

Lenacapavir as part of a Combination Regimen in Treatment-Naïve People with HIV: Week 54 Results

Samir K. Gupta,¹ James Sims,² Cynthia Brinson,³ Frederick A. Cruickshank,⁴ Godson Oguchi,⁵ Javier Morales,⁶ Theo Hodge,⁷ Craig Dietz,⁸ Angela S. Liu,⁹ Laurie VanderVeen,⁹ Hadas Dvory-Sobol,⁹ Martin S. Rhee,⁹ Jared M. Baeten,⁹ Ellen Koenig¹⁰

¹Indiana University School of Medicine, Indianapolis, IN, USA; ²St. Hope Foundation, Bellaire, TX, USA; ³Central Texas Clinical Research, Austin, TX, USA; ⁴Rosedale Infectious Diseases, Huntersville, NC, USA; ⁵Midland Florida Clinical Research Center, LLC, Deland, FL, USA; ⁶Clinical Research Puerto Rico Inc, San Juan, Puerto Rico, USA; ⁷Washington Health Institute, Washington DC, USA; ⁸Kansas City Care Health Center, Kansas City, MO, USA; ⁹Gilead Sciences Inc., Foster City, CA, USA; ¹⁰Instituto Dominicano de Estudios Viroológicos, Santo Domingo, Dominican Republic

Disclosures

SKG receives unrestricted research grant support from the NIH, Indiana University School of Medicine, and GSK/ViiV and receives advisory board fees from Gilead Sciences, Inc., and GSK/ViiV.

Acknowledgments

We extend our thanks to:

The study participants and their families

Participating study investigators and staff:

Dominican Republic: E Koenig

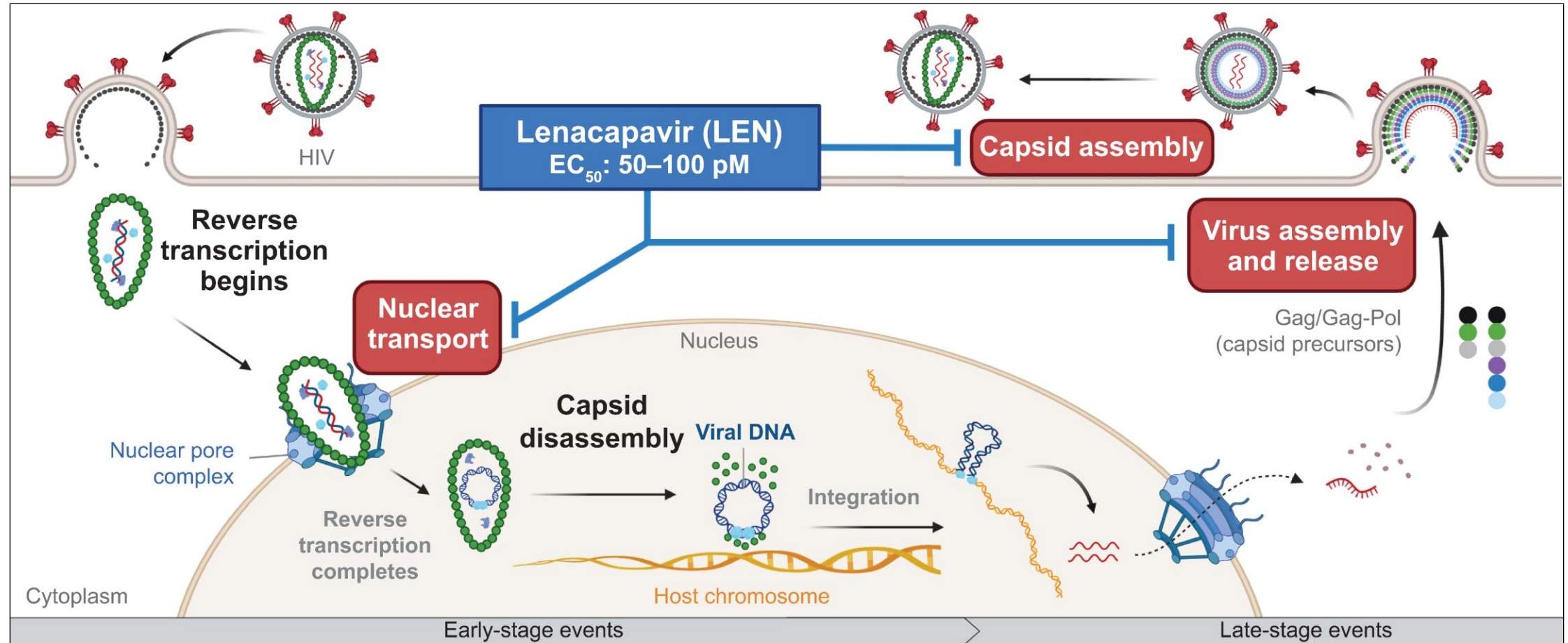
United States: P Benson; DS Berger; M Berhe; C Brinson; P Cook; DR Coulston; GE Crofoot; FA Cruickshank; D Cunningham; E DeJesus; C Dietz; V Drelichman; E Gardner; A Gaur; D Goldstein; SK Gupta; D Hagins; R Hengel; T Hodge; C-B Hsiao; A Khalsa; CA Kinder; P Kumar; C McDonald; A Mills; JO Morales-Ramirez; C Newman; G Oguchi; O Osiyemi; MN Ramgopal; PJ Ruane; W Sanchez; JL Santana-Bagur; L Santiago; A Scribner; J Sims; GI Sinclair; JL Stephens; M Wohlfeiler; AK Wurapa



