

Week 52 Subgroup Efficacy of Lenacapavir in Heavily Treatment-Experienced PWH

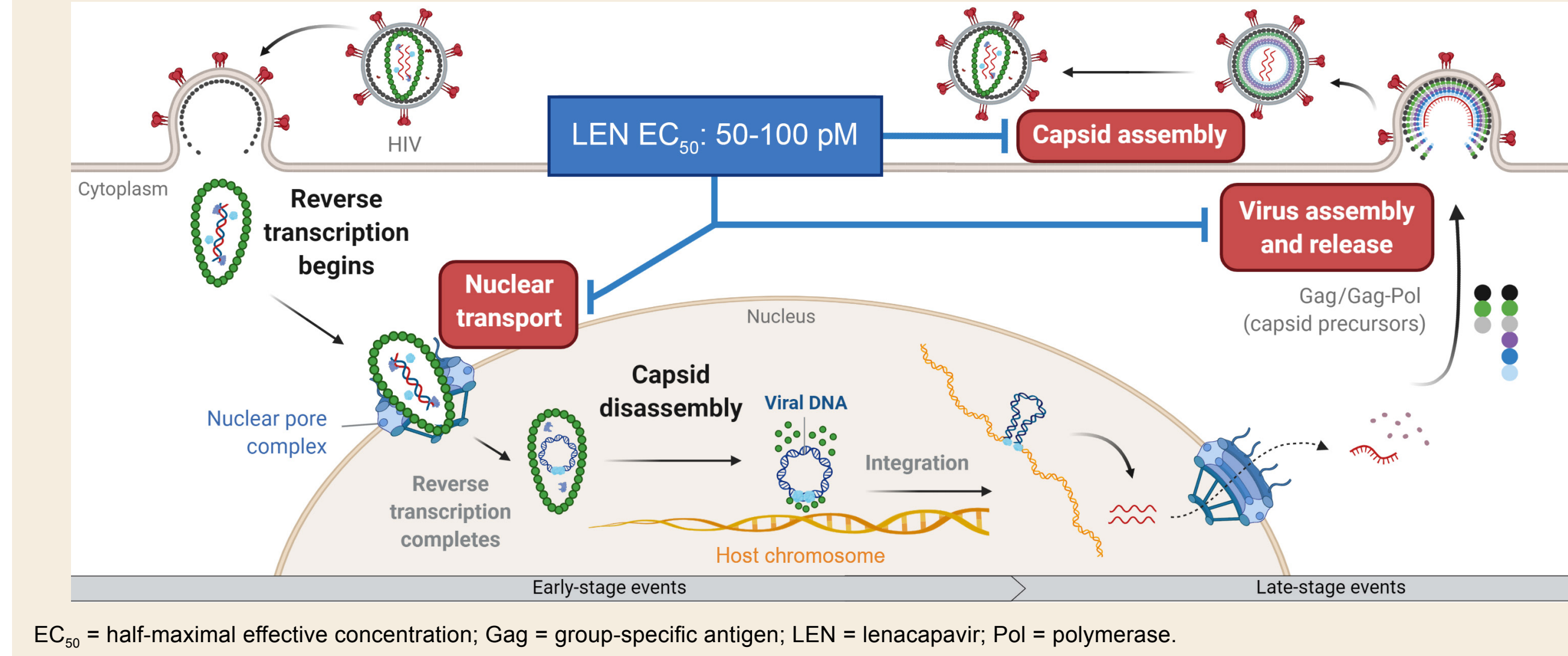
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Introduction

