant discontinued LEN due to a non-ISR AE

Most Common AEs in SC LEN

AEs > 10% in Either Study, %	CAPELLA SC LEN n = 72	CALIBRATE SC LEN n = 105	CALIBRATE Oral LEN n = 52
Nausea	13	14	12
Diarrhea	13	7	10
Headache	8	13	13
Considered related to study drug by investigator			
Nausea	4	6	4
Diarrhea	3	2	4
Headache	3	3	2

- Investigators considered AEs of nausea, diarrhea, and headache related to LEN in 2%-6% of participants in each study group
- In CALIBRATE, gastrointestinal AEs were similar in the SC LEN vs oral LEN groups (nausea: 14% vs 12%; diarrhea: 7% vs 10%; and vomiting: 4% vs 8%)

Incidence and Prevalence of Most Common AEs



Duration, Median (range), wk	CAPELLA SC LEN n = 72	CALIBRATE SC LEN n = 105	CALIBRATE Oral LEN n = 52
Nausea	13.6 (0.1-75.9)	1.6 (0.1-21.9)	0.7 (0.3-9.7)
Diarrhea	14.3 (0.4-75.9)	0.7 (0.3-12.0)	0.4 (0.3-0.7)
Headache	1.3 (0.3-4.4)	2.1 (0.1-13.1)	0.6 (0.1-4.3)

Conclusions

- Among a range of PWH using oral and/or SC LEN, LEN was well tolerated with no non-ISR AEs related to LEN leading to discontinuation
- The most common non-ISR AEs in participants who received SC LEN were nausea, diarrhea, and headache

References: **1.** Link JO, et al. *Nature.* 2020;584:614-8; **2.** Zila V, et al. *Cell.* 2021;184:1032-46; **3.** Begley R, et al. AIDS 2020, abstr PEB0265; **4.** Begley R, et al. CROI 2020, abstr 470; **5.** Daar EM, et al. CROI 2020, poster 3691; **6.** Gupta SK, et al. CROI 2022, abstr 1292; **7.** Ogbuagu O, et al. CROI 2022, poster 491; **8.** Segal-Maurer S, et al. *N Engl J Med.* 2022;386:1793-1803; **9.** Kumar P, et al. AIDS 2022, poster EPB184.

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