

Long-Acting Lenacapavir in a Combination Regimen for Treatment Naïve PWH: Week 80

Debbie Hagins,^{1*} Ellen Koenig,² Rachel Safran,³ Lizette Santiago,⁴ Michael Wohlfeiler,⁵ Chiu-Bin Hsiao,⁶ Shan-Yu Liu,⁷ Laurie A. VanderVeen,⁷ Hadas Dvory-Sobel,⁷ Martin S. Rhee,⁷ Jared Baeten,⁷ Samir Gupta⁸

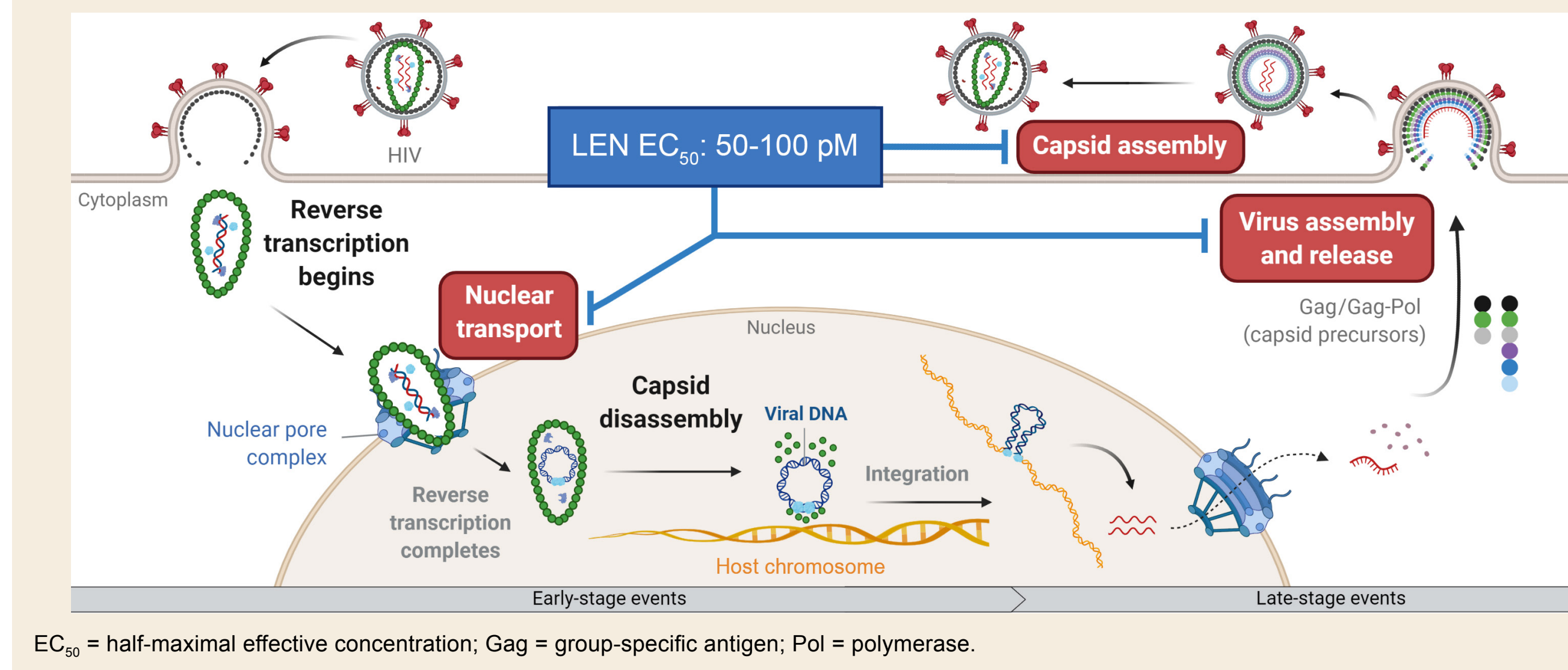
¹Chatham County Health Department, Savannah, GA; ²IDEV: Instituto Dominicano de Estudios Virologicos, Santo Domingo, Dominican Republic; ³MultiCare Rockwood Internal Medicine & HIV Clinic, Spokane, WA; ⁴Hope Clinical Research, Inc., San Juan, PR; ⁵AIDS Healthcare Foundation-South Beach, Miami Beach, FL; ⁶Allegheny Health Network, Pittsburgh, PA; ⁷Gilead Sciences, Inc., Foster City, CA; ⁸Indiana University-Purdue University, Indianapolis, IN

*Presenting author.