Lenacapavir (GS-6207) Inhibits Multiple Stages of HIV Replication Cycle^{1,2}



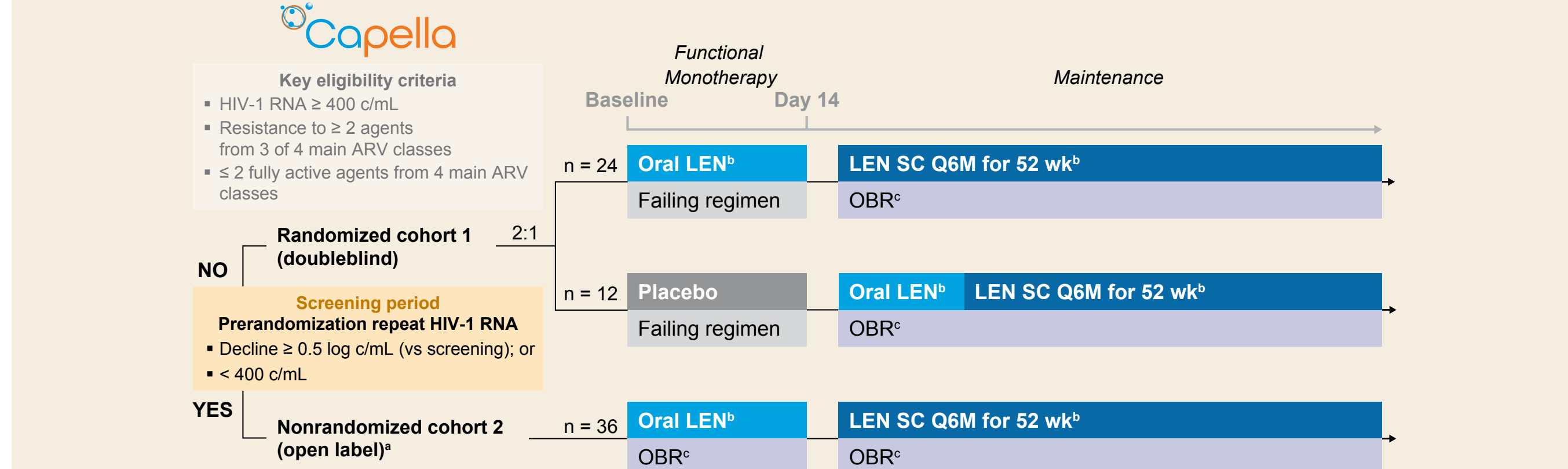
- LEN is a novel, highly potent, long-acting, first-in-class inhibitor of HIV-1 capsid protein approved in Canada, the EU, and the US for the treatment of HIV-1 infection in adults with multidrug resistance in combination with other antiretrovirals (ARVs)³⁻⁵
- LEN can meet significant unmet HIV treatment and prevention needs:
 - A new mechanism of action for people with multidrug-resistant (MDR) HIV-1 who are heavily treatment-experienced (HTE) and have limited treatment options
 - Reduction of daily pill burden through less frequent dosing for treatment and prevention
- Highly desirable in vitro profile with picomolar antiviral activity (EC₅₀: 50-100 pM)
 - Retains full activity against mutants resistant to nucleoside reverse-transcriptase inhibitors (NRTIs), non-nucleoside reverse-transcriptase inhibitors (NNRTIs), integrase strand transfer inhibitors (INSTIs), protease inhibitors (PIs), and entry inhibitors⁶⁻⁹
 - No observed preexisting resistance¹⁰
- The CAPELLA study (NCT04150068) is an ongoing Phase 2/3 study in people with HIV (PWH) who are HTE and viremic on their current regimen with MDR HIV-1¹¹:
 - At Week 52, LEN + an optimized background regimen (OBR) led to 78% (56/72) virologic suppression and a median cluster of differentiation-4 (CD4) increase of 84 cells/μL

Objective

- To evaluate Week 52 efficacy by subgroup analyses using FDA Snapshot algorithm

Methods

Study Design



*3 participants were enrolled in Cohort 2 as they did not meet randomization criteria, while Cohort 1 was still enrolling; 33 enrolled in Cohort 2 after enrollment of Cohort 1 was completed; †Administered as 600 mg on Days 1 and 2, and 300 mg on Day 8; LEN SC administered as 927 mg (2 x 1.5 mL) in abdomen on Day 15; ‡Investigational agents, such as fostemsavir, were allowed; ††azanavir (ATV), ATV/cobicistat, ATV/ritonavir, efavirenz, entecavir, tipranavir, and nevirapine were not allowed.

Results

Baseline Characteristics

	Randomized Cohort n = 36	Nonrandomized Cohort n = 36	Total N = 72
Age, median (range), years	54 (24-71)	49 (23-78)	52 (23-78)
Sex, % female at birth	28	22	25
Race, % Black	46*	31	38
Ethnicity, % Hispanic/Latinx	29*	14	21
HIV-1 RNA, median (range), log ₁₀ c/mL	4.5 (2.3-5.4)	4.5 (1.3-5.7)	4.5 (1.3-5.7)
> 100,000 c/mL, %	19	19	19
CD4 count, median (range), cells/μL	127 (6-827)	195 (3-1296)	150 (3-1296)
≤ 200 cells/μL, %	75	53	64
No. of prior ARV agents, median (range)	9 (2-24)	13 (3-25)	11 (2-25)
No. of fully active agents in OBR, %			
0	17	17	17
1	39	36	38
≥ 2	44	47	46
Known resistance to ≥ 2 drugs in class, %			
NRTI	97	100	99
NNRTI	94	100	97
PI	78	83	81
INSTI	75	64	69
4-class resistance %	47	44	46

