

Efficacy and Safety of a Twice-Yearly Regimen of Lenacapavir, Teropavimab, and Zinlirvimab: Phase 2 Week 52 Results

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Disclosures

Onyema Ogbuagu has served as an advisor/consultant to Gilead Sciences, Inc. and ViiV, and has received honoraria from Gilead Sciences, Inc.

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Joseph Eron has received grants/contract payment made to their institution from Gilead Sciences, Inc., has served as an advisor/consultant to Gilead Sciences, Inc., ViiV, Merck, and AbbVie, and has participated in Data Safety Monitoring Boards and Advisory Boards for Invivyd and Taimed.

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Background

- Antiretroviral therapy (ART) with less frequent dosing may offer advantages over daily oral options for some people with HIV-1, such as improved adherence and reduced pill burden¹
- Lenacapavir (LEN), the first-in-class HIV-1 capsid inhibitor, is approved for the treatment of multidrug-resistant HIV-1 in the EU, UK, US, Canada, and other countries, and can be administered subcutaneously twice yearly^{2–5}
- Teropavimab (TAB; 3BNC117-LS) and zinlirvimab (ZAB; 10-1074-LS), broadly neutralising antibodies (bNAbs) that target the HIV envelope, can also be dosed twice yearly⁶
 - TAB targets the CD4-binding site of gp120 while ZAB targets the V3 glycan on the HIV-1 envelope
- In this Phase 2 study (NCT05729568) of the combination of LEN, TAB, and ZAB, 96% of participants maintained virologic suppression at Week 26⁷

Objective: To evaluate the 1-year efficacy and safety of switching to twice-yearly LEN, TAB, and ZAB versus continuing stable baseline daily oral ART

1. Claborn KR, et al. *Psychol Health Med* 2015; 20(3): 255-65. 2. Sunlenca® UK Prescribing Information, available at <https://www.medicines.org.uk/emc/files/pil.14102.pdf> [Accessed October 2025]. 3. Sunlenca® EU Summary of Product Characteristics, available at https://www.ema.europa.eu/en/documents/product-information/sunlenca-epar-product-information_en.pdf [Accessed October 2025]. 4. Sunlenca® US Prescribing Information, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215973s000lbl.pdf [Accessed October 2025]. 5. Sunlenca® Canada Product Monograph, available at https://pdf.hres.ca/dpd_pm/00081120.PDF [Accessed October 2025].

6. Gautam R, et al. *Nat Med*. 2018;24:610–6. 7. Ogbuagu O, et al. CROI 2025. Presentation #151.

ART, antiretroviral therapy; bNAbs, broadly neutralising antibody; LEN, lenacapavir; TAB, teropavimab; ZAB, zinlirvimab.