Introduction

- Lenacapavir (LEN) is a novel, highly potent, long-acting, first-in-class inhibitor of the HIV-1 capsid protein approved in Canada, the EU, and the US for the treatment of HIV-1 infection in adults with multidrug resistance in combination with other antiretrovirals¹⁻³
 - Can be administered SC (2 x 1.5 mL [927 mg] in abdomen Q6M) or orally (daily or weekly)⁴⁻⁶
 - In development as a long-acting agent for treatment and prevention of HIV
- CALIBRATE (NCT04143594) is an ongoing, Phase 2, open-label, active-controlled study designed to generate exploratory clinical data to support the future development of LEN-containing regimens
- At the Week 54 primary endpoint, SC LEN Q6M or oral LEN QD in combination with oral tenofovir alafenamide (TAF), bicitegravir (BIC), or emtricitabine (F)/TAF maintained high rates of virologic suppression (90%, 85%, and 85%, respectively) and was generally well tolerated⁷

Lenacapavir Inhibits Multiple Stages of HIV Replication Cycle^{8,9}

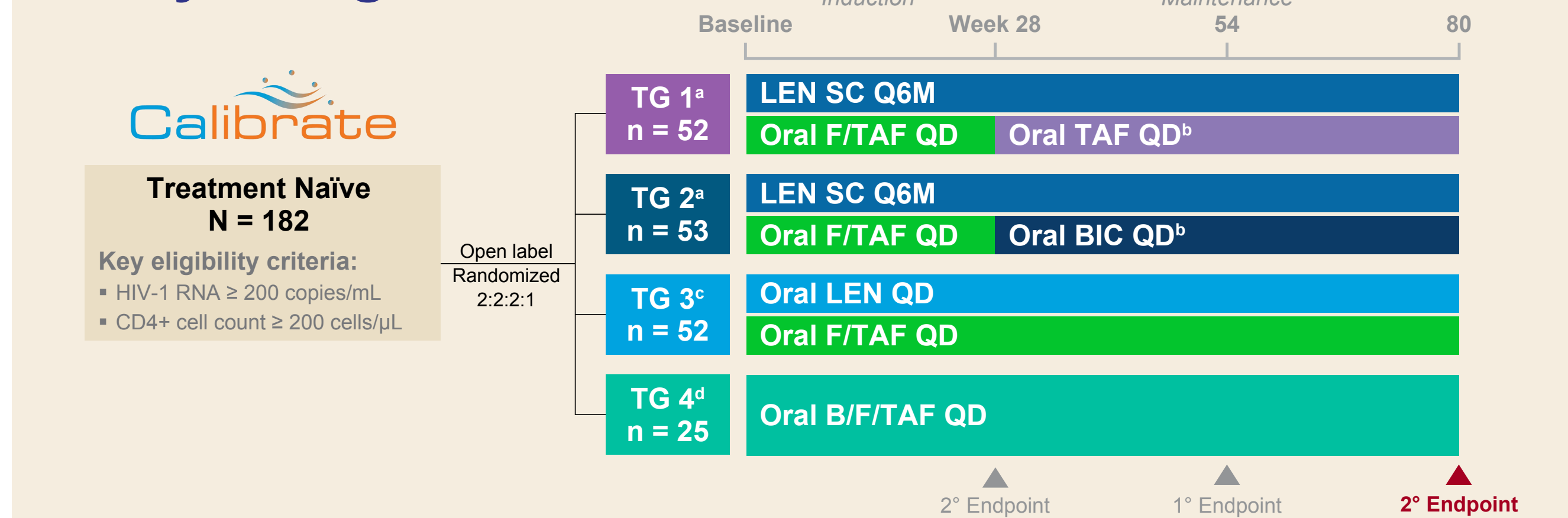


Objectives

- To report the secondary efficacy endpoint and safety at Week 80

Methods

Study Design



- There were no prespecified formal statistical comparisons between TGs

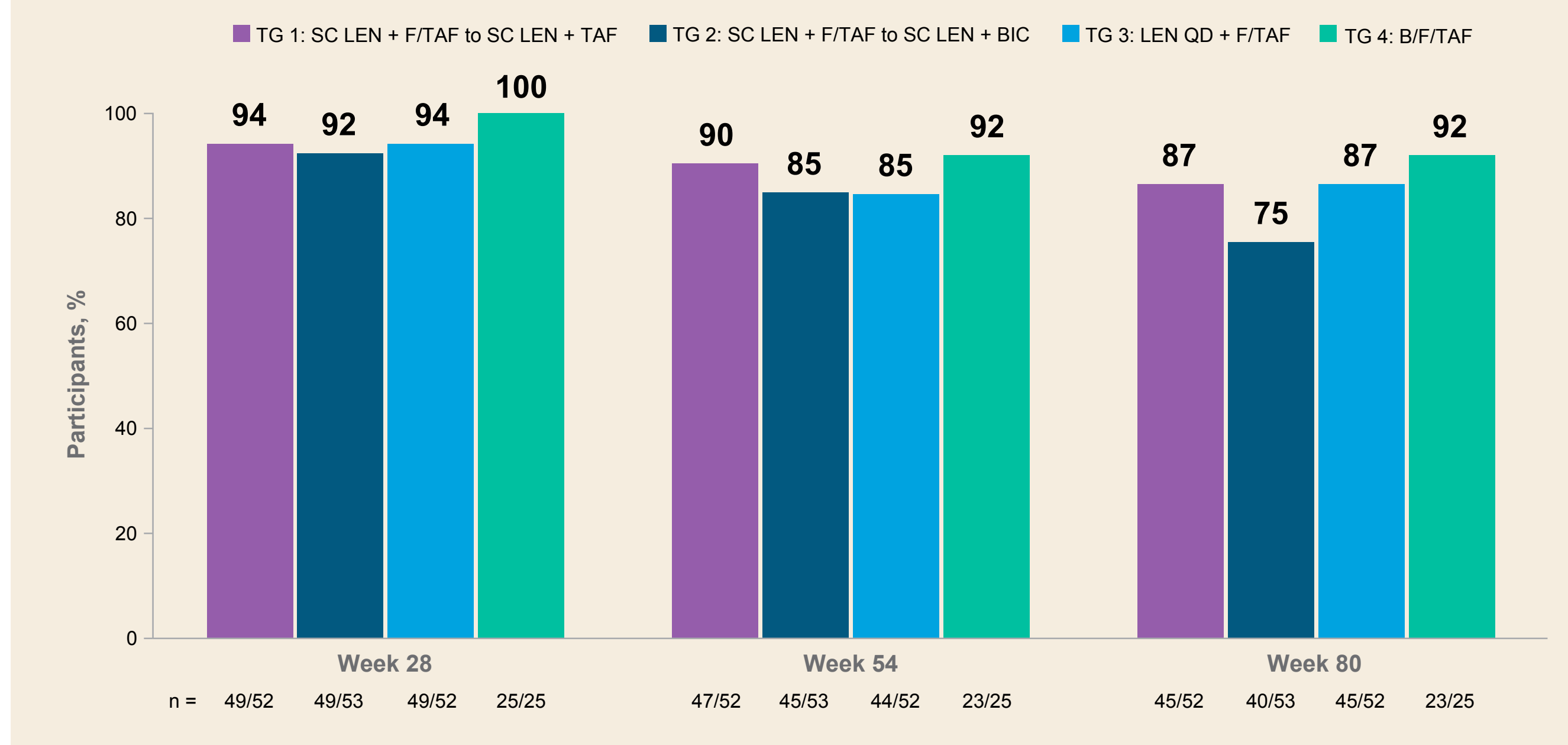
Results

Baseline Characteristics

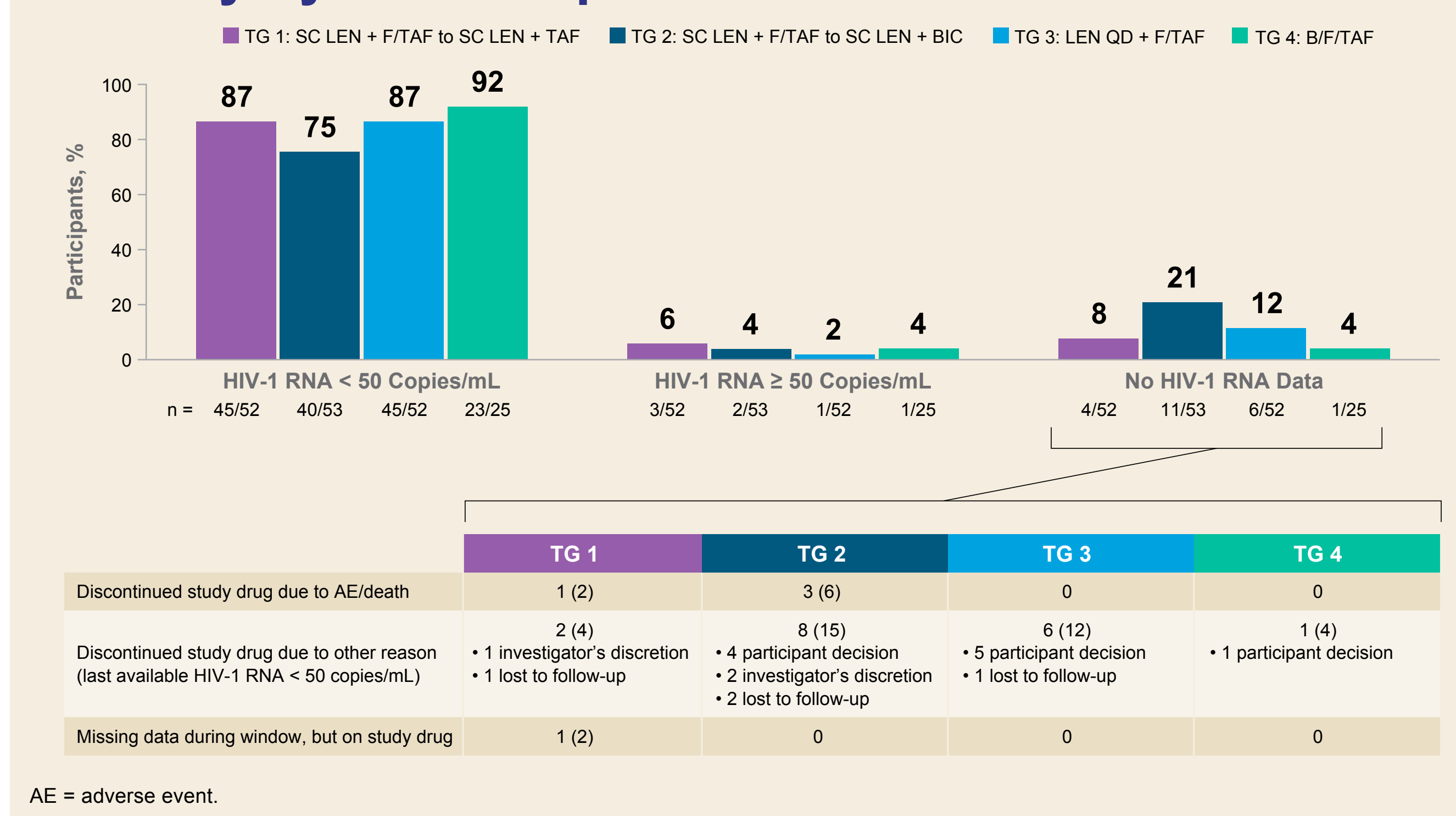
	TG 1 n = 52	TG 2 n = 53	TG 3 n = 52	TG 4 n = 25	Overall N = 182
Age, median (range), years	31 (19-61)	28 (19-56)	28 (19-72)	29 (21-61)	29 (19-72)
Sex, % female at birth	10	2	12	0	7
Race, % Black	46	45	60	64	52
Ethnicity, % Hispanic/Latinx	48	40	46	48	45
HIV-1 RNA, median log ₁₀ copies/mL	4.27	4.32	4.53	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/ μ L	404	450	409	482	437
Q1, Q3	320, 599	332, 599	301, 600	393, 527	332, 599
< 200 cells/ μ L, %	0	2	6	0	2

CD4 = cluster of differentiation-4; Q = quartile.