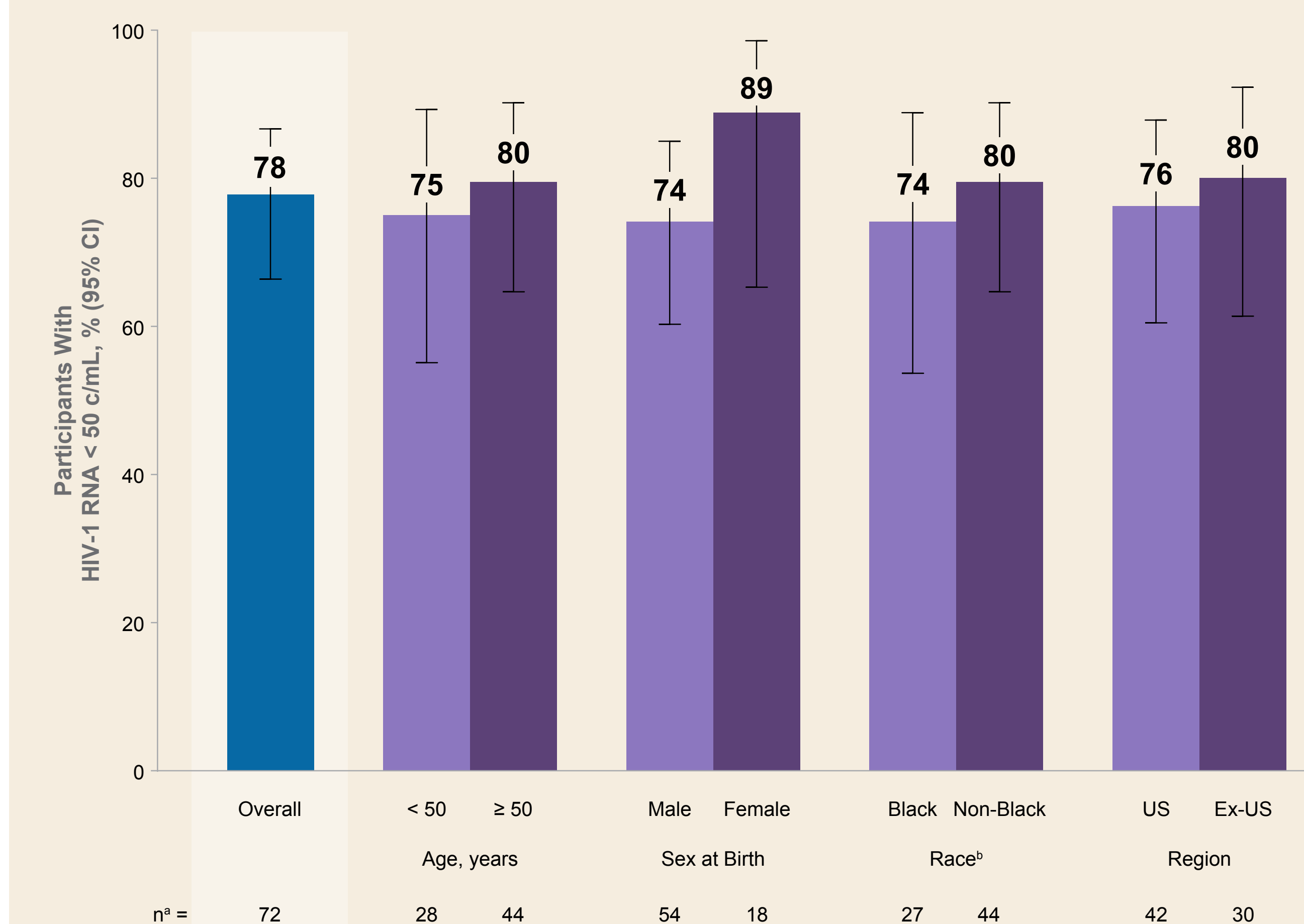
*Local regulators did not allow collection of race or ethnicity information for 1 participant.

Composition of Failing Regimen and OBR

Class/agent	Total: N = 72	
	Failing Regimen	OBR
NRTI	82%	85%
INSTI	68%	65%
PI	63%	63%
NNRTI	31%	33%
IMAB (CD4-directed postattachment inhibitor)	18%	24%
Maraviroc (CCR5 entry inhibitor)	14%	14%
FTR (attachment inhibitor)	6%	11%
Enfuvirtide (fusion inhibitor)	6%	7%
No. of fully active ARVs		
0	42%	17%
1	36%	38%
≥ 2	22%	46%
OSS, median*	1	2