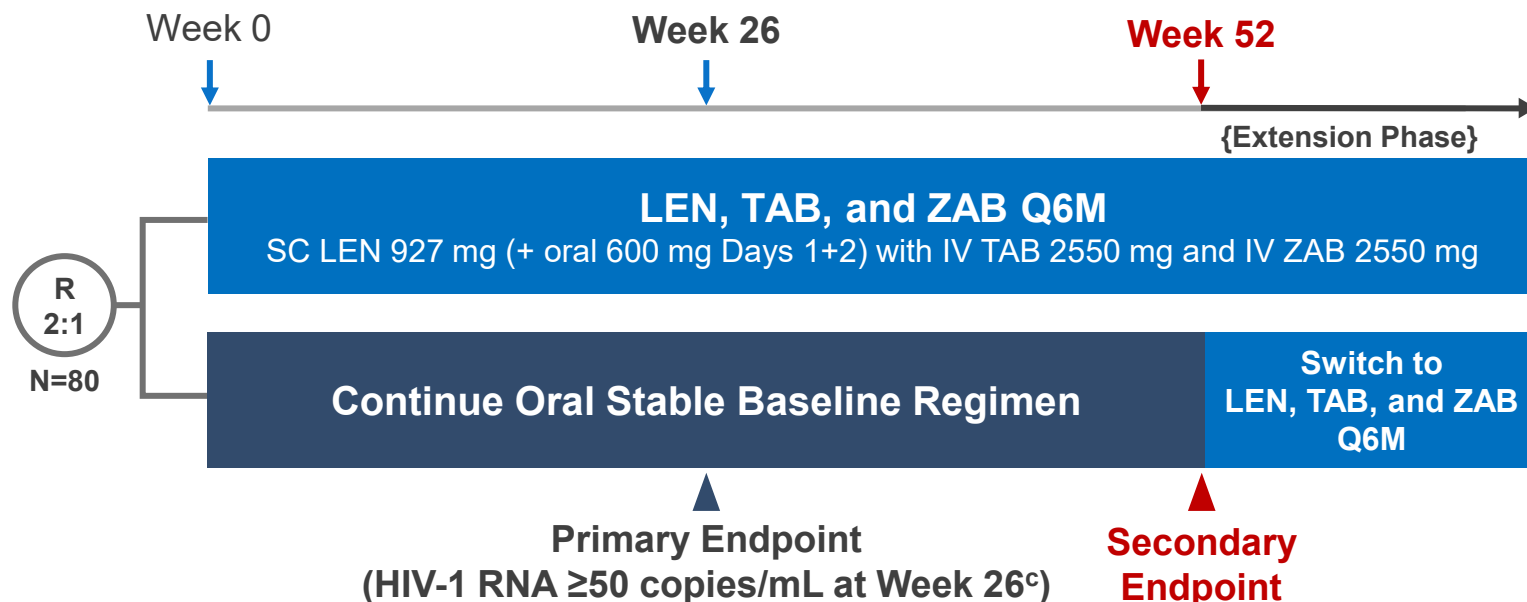
Phase 2 Study Design

— Randomised, open-label, active-controlled, multicenter study^a



Key inclusion criteria

- Age 18–65 years
- HIV-1 RNA <50 copies/mL for ≥12 months
- On stable oral ART (≤2 classes) for ≥12 months
- CD4+ T-cell count ≥200 cells/μL
- HBV negative
- Highly susceptible to **both** bNAbs (IC₉₀ ≤2 μg/mL)^b



Week 52 Secondary Outcomes:

- HIV-1 RNA <50 copies/mL and ≥50 copies/mL per FDA Snapshot algorithm
- Change from baseline in CD4+ T-cell count; safety (adverse events); pharmacokinetics of LEN, TAB, and ZAB; anti-drug antibodies (ADAs)

^aNCT05729568. ^bBy PhenoSense® mAb Assay (Monogram Biosciences).

ADA, anti-drug antibody; **ART**, antiretroviral therapy; **bNAb**, broadly neutralising antibody; **HBV**, hepatitis B virus; **IC₉₀**, 90% inhibitory concentration; **IV**, intravenous; **LEN**, lenacapavir; **Q6M**, every 6 months; **R**, randomised; **SC**, subcutaneous; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Participant Disposition and bNAb Susceptibility

Screened (N=241)
Randomized and dosed (N=80)^a

LEN, TAB, and ZAB
Dosing Period 1: D1 to W26
n=53

**Continue Oral Stable
Baseline Regimen**
n=27

Discontinued study treatment prior to W26
• n=1; Relocated (moved cities)
Discontinued study treatment at W26
• n=2; Participant decision
• n=1; Lack of efficacy

Discontinued study treatment
• n=1; Adverse event
(metastatic pancreatic carcinoma)

Dosing Period 2: W26 to W52
n=49

Completed Study Treatment to W26
n=26

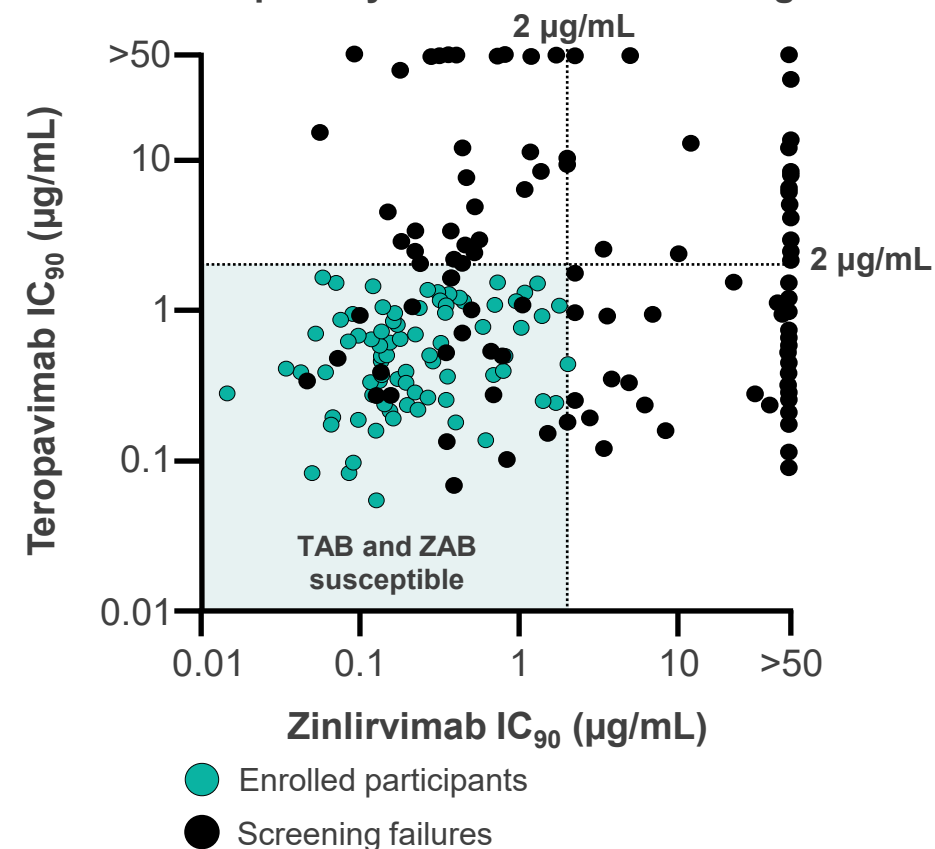
Completed Study Treatment to W52
n=49

Completed Study Treatment to W52
n=25

Discontinued study treatment
• n=1; Participant decision

Successful susceptibility assay (n=200)
(41/241 with assay failure)
Susceptible to TAB and ZAB (n=99)^b