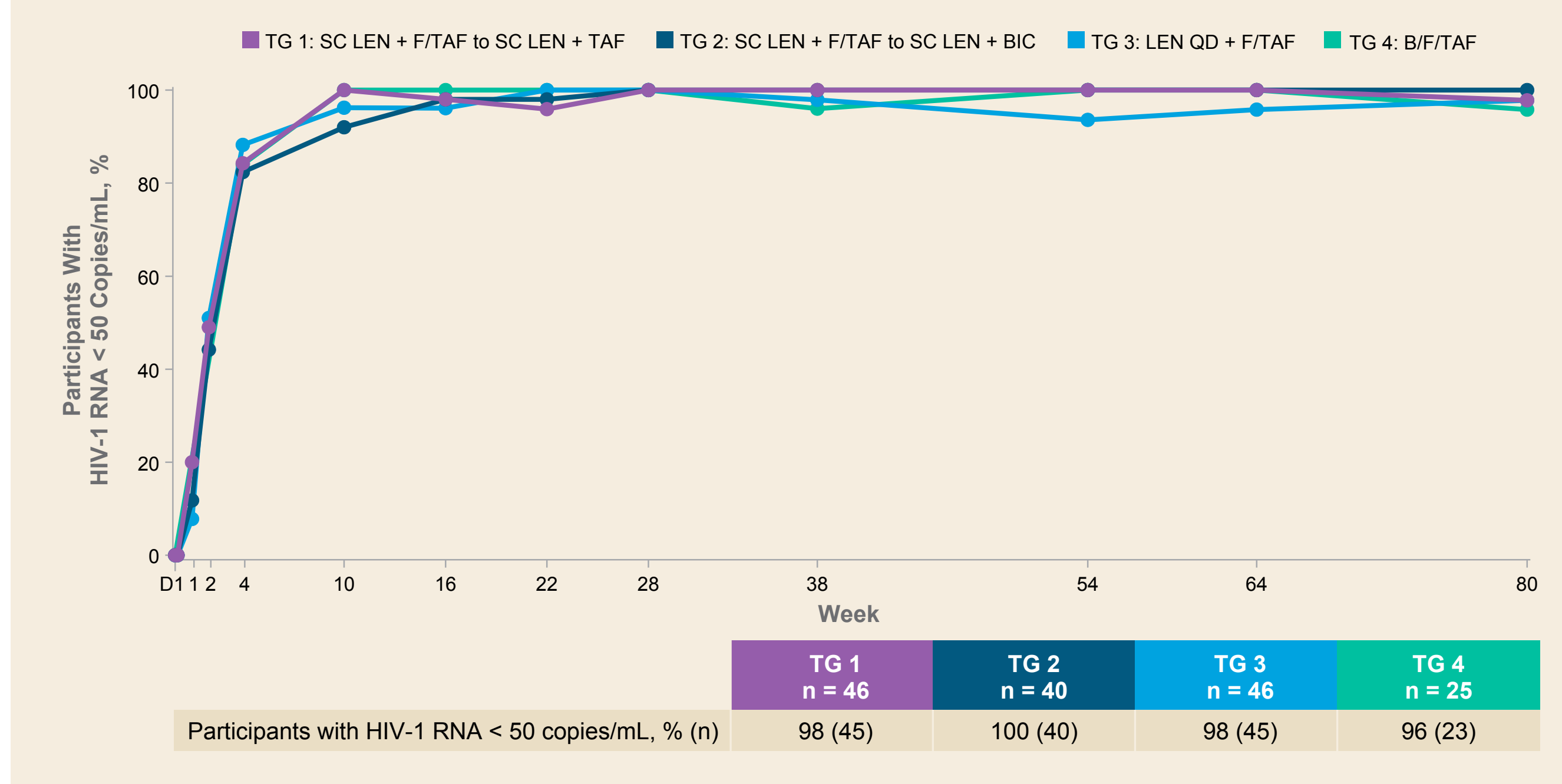
Efficacy by FDA Snapshot: HIV-1 RNA < 50 Copies/mL