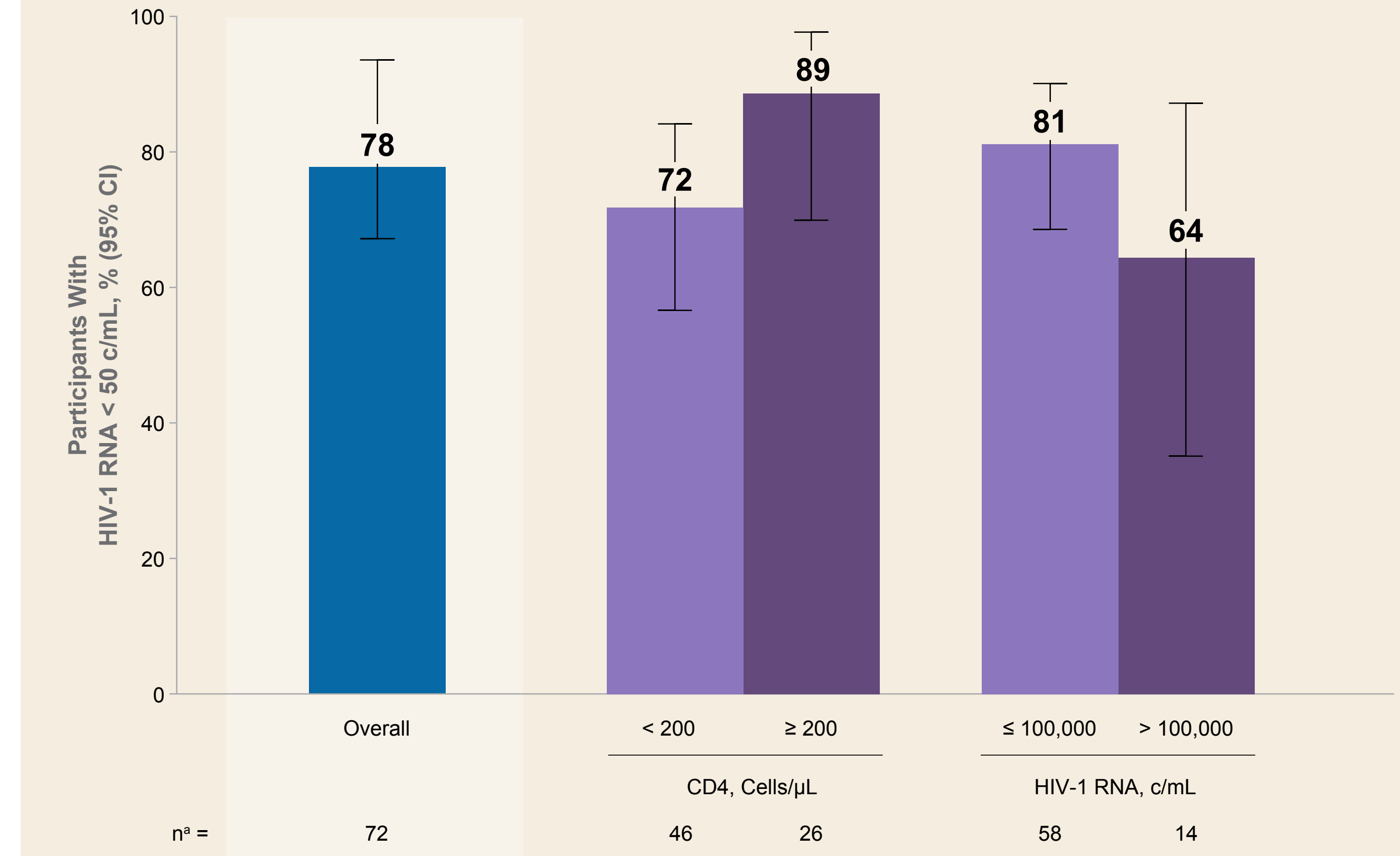
*Overall susceptibility scores (OSS; 1, 0.5, or 0 for full, partial, or no susceptibility, respectively) were determined based on proprietary algorithm (Monogram Biosciences Inc., South San Francisco, CA), for historical resistance reports, scores were derived from data provided by investigators. OSS of OBR was sum of individual scores. CCR5 = C-C chemokine receptor type-5; FTR = fostemsavir; IMAB = ibalizumab.