Susceptibility to bNAbs at Screening



^a84 participants met all eligibility criteria; 1 eligible but not randomized (participant decision); 3 randomized but not dosed (participant decision). ^bTAB only: 47 (24%); ZAB only: 31 (16%); neither: 23 (12%).
bNAb, broadly neutralising antibody; D, day; IC₉₀, 90% inhibitory concentration; LEN, lenacapavir; TAB, teropavimab; W, week; ZAB, zinlirvimab.

Baseline Characteristics

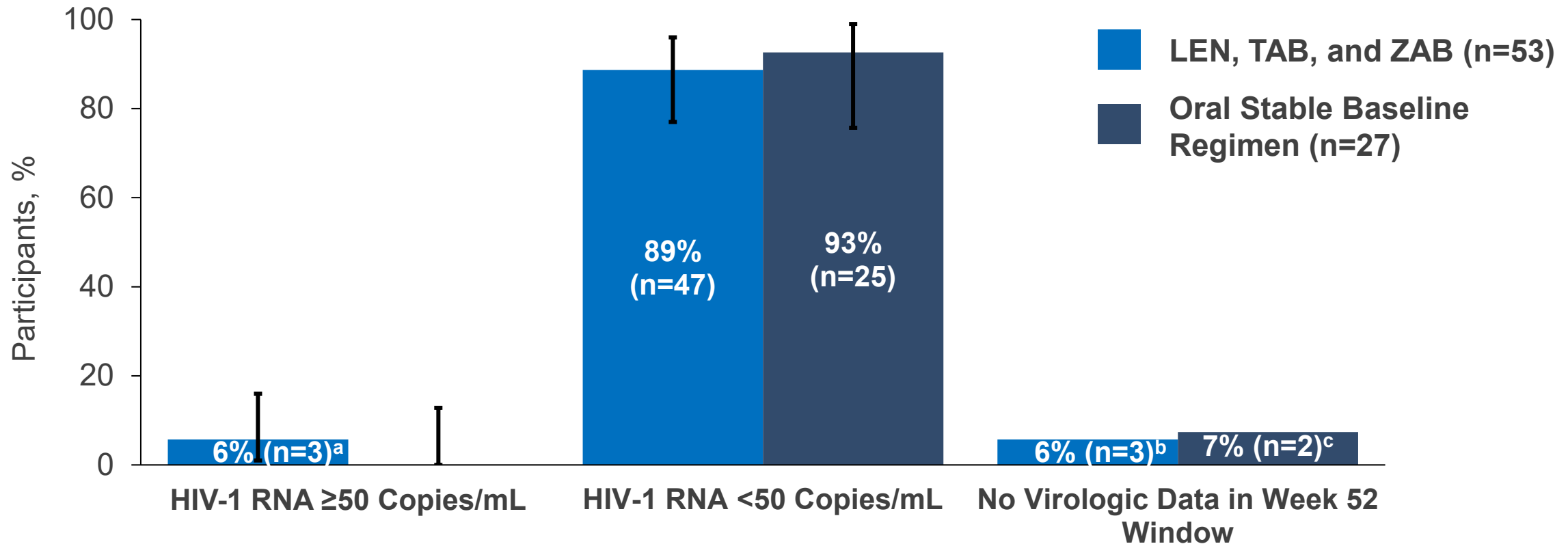
	LEN, TAB, and ZAB n=53	Oral Stable Baseline Regimen n=27
Median (range) age, years	46 (20–65)	57 (28–65)
Female sex at birth, n (%)	8 (15)	4 (15)
Race, n (%)		
Asian	1 (2)	1 (4)
Black	21 (40)	8 (30)
White	28 (53)	16 (59)
Other	3 (6)	2 (7)
Hispanic or Latine ethnicity, n (%)	13 (25)	7 (26)
Median (range) weight, kg	93 (56–156)	87 (58–157)
Median (range) BMI, kg/m ²	29.2 (20.4–48.9)	29.2 (19.1–51.4)
BMI ≥30 kg/m ² , n (%)	23 (43)	9 (33)
Median (IQR) CD4+ T-cell count, cells/μL	710 (552–895)	738 (583–869)
Median (IQR) duration of all prior ARVs (years) ^a	12.2 (7.5–16.5)	16.4 (10.4–23.4)
Baseline ARV containing INSTI + NRTI(s), n (%)	42 (79)	23 (85)
USA region, ^b n (%)	48 (91)	19 (70)

^aThese durations are estimates based on self-reported data.