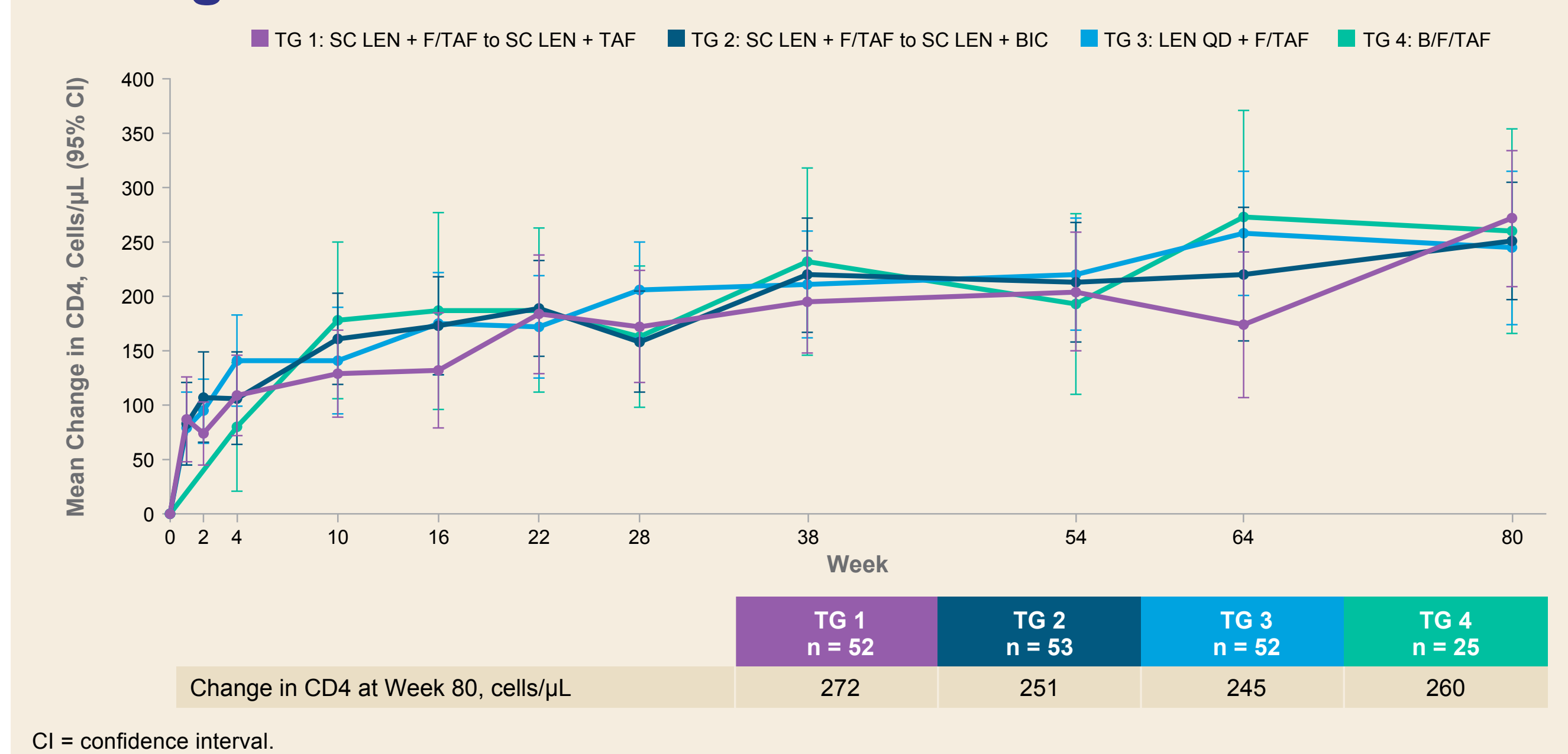
Efficacy by FDA Snapshot at Week 80



Participants With HIV-1 RNA < 50 Copies/mL by Visit Missing = Excluded (on Treatment)



Changes in CD4



- For participants in TGs 1-3, CD4 count increased by a mean of 256 cells/ μ L (minimum, maximum: -384, 843) at Week 80

Resistance Analysis

Participants, n	TG 1 n = 52	TG 2 n = 53	TG 3 n = 52	TG 4 n = 25
Met resistance testing criteria	2	1	3	1
Emergent LEN resistance	1	1	1	0
Q67H	1	1	1	0
K70R	1	1	1	0

Genotypic and phenotypic resistance testing performed on any participants with confirmed HIV-1 RNA \geq 50 copies/mL and < 1-log₁₀ HIV-1 RNA reduction