Week 52 Efficacy by Demographics



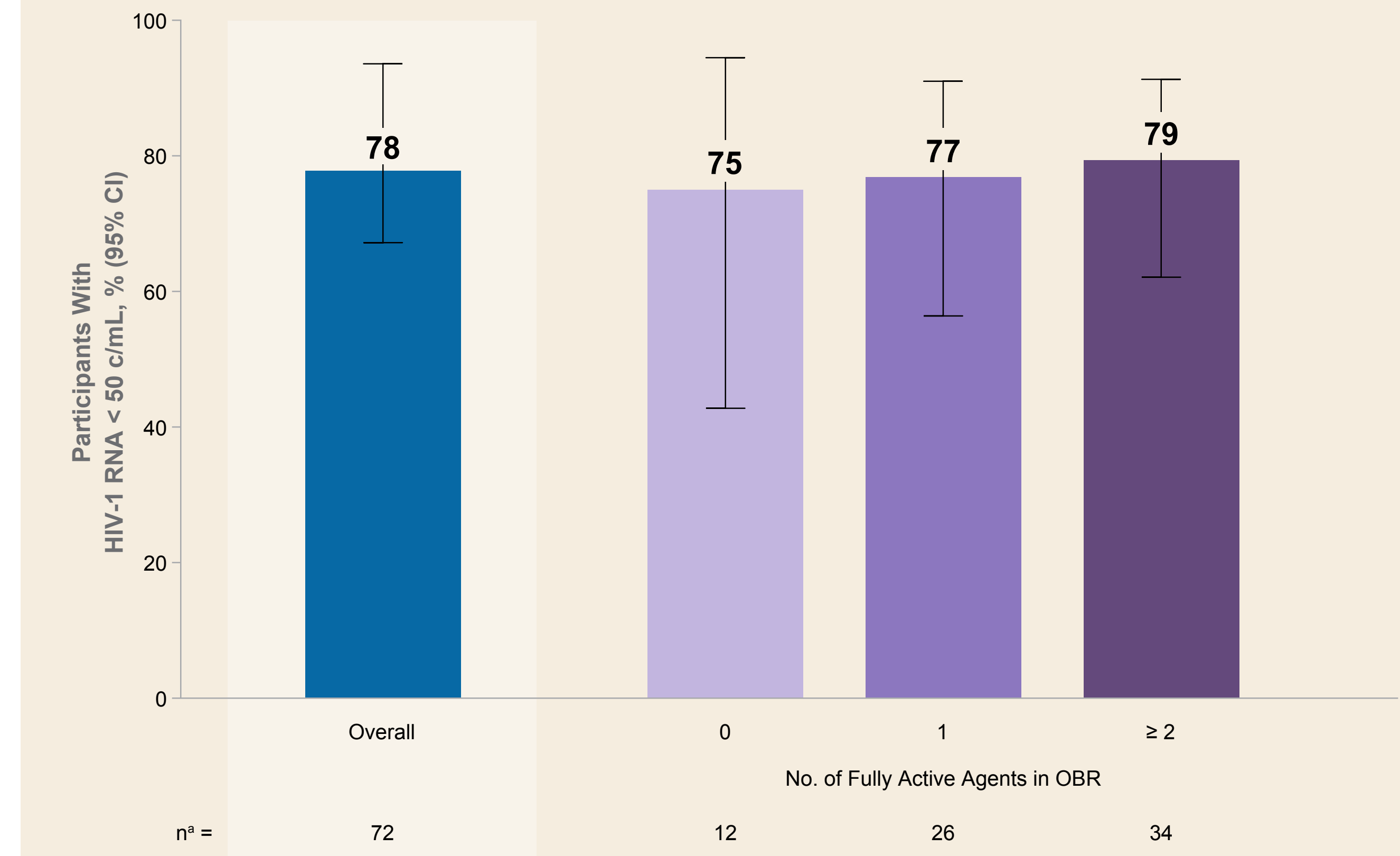
Prespecified subgroup analyses of efficacy at Week 52; post-hoc analyses indicated no significant differences between groups (P > 0.05). *Total n in each subgroup; †1 participant with race reported as 'not permitted.' CI = confidence interval.