^bEx-USA regions include Australia, Canada, and Puerto Rico. Participants were enrolled across 34 sites.

ARV, antiretroviral; **BMI**, body mass index; **INSTI**, integrase strand transfer inhibitor; **IQR**, interquartile range; **LEN**, lenacapavir; **NRTI**, nucleoside reverse transcriptase inhibitor; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Week 52 Virologic Outcomes (FDA Snapshot Algorithm)



— Median (IQR) CD4+ T-cell count increased from baseline at Week 52:

- +32 (–43 to 119) cells/μl in the LEN, TAB, and ZAB group
- +38 (–30 to 146) cells/μl in the oral stable baseline regimen group

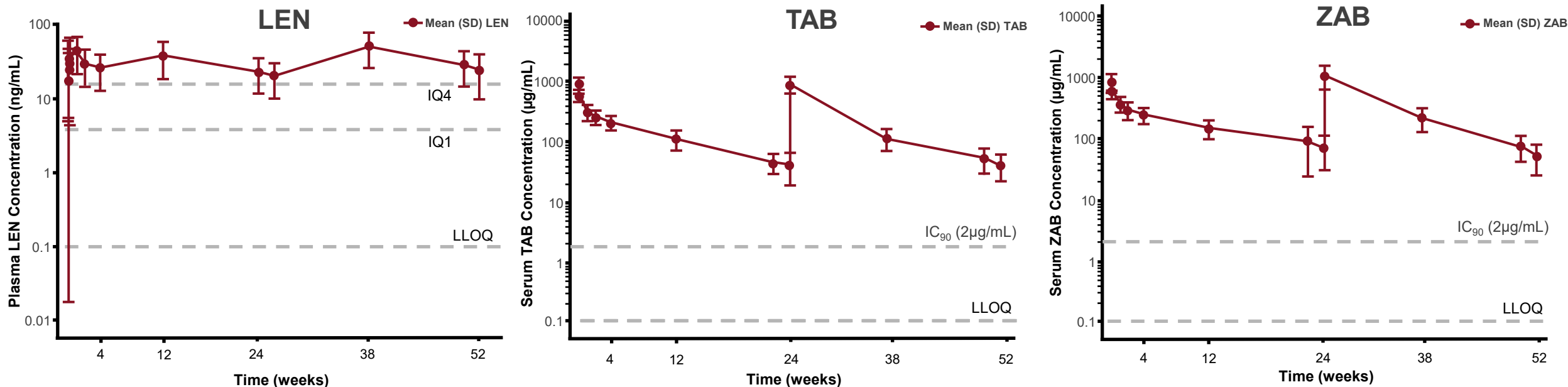
^an=2 with HIV-1 RNA ≥50 copies/mL in W52 window, n=1 with HIV-1 RNA ≥50 copies/mL discontinued study drug due to lack of efficacy at W26. All 3 participants restarted standard first-line oral ART (B/F/TAF) and resuppressed in follow-up. ^bn=2 discontinued study drug due to participant decision and n=1 discontinued study drug due to relocation, all with last HIV-1 RNA <50 copies/mL.

^cn=1 discontinued study drug due to participant decision and n=1 discontinued study drug due to adverse event, both with last HIV-1 RNA <50 copies/mL.

ART, antiretroviral therapy; **IQR**, interquartile range; **LEN**, lenacapavir; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Pharmacokinetics and Anti-Drug Antibodies

— Mean concentrations of LEN, TAB, and ZAB were maintained through Week 52



- Treatment-emergent ADAs against: TAB, n=6 (11%); ZAB, n=9 (17%)
- PK profiles of participants with and without ADAs were similar
- ADAs were not associated with adverse events or virologic rebound
- Further PK and ADA data will be presented at IDWeek 2025 (Poster P-1248)

Safety Overview (Excluding ISRs related to SC LEN)

Participants, n (%)	LEN, TAB, and ZAB n=53	Oral Stable Baseline Regimen n=27
AEs	40 (76) ^a	21 (78)
Grade ≥3	4 (8) ^b	2 (7)
Treatment-related AEs	5 (9) ^c	0
Grade ≥3	0	0
Serious AEs	1 (2) ^d	1 (4) ^e
AEs leading to study drug discontinuation	0	1 (4) ^e
AEs in ≥5% of participants^f		
Diarrhea	7 (13)	1 (4)
Upper respiratory tract infection	5 (9)	0
COVID-19	3 (6)	2 (7)
Viral upper respiratory tract infection	3 (6)	1 (4)
Sinusitis	3 (6)	1 (4)
Constipation	3 (6)	0
Nausea	3 (6)	1 (4)
Hemorrhoids	3 (6)	1 (4)
Cough	3 (6)	0

Safety data through the Week 52 data cut (up to last participant Week 52 visit) were included. ^a47 participants (89%) including ISRs. ^bPerineal abscess, acute pyelonephritis, scrotal abscess, ureteritis, abnormal weight loss, glycosuria, and nephrolithiasis in four participants. ^cLacrimation increased, nausea, device dislocation, abnormal dreams, and insomnia. 37 participants (70%) including ISRs.