from Day 1 at Week 10 visit, any visit after achieving HIV-1 RNA < 50 copies/mL and rebound to \geq 50 copies/mL, and any visit with > 1-log₁₀ increase from nadir.

- Emergent LEN resistance in 3/157 participants (2%) through Week 80
 - 1 participant (TG 1) developed Q67H + K70R at Week 80
 - 1 participant (TG 2) developed M184M/I in reverse transcriptase prior to Q67H + K70R in capsid at Week 10^{10,11}
 - 1 participant (TG 3) developed Q67H in capsid at Week 54 with subsequent emergence of K70R, and demonstrated nonadherence by pill count and drug levels^{12,13}

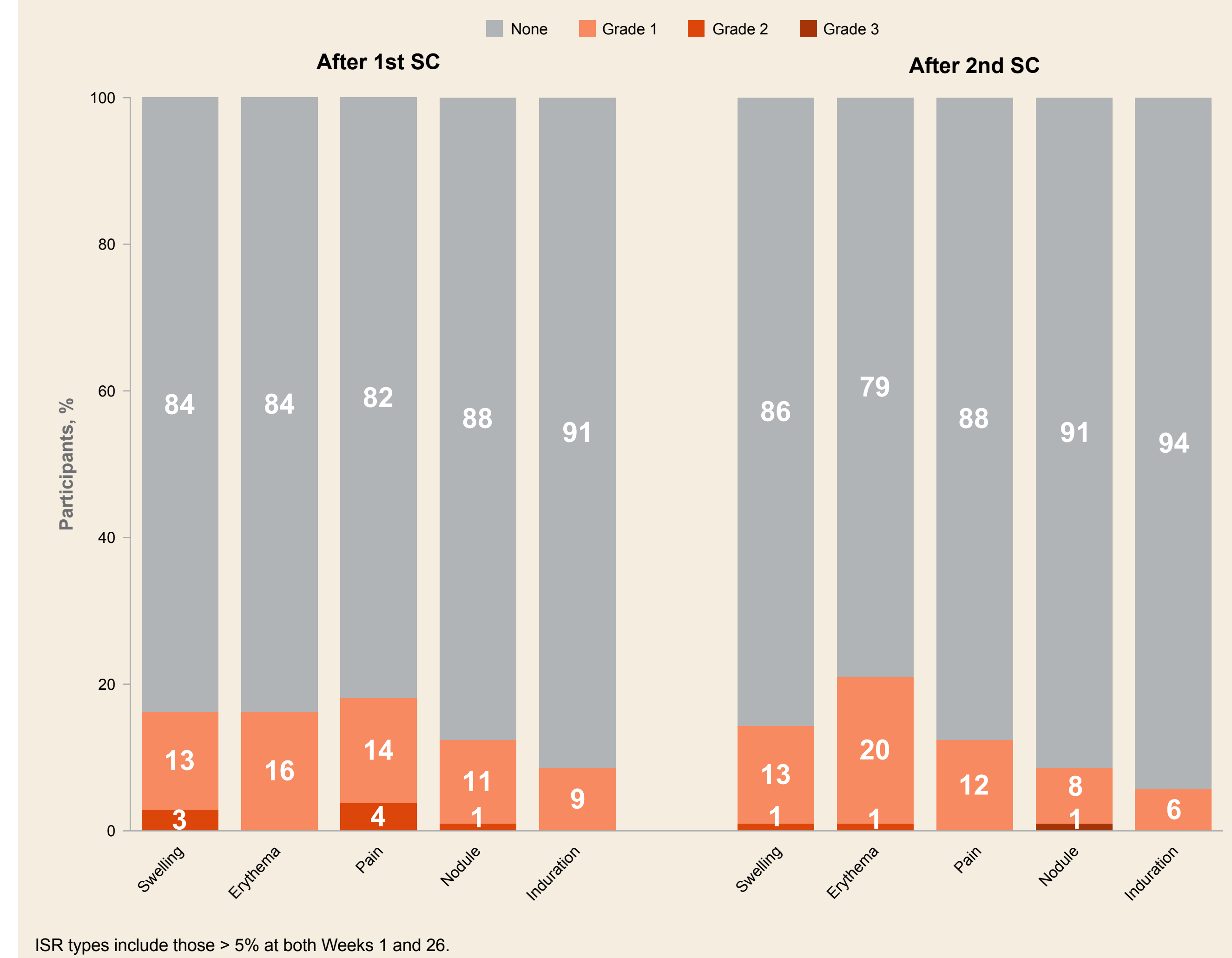
Adverse Events (Excluding ISRs)