Week 52 Efficacy by Baseline CD4 and HIV-1 RNA



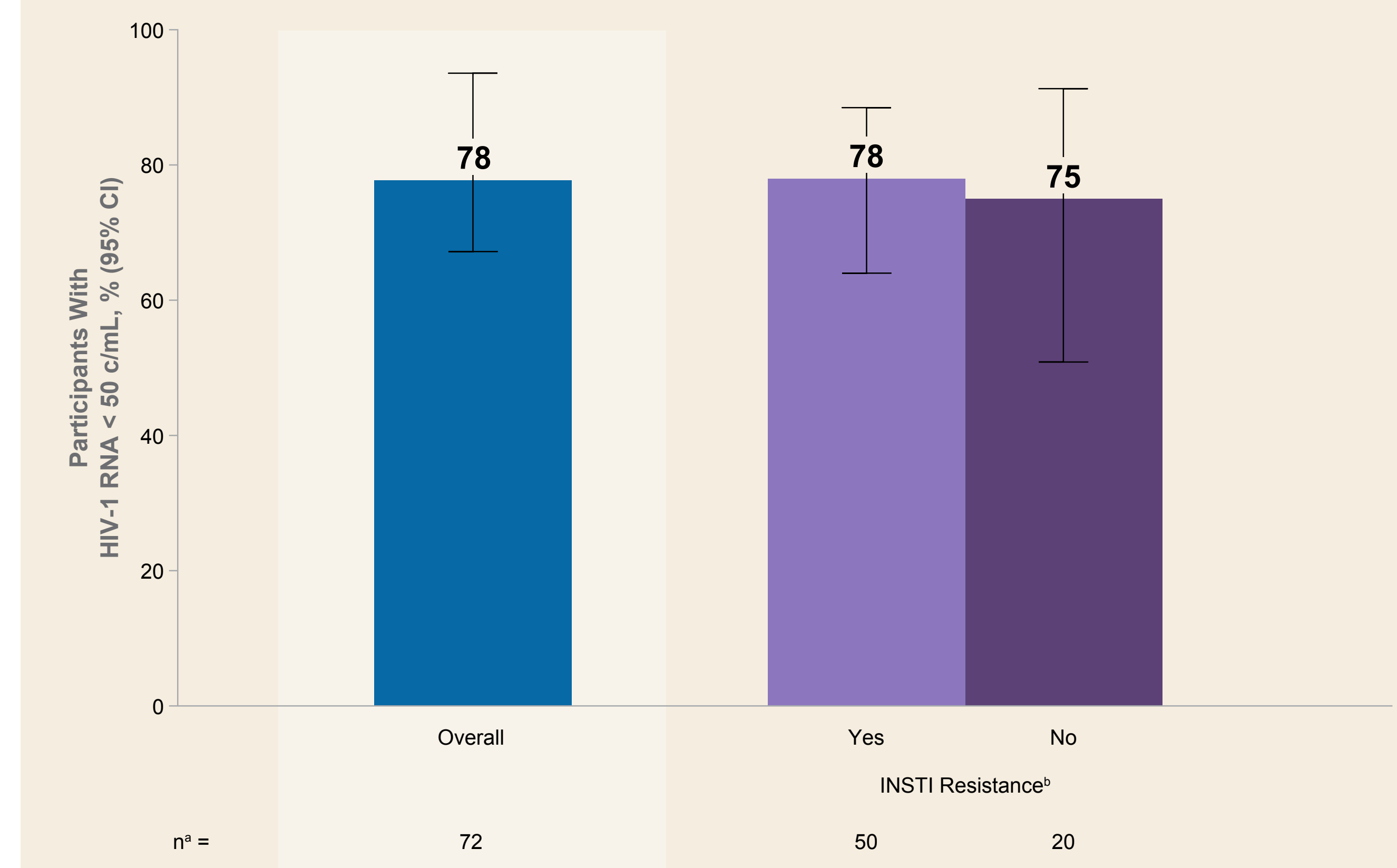
Prespecified subgroup analyses of efficacy at Week 52; in post-hoc analysis, differences between CD4 < and ≥ 200 cells/μL (P = 0.07), and between HIV-1 RNA ≤ and > 100,000 c/mL (P = 0.11) were not statistically significant. *Total n in each subgroup.

Week 52 Efficacy by Number of Fully Active Agents in OBR



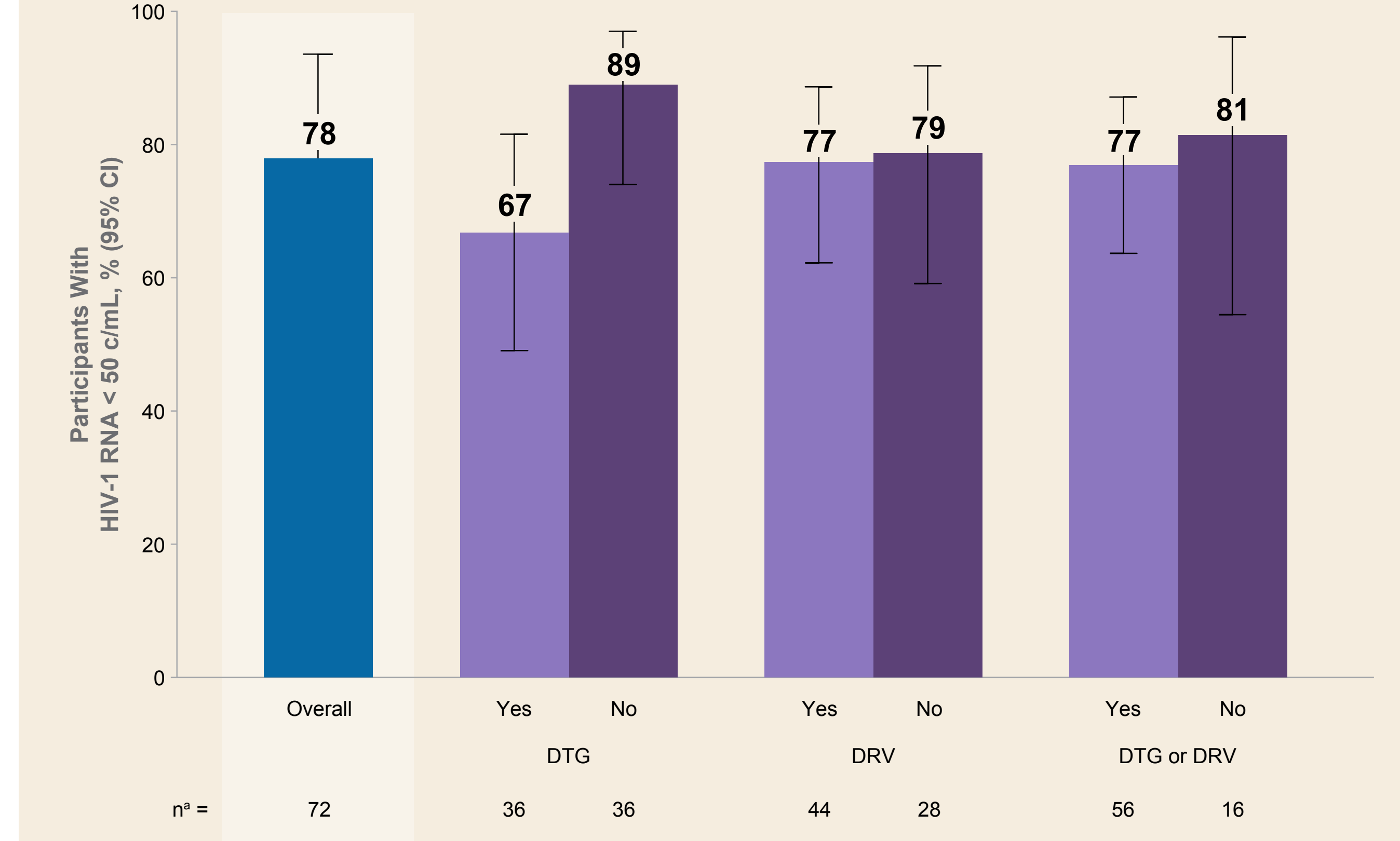
Post hoc subgroup analyses of efficacy at Week 52; post hoc analyses indicated no significant differences between groups (P > 0.05). *Total n in each subgroup.