^dPerineal abscess and scrotal abscess in one participant. ^eMetastatic pancreatic carcinoma in one participant. ^f≥5% of participants in either group, excluding ISRs.

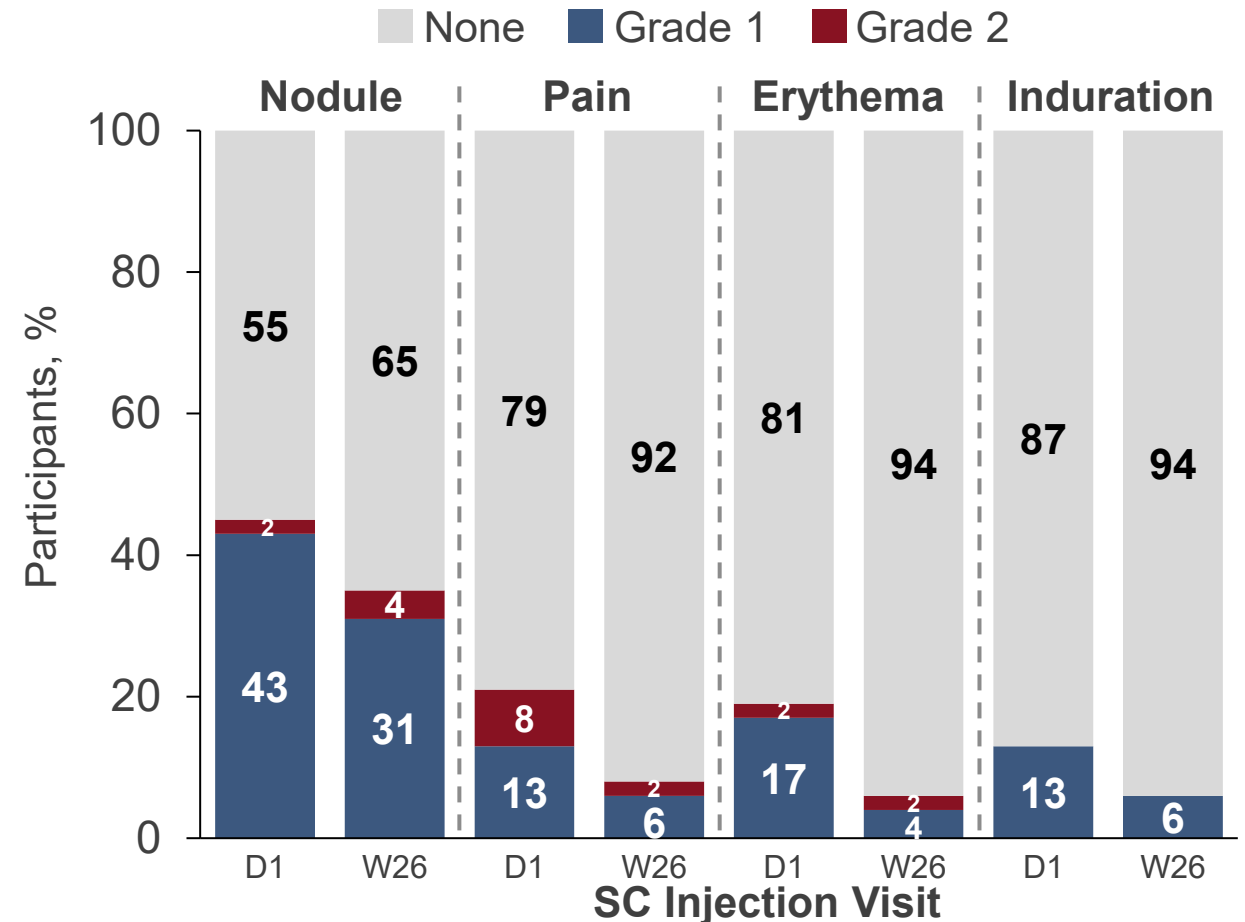
AE, adverse event; **ISR**, injection site reaction; **LEN**, lenacapavir; **SC**, subcutaneous; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Injection Site Reactions and Infusion-Related Reactions

- The most common AEs were Grade 1 or Grade 2 ISRs related to SC LEN in 36 (68%) participants^a
 - Grade 1: 30 (57%) participants
 - Grade 2: 6 (11%) participants
- No participants discontinued due to ISRs