≥ 10% of Participants in LEN total, %	LEN Total TGs 1-3 n = 157	B/F/TAF TG 4 n = 25
Headache	16	12
Nausea	13	4
COVID-19	13	16
Syphilis	11	16
Influenza	11	0
Diarrhea	10	8

ISRs = injection-site reactions.

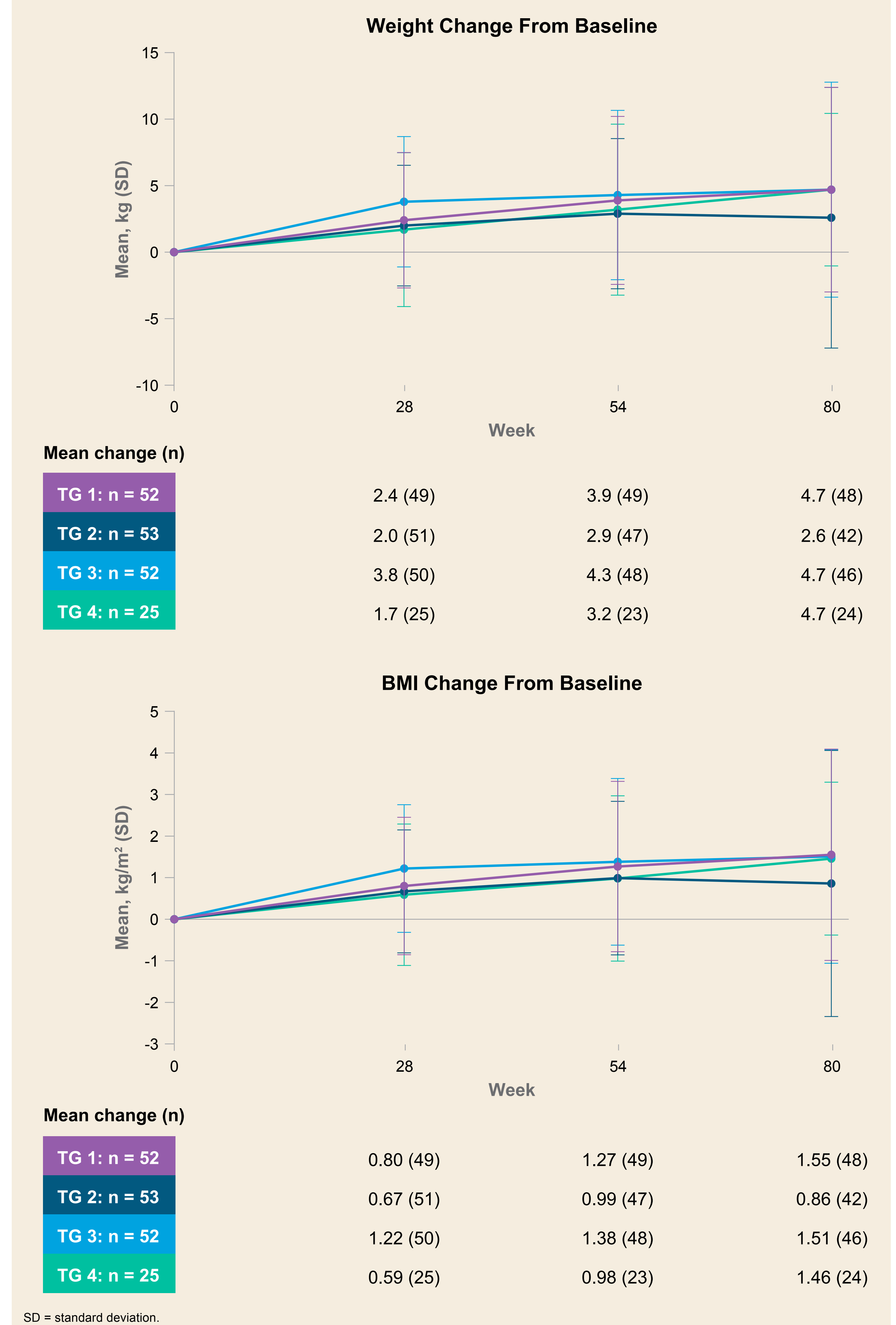
- 1 participant (TG 1) had a serious AE of non-small-cell lung cancer with a fatal outcome and not related to study drug (Day 273)
- No serious AEs related to study drug
- No Grade 4 AEs related to study drug
- No discontinuations due to non-ISR AEs
- Gastrointestinal AEs: SC LEN (TG 1+2) vs oral LEN (TG 3)
 - Nausea: 14% vs 12%
 - Diarrhea: 10% vs 12%
 - Vomiting: 5% vs 10%