Week 52 Efficacy by Baseline INSTI Resistance



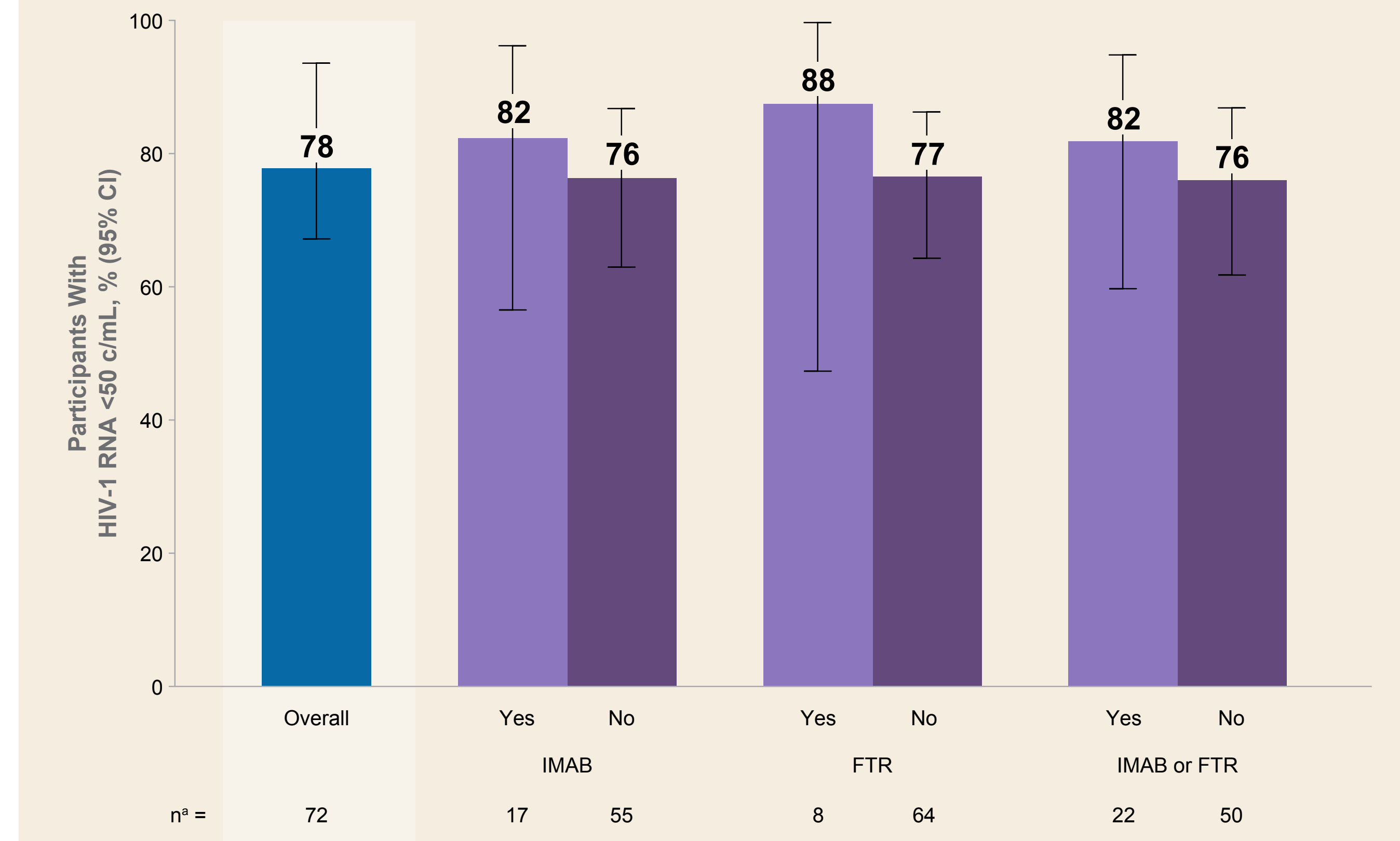
Prespecified subgroup analyses of efficacy at Week 52; includes all participants with and without INSTI agents in OBR; post-hoc analyses indicated no significant differences between groups (P > 0.05). *Total n in each subgroup; †Included phenotypic and genotypic resistance to dolutegravir, cabotegravir, dolutegravir (DTG), elvitegravir, and raltegravir; 2 participants had missing baseline INSTI resistance data.