There were no infusion-related reactions to TAB or ZAB

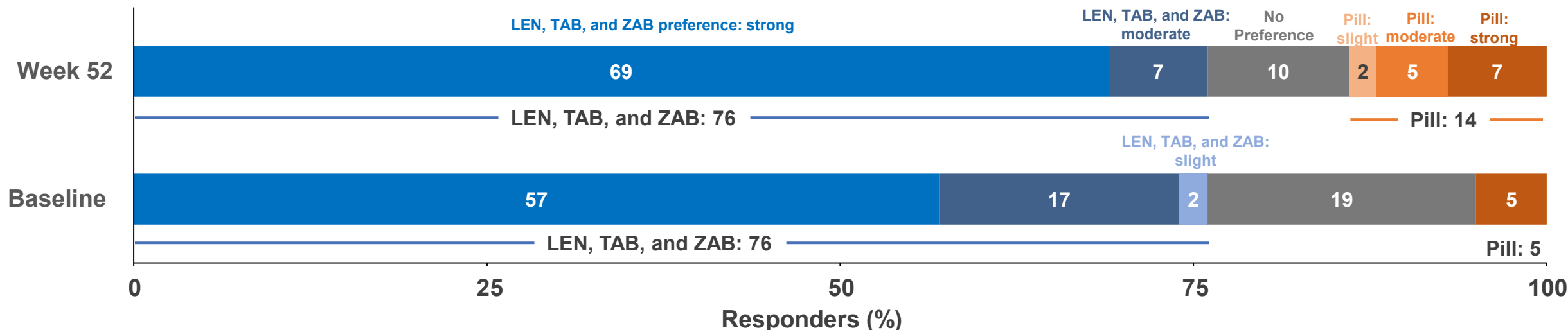
Injection Site Reactions Related to SC LEN Occurring in ≥10% of Participants Receiving LEN, TAB, and ZAB^b



^aParticipants who received one or both SC injections at Day 1 or Week 26. ^bIn total, 53 and 49 participants received SC LEN injection at D1 and W26, respectively. AE, adverse event; D, day; ISR, injection site reaction; LEN, lenacapavir; SC, subcutaneous; TAB, teropavimab; W, week; ZAB, zinlirvimab.

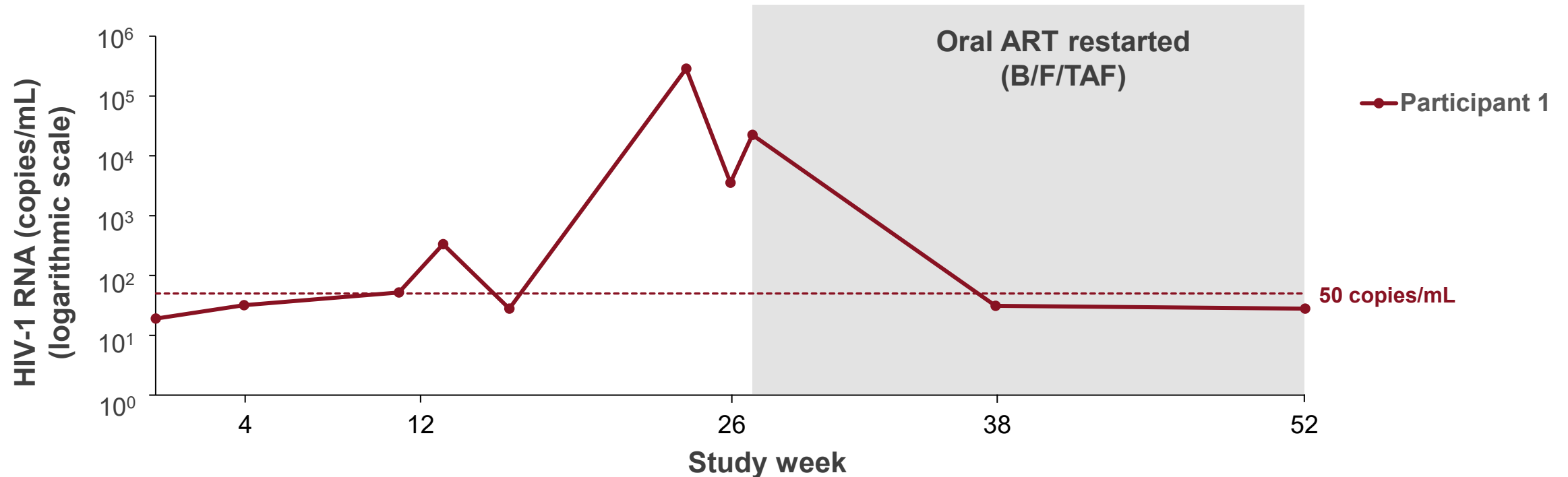
Patient-Reported Outcomes

HIV Treatment Preference Questionnaire (HIVTPQ) (Twice-Yearly LEN, TAB, and ZAB vs Daily Oral Pill)