This study was funded by Gilead Sciences, Inc.



Editorial and production assistance were provided by BioScience Communications, New York, NY, funded by Gilead.

LEN Targets Multiple Stages of HIV Replication Cycle



Introduction

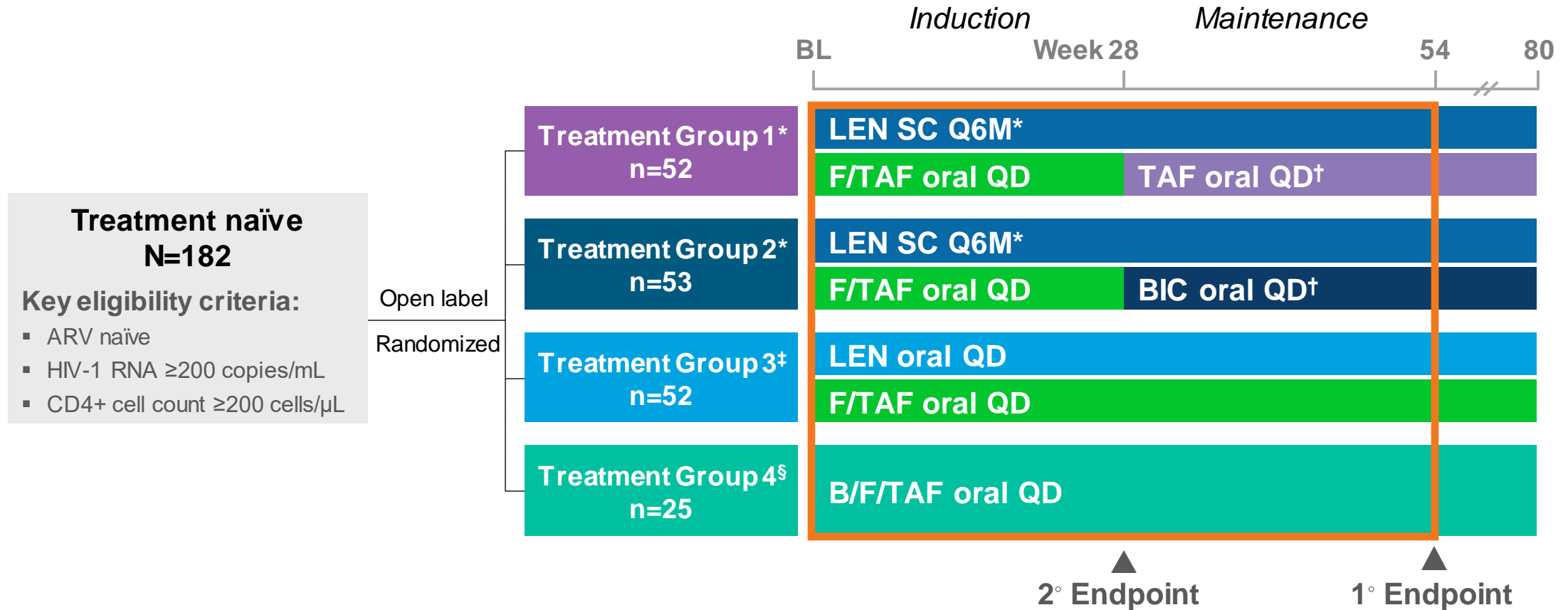
- ◆ Lenacapavir (LEN, GS-6207) is a long-acting first-in-class inhibitor of HIV-1 capsid protein
 - In clinical development for treatment and prevention of HIV-1 infection
- ◆ Highly potent activity (EC_{50} : 50–100 pM), with a low clearance and slow release kinetics¹
 - Can be administered orally (daily or weekly) or subcutaneously (every 6 months)²⁻⁴
- ◆ CALIBRATE was designed to generate exploratory clinical data to support the future development of LEN-containing regimens