Week 52 Efficacy by Baseline Use of Dolutegravir or Darunavir



Post hoc subgroup analyses. *Total n in each subgroup. DRV = darunavir.

Week 52 Efficacy by Baseline Use of Ibalizumab or Fostemsavir



Prespecified subgroup analyses of efficacy at Week 52; post-hoc analyses indicated no significant differences between groups (P > 0.05). *Total n in each subgroup.

Conclusions

- In people with MDR HIV-1 and limited treatment options, LEN in combination with an OBR led to high rates of virologic suppression at Week 52 overall
- The efficacy of LEN in combination with an OBR was consistent across diverse demographics, baseline characteristics, and OBR
- LEN is an important option for people with MDR HIV-1 and limited treatment options
- These data support the ongoing evaluation of LEN for treatment and prevention of HIV

References: 1. Link JO, et al. Nature 2020;584:614-8. 2. Zila V, et al. Cell 2021;184:1032-46.e18. 3. Sunlenca [package insert]. Foster City, CA: Gilead Sciences, Inc; 2022. 4. Sunlenca [product monograph]. Mississauga, ON: Gilead Sciences Canada, Inc; 2022. 5. Sunlenca [summary of product characteristics]. Carrigrohilly, Ireland: Gilead Sciences Ireland UC; 2022. 6. Margot N, et al. CROI 2020, poster 529. 7. Margot N, et al. CROI 2022, poster 508. 8. VanderWeert L, et al. CROI 2021, oral 01781. 9. Yant SR, et al. CROI 2019, poster 490. 10. VanderWeert L, et al. IDWeek 2021, oral 73. 11. Segal-Maurer S, et al. N Engl J Med 2022;386:1750-1803. Acknowledgments: We extend our thanks to the study participants and their families, and the participating study investigators and staff: Canada: J Brunetta, B Trotter, Dominican Republic: E Koenig, France: J-M Molina, S Ronot-Briegleb, Y Yazdangar, Germany: H-J Stelbrink, Italy: A Arlinori, A Castagna, F Castelli, Japan: T Shirasaka, Y Yokomaku, South Africa: M Rassoul, Spain: J Malloa, Taiwan: C-C Hung, Thailand: A Avihingsanon, P Chetchotsakd, K Siripassorn, W Ratanasawan, USA: DS Berger, M Berhe, C Brinson, CM Cretons, GE Crofoot, E DeJesus, D Hagins, T Hodge, K Lichtenstein, JP McGowan, O Ogbuagu, O Osiyemi, GJ Richmond, MN Rangopoul, PJ Ruane, W Sanchez, S Segal-Maurer, J Sims, GJ Sinclair, DA Wheeler, A Wozna, K Workowski, C Zurawski. This study was funded by Gilead Sciences, Inc. Editing and production assistance were provided by BioScience Communications, New York, NY, funded by Gilead. Disclosures: O Ogbuagu: consulting fees from Gilead, Janssen, VIV, speaking honoraria from Gilead, Janssen, MSD, Theratechnologies, VIV, E DeJesus: grants and personal, advisory board and speakers bureau fees from Gilead, advisory board fees from Janssen, Theratechnologies, VIV, A Avihingsanon: support from Gilead, VIV, C Zurawski: advisory board and speaker fees from Gilead, O Osiyemi: consultancy fees from Gilead, MSD, VIV, stockholder of Gilead, GSK, Pfizer, T Hodge: funding from Gilead, Janssen, VIV, GE Crofoot: support from Gilead, H Wang, H Dvory-Sobol, MS Rhee, J Baeten: employees and shareholders of Gilead, J-M Molina: grant from Gilead, advisory board fees from Gilead, MSD, VIV.