- Overall, 42/53 participants completed the HIVTPQ at baseline, Week 26, and Week 52
- At Week 52, 32/42 (76%) participants **preferred LEN, TAB, and ZAB** (strong, n=29; moderate, n=3) over daily oral ART
- At Week 52, 38/42 (90%) participants indicated **twice-yearly LEN, TAB, and ZAB would be easier to adhere to** compared to daily oral ART

Participants with Virologic Rebound: Participant 1



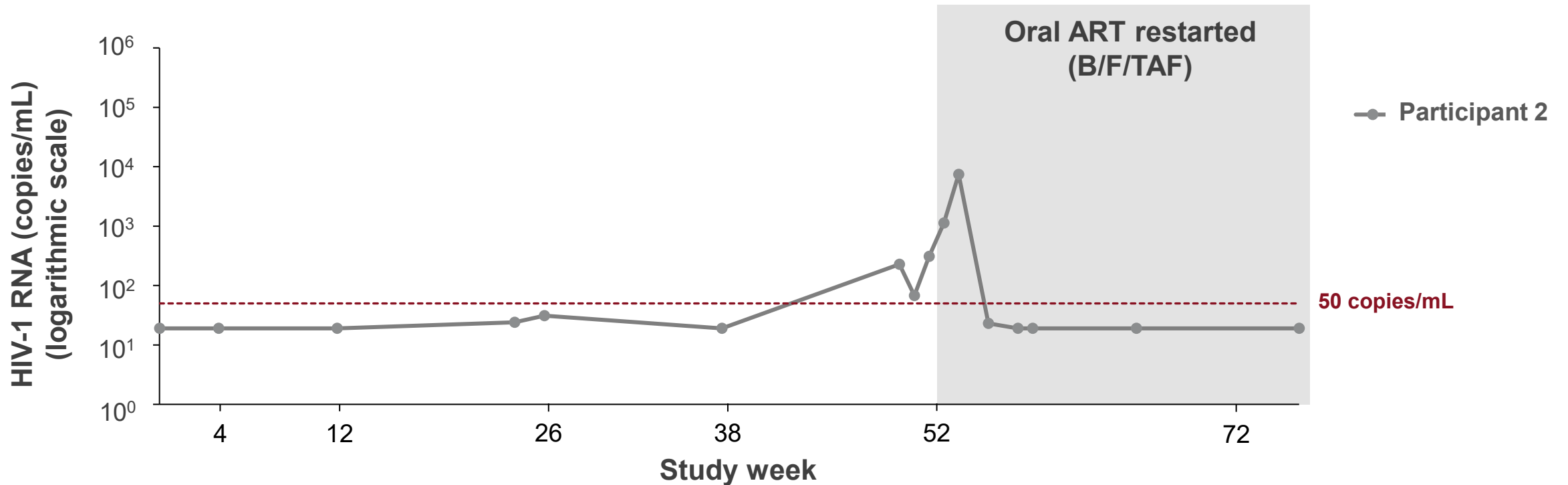
- Week 12: Upper respiratory tract infection and steroid usage
- Week 24: Developed resistance to LEN and lost susceptibility to ZAB^a
- No ADAs to TAB or ZAB

Confirmed virologic rebound: HIV-1 RNA ≥ 50 copies/mL, confirmed at the following visit. Week 12 virologic rebound was confirmed in the setting of viral upper respiratory tract infection (Weeks 11–14) and steroid usage (methylprednisolone Weeks 12–13). Virologic failure was confirmed at Week 24 following Grade 1 sinusitis at Weeks 19–20 (treated with Amox-Clav).

1. Ogbuagu O, et al. CROI 2025. Presentation #151. ^aDeveloped resistance to LEN (Q67H in capsid) and lost susceptibility to ZAB ($IC_{50} > 50$ μ g/mL).

ADA, anti-drug antibody; ART, antiretroviral therapy; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; LEN, lenacapavir; TAB, teropavimab; ZAB, zinlirvimab.