	Phase 2/3 in heavily Tx-experienced PWH ^{5,6}	LEN + OBR	Week 52	83% virologic suppression (CROI 2022) ⁷
	Phase 2 in Tx-naïve PWH ⁸	LEN + F/TAF	Week 28	94% virologic suppression

F/TAF, emtricitabine/tenofovir alafenamide; OBR, optimized background regimen; PWH, people with HIV; Tx, treatment.

1. Link JO, et al. Nature 2020;584:614-8; 2. Begley R, et al. AIDS 2020, abstr PEB0265; 3. Begley R, et al. CROI 2020, abstr 470; 4. Daar E, et al. CROI 2020, abstr 469; 5. Segal-Maurer S, et al. CROI 2021, abstr 127; 6. Molina J-M, et al. IAS 2021, abstr OALX01LB02; 7. Ogbuagu O, et al. CROI 2022, abstr 1047; 8. Gupta SK, et al. IAS 2021, abstr OALB0302.

Study Design



*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 Weeks 16 and 22 to initiate either TAF 25 mg or BIC 75 mg at Week 28; those with HIV-1 RNA ≥50 copies/mL will discontinue study at Week 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; QD, once daily; Q6M, every 6 months; SC, subcutaneous; TG, treatment group.

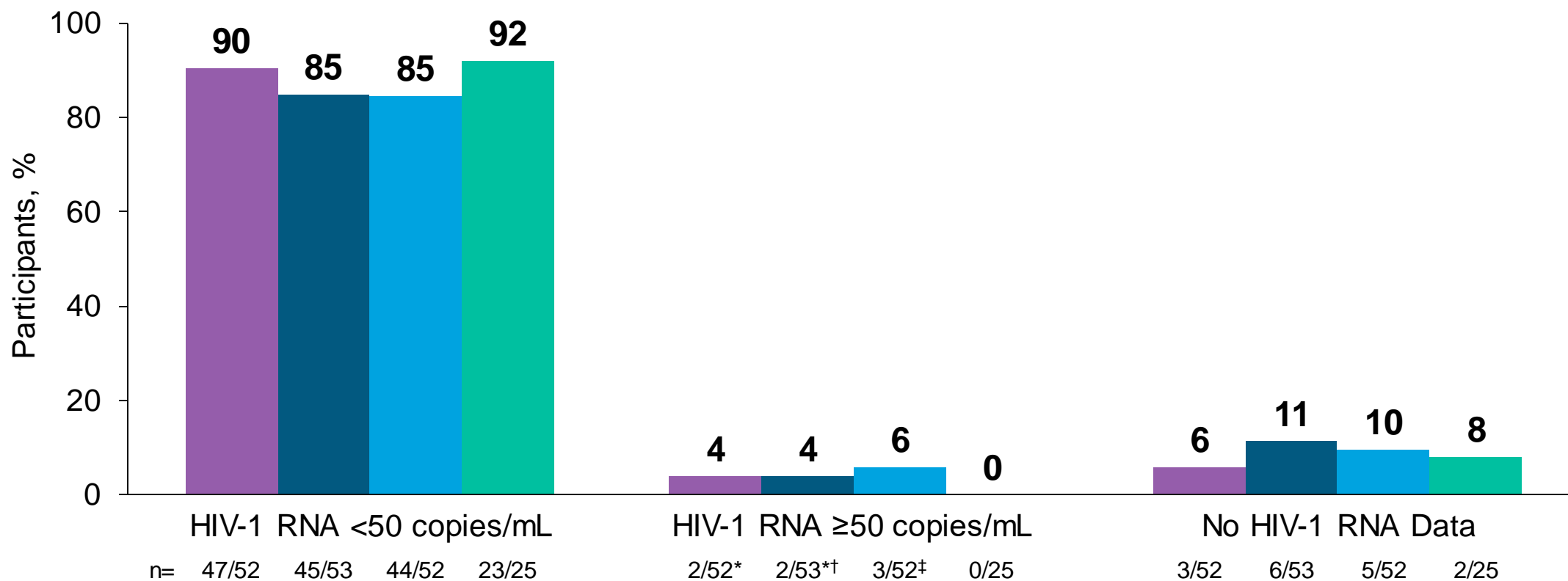
Baseline Characteristics