Injection-Site Reactions



- LEN-related ISRs were mostly mild to moderate
 - 1 Grade 3 ISR (nodule) after the 2nd SC dose
- 4 participants discontinued due to ISRs:
 - 3 due to induration (all Grade 1; 2 after the 1st SC dose and 1 after the 3rd SC dose)
 - 1 due to erythema and swelling (Grade 1 after the 2nd SC dose)

Weight and BMI Changes



Conclusions

- In treatment-naïve people with HIV (PWH), SC LEN in combination with TAF or BIC and oral LEN with F/TAF maintained high rates of virologic suppression through Week 80
- LEN was well tolerated; discontinuations due to AEs were infrequent
- These long-term results support ongoing evaluation of LEN in combination with other long-acting partner agents for the treatment of HIV-1 infection, and support Gilead's long-acting oral and injectable development program

References: 1. Sunlenca [package insert] Foster City, CA: Gilead Sciences, Inc; 2022. 2. Sunlenca [product monograph]. Mississauga, ON: Gilead Sciences Canada, Inc; 2022. 3. Sunlenca [summary of product characteristics]. Carrigrohilly, Ireland: Gilead Sciences Ireland UC; 2022. 4. Begley R, et al. AIDS 2020, abstr PEB0265. 5. Begley R, et al. CROI 2020, abstr 470. 6. Daar EM, et al. CROI 2020, poster 3691. 7. Gupta SK, et al. CROI 2022, abstr 1292. 8. Link V, et al. Nature 2020;584:614-8. 9. Zia V, et al. Cell 2021;184:1032-46. 10. Gupta SK, et al. IAS 2021, abstr OALB0302. 11. VanderVeen L, et al. IDWeek 2021, oral 73. 12. Gupta SK, et al. CROI 2022, oral 138. 13. VanderVeen L, et al. AIDS 2022, abstr. EPB239.

Acknowledgments: We extend our thanks to the participants, their families, and all participating investigators: Dominican Republic: E Koenig; US: P Benson, DS Berger, M Berke, 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 Holdge, 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, J Stephens, M Wohlfeiler, AK Wurapa. This study was funded by Gilead Sciences, Inc. Editing and production assistance were provided by BioScience Communications, New York, NY, funded by Gilead. Disclosures: D Hagins, E Koenig, R Safran, C-B Hsiao: nothing to disclose; L Santiago: consulting fees, speaking honoraria, and research funding from Gilead, GSK, Janssen, MSD, Pfizer; M Wohlfeiler: CROI and IAC advisory boards; principal investigator for HIV; S-Y Liu, LA VanderVeen, H Dvory-Sobel, MS Rhee, J Baeten: employees and shareholders of Gilead; S Gupta: advisory board fees from Gilead, GSK/IVV; research grant support from NIH, Indiana University School of Medicine, GSK/IVV.