Participants with Virologic Rebound: Participant 2

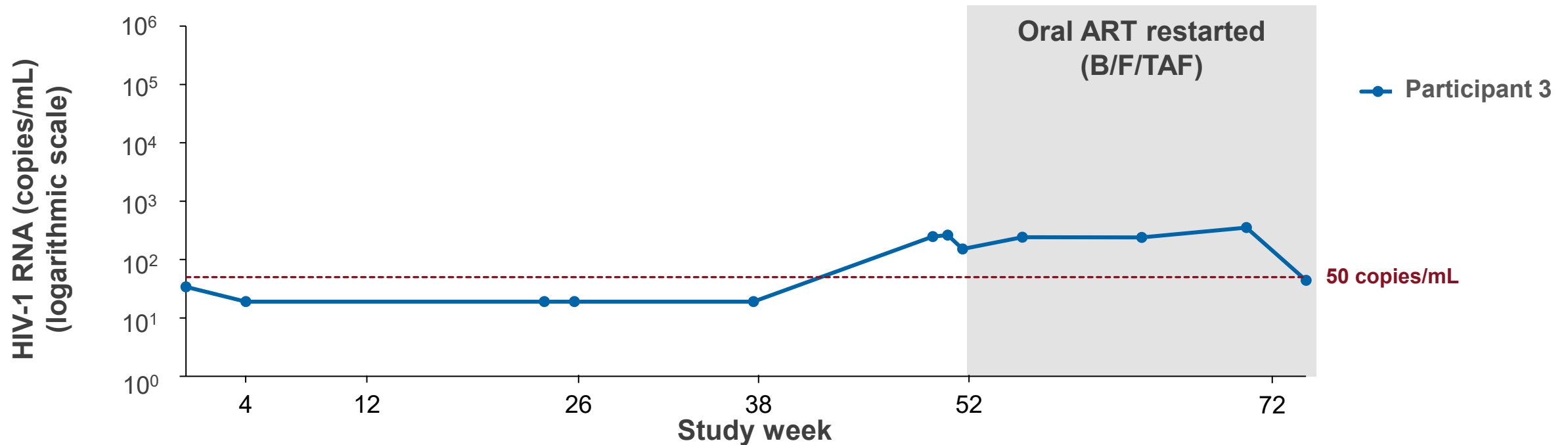


- Week 50: Lost susceptibility to ZAB (genotype only)
- No ADAs to TAB or ZAB

Confirmed virologic rebound: HIV-1 RNA ≥ 50 copies/mL, confirmed at the following visit.

ADA, antidrug antibody; **ART**, antiretroviral therapy; **B/F/TAF**, bictegravir/emtricitabine/tenofovir alafenamide; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Participants with Virologic Rebound: Participant 3



- Low level viremia persisted post-ART restart, with peak viral load at Week 71 (353 copies/mL)
- No resistance detected
- First ADAs to TAB detected at Week 26 and persistent at Weeks 38 and 52; ADAs to ZAB first detected at Week 12 and persistent to Week 26
 - ADAs did not impact PK

Confirmed virologic rebound: HIV-1 RNA ≥ 50 copies/mL, confirmed at the following visit.

ADA, antidrug antibody; **ART**, antiretroviral therapy; **B/F/TAF**, bictegravir/emtricitabine/tenofovir alafenamide; **PK**, pharmacokinetics; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Assessment of Confirmed Virologic Rebound in 3 Participants

- All three participants were male, had HIV-1 subtype B, and had confirmed virologic rebound late in the dosing interval

	Participant 1	Participant 2	Participant 3
Baseline BMI, kg/m²	30.8	38.3	36.3
Baseline weight, kg	109	143	118
Time of rebound	Week 24	Week 50	Week 50
LEN C_{trough}	4 th percentile	13 th percentile	66 th percentile
TAB C_{trough}	25 th percentile	18 th percentile	12 th percentile
ZAB C_{trough}	37 th percentile	18 th percentile	6 th percentile
Baseline susceptibility TAB IC₉₀, µg/mL	1.53	0.08	0.36
Baseline susceptibility ZAB IC₉₀, µg/mL	0.72	0.09	0.17

- All three virologic rebound participants weighed >100kg, with lower bNAbs exposures
- Weight is a clinically significant covariate that affects antibody exposure
- Data are not sufficient to establish a statistical association between TAB and ZAB exposures and risk of virologic rebound

All eligible study participants were highly susceptible to both bNAbs (IC₉₀ ≤2 µg/mL) at study start.

BMI, body mass index; **bNAbs**, broadly neutralising antibody; **C_{trough}**, trough concentration; **IC₉₀**, 90% inhibitory concentration; **LEN**, lenacapavir; **PK**, pharmacokinetics;

PopPK, population pharmacokinetic; **TAB**, teropavimab; **ZAB**, zinlirvimab.

Conclusions

- Overall, 89% of participants receiving LEN, TAB, and ZAB remained suppressed at Week 52 by FDA Snapshot algorithm
 - Efficacy of LEN, TAB, and ZAB was similar to standard-of-care daily oral ART
 - Three participants met confirmed virologic rebound criteria; two had emergent resistance (one each to LEN and ZAB) and one had low level viremia that persisted on oral therapy with no emergent resistance
 - All three participants resuppressed on oral therapy
 - The relationship between viral rebound and PK is being explored
- Through Week 52, LEN, TAB, and ZAB was well tolerated
- The majority of participants having experienced both modalities of treatment preferred LEN, TAB, and ZAB over daily oral ART through Week 52
- These data support further evaluation of LEN, TAB, and ZAB in Phase 3 studies
- This long-acting combination regimen has potential as the first complete twice-yearly combination treatment for people with HIV-1

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