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

	LEN Total			B/F/TAF	Overall N=182
	TG 1 n=52	TG 2 n=53	TG 3 n=52	TG 4 n=25	
Age, median (range), years	31 (19, 61)	28 (19, 56)	28 (19, 72)	29 (21, 61)	29 (19, 72)
Sex, % female at birth	10	2	12	0	7
Race, % Black	46	45	60	64	52
Ethnicity, % Hispanic/Latinx	48	40	46	48	45
HIV-1 RNA, median log ₁₀ copies/mL	4.27	4.32	4.53	4.37	4.37
Q1, Q3	3.77, 4.63	3.96, 4.74	3.82, 4.83	4.09, 4.77	3.86, 4.74
>100,000 copies/mL, %	10	17	17	16	15
CD4 count, median cells/μL	404	450	409	482	437
Q1, Q3	320, 599	332, 599	301, 600	393, 527	332, 599
<200 cells/μL, %	0	2	6	0	2

Efficacy at Week 54 (FDA Snapshot)

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



- ◆ In the pooled SC LEN group (TG 1+2: initially in combination with F/TAF, then with TAF or BIC), 88% (92/105) achieved and maintained virologic suppression at Week 54

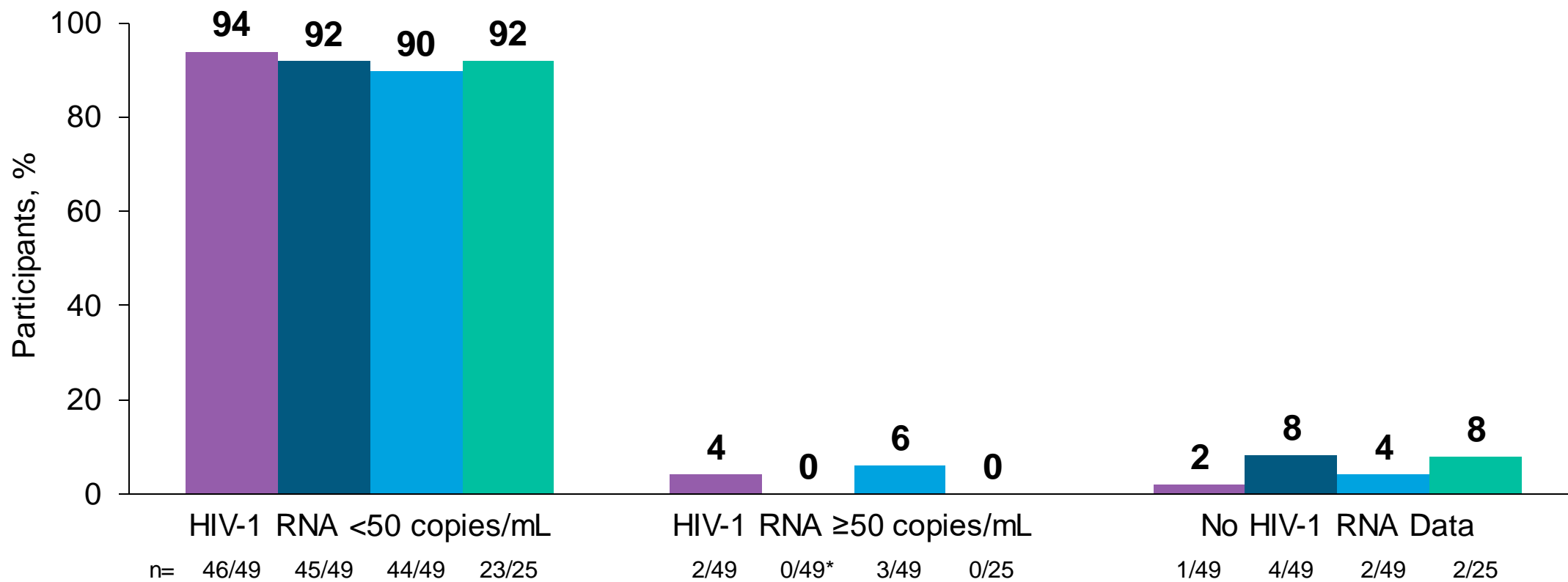
*3 participants (2 in TG 1 and 1 in TG 2) discontinued due to not meeting the protocol criteria of having HIV-1 RNA <50 copies/mL prior to Week 28;

†1 participant discontinued on Day 2; ‡2 of the 3 participants with HIV-1 RNA ≥50 copies/mL at Week 54 were suppressed in subsequent visit.

Efficacy at Week 54 (FDA Snapshot)

Among Participants who were Virologically Suppressed at Week 28

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



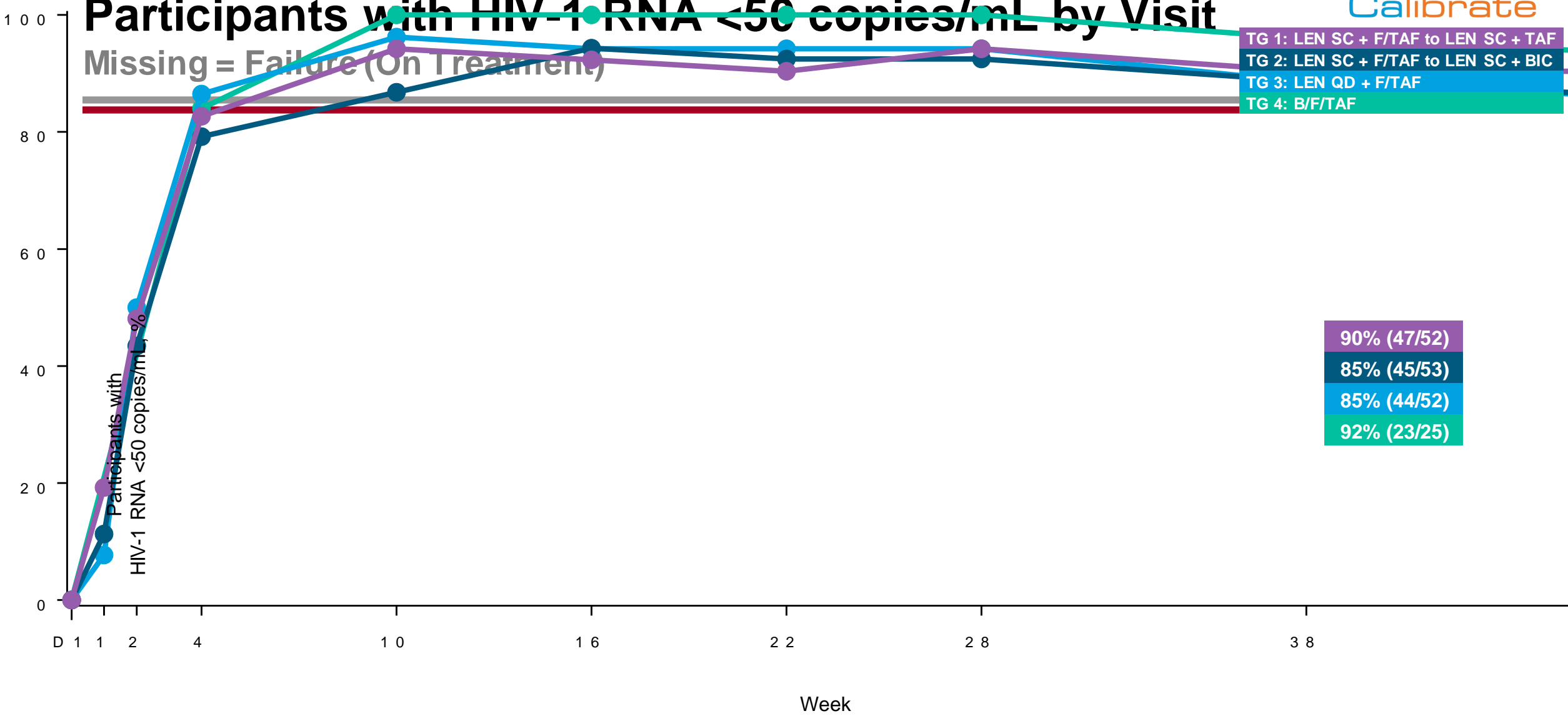
- ◆ In the pooled SC LEN group (TG 1+2: initially in combination with F/TAF, then with TAF or BIC), among participants who were virologically suppressed at Week 28, 93% (91/98) maintained virologic suppression at Week 54

*1 participant discontinued due to not meeting the protocol criteria of having HIV-1 RNA <50 copies/mL prior to Week 28; 1 participant discontinued on Day 2.

Participants with HIV-1 RNA <50 copies/mL by Visit

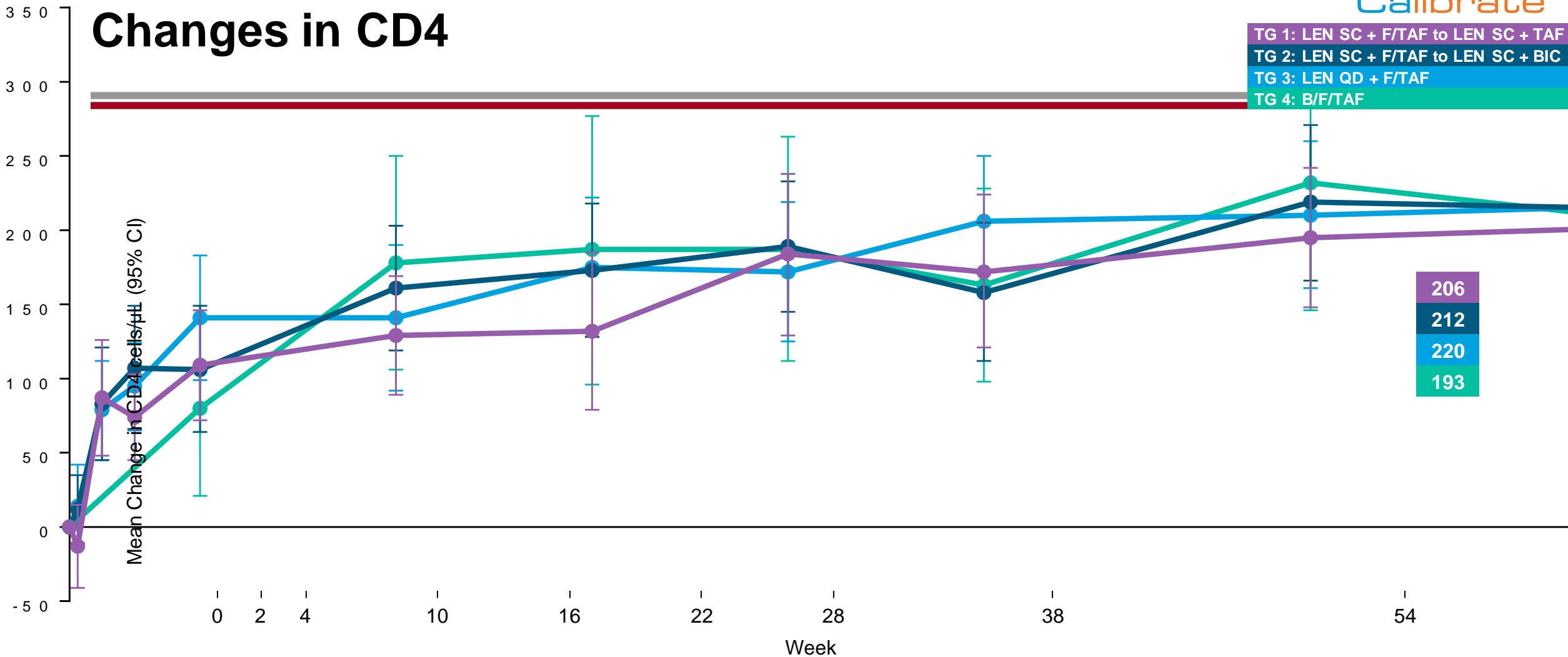
Missing = Failure (On Treatment)

- 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



90% (47/52)
85% (45/53)
85% (44/52)
92% (23/25)

Changes in CD4



◆ Baseline CD4 of the overall study population: median 437 cells/μL

Resistance Analysis*

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

Participants, n	TG 1 n=52	TG 2 n=53	TG 3 n=52	TG 4 n=25
Participants meeting the resistance testing criteria	1	1	3	1
Emergent LEN resistance	0	1	1	0

- ◆ Emergent LEN resistance in 2/157 (1.5%) participants
 - One participant in TG 2 developed Q67H+K70R (LEN fold change=20) in CA at Week 10, preceded by M184M/I in RT (IDWeek 2021)[†]
 - Pattern of mutation emergence suggests incomplete adherence to F/TAF
 - One participant in TG 3 developed Q67H (LEN fold change=7) in CA at Week 54
 - Nonadherence to F/TAF as assessed by pill count and drug levels
 - Both participants later re-suppressed on a regimen of INSTI + 2 NRTI

*Genotypic and phenotypic resistance testing performed on any participants with confirmed HIV-1 RNA ≥ 50 copies/mL and $< 1 \log_{10}$ HIV-1 RNA reduction from Day 1 at the Week 10 visit, at any visit after achieving HIV-1 RNA < 50 copies/mL and a rebound to ≥ 50 copies/mL, and at any visit, with $> 1 \log_{10}$ increase from the nadir; [†]Previously presented (Gupta SK, et al. IAS 2021, abstr OALB0302, VanderVeen L, et al. IDWeek 2021, oral 73).

CA, HIV capsid; INSTI, integrase strand transfer inhibitor; NRTI, nucleotide reverse transcriptase; RT, reverse transcriptase.

Adverse Events (excluding ISRs)

≥10% Participants in LEN total, %	LEN Total TG 1+2+3 n=157	B/F/TAF TG 4 n=25
Headache	13%	12%
Nausea	13%	4%
COVID-19	10%	12%

- ◆ No SAEs related to study drug
- ◆ No Grade 4 AEs related to study drug
- ◆ No discontinuations due to non-ISR AEs
- ◆ Gastrointestinal AEs: SC LEN (TG 1+2) vs oral LEN (TG 3)
 - Nausea: 14% vs 12%
 - Diarrhea: 7% vs 10%
 - Vomiting: 4% vs 8%

Injection Site Reactions

ISR Types*	After 1 st SC Dose at Week 1 n=103 [†]	After 2 nd SC dose at Week 26 n=95 [†]	Median duration (days)
Swelling	14%	12%	11
Erythema	14%	18%	5
Pain	15%	9%	4
Nodule	11%	8%	195
Induration	9%	6%	202

- ◆ Mostly Grade 1 or 2 ISRs
 - One Grade 3 ISR (nodule) after the second SC dose
- ◆ Three participants discontinued due to ISRs:
 - Two due to induration (both Grade 1, after the first SC dose)
 - One due to erythema and swelling (Grade 1, after the second SC dose)

*Includes those >5% at both Weeks 1 and 26; [†]TG 1+2 (ie, those who received ≥1 dose of SC LEN and still on study or last study date in 2-week interval).

Laboratory Abnormalities

Participants, %	LEN Total TG 1+2+3 n=157	B/F/TAF TG 4 n=25
Any Grade 3 or 4 lab abnormality	25%	24%
≥5% in LEN total		
Low creatinine clearance/eGFR*	8%	12%
High creatine kinase	7%	4%

- ◆ No clinically relevant Grade 3 or 4 lab abnormalities
- ◆ No discontinuations associated with Grade 3 or 4 lab abnormalities

*Per Division of AIDS scale, Grade 3 creatinine clearance is <60–30 mL/min or 30–<50% decrease from baseline. eGFR, estimated glomerular filtration rate.

- ◆ In treatment naïve PWH, SC LEN, initially in combination with F/TAF and later with oral TAF or BIC, achieved and maintained high rates of virologic suppression through 1 year (90% and 85%, respectively)
 - Oral LEN in combination with F/TAF had similar efficacy (85%)
- ◆ LEN was well tolerated; discontinuations due to adverse events were infrequent
- ◆ These Phase 2 data support the ongoing evaluation of LEN for treatment and prevention of HIV-1 infection
 - In heavily treatment-experienced PWH in the ongoing CAPELLA study
 - In treatment-naïve and -experienced PWH in combination with other agent(s)
 - In people who could benefit from pre-exposure prophylaxis (PrEP)