Efficacy and Safety of Twice-Yearly Lenacapavir, Teropavimab, and Zinlirvimab as an HIV-1 Treatment for Up to 104 Weeks

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Summary

What was our main question?	What is the efficacy and safety of switching to twice-yearly lenacapavir (LEN) + teropavimab (TAB) + zinlirvimab (ZAB) after up to 104 weeks of treatment?
What did we find?	Twice-yearly LEN + TAB + ZAB maintained high rates of virologic suppression through 52 and 104 weeks of treatment and demonstrated a favorable safety profile
Why is this important?	These data support LEN + TAB + ZAB as the first potential complete twice-yearly combination treatment for people with HIV-1 (PWH)

LEN, lenacapavir; **PWH,** people with HIV-1; **TAB,** teropavimab; **ZAB,** zinlirvimab.

Background

- Antiretroviral therapy (ART) with longer dosing intervals may provide advantages over daily oral options for some PWH by minimizing pill burden and reducing barriers to adherence[1]
- LEN is an HIV-1 capsid inhibitor that can be administered subcutaneously twice yearly[2–5]
  - LEN is approved for the treatment of multidrug-resistant HIV-1 and for pre-exposure prophylaxis in many countries
- TAB[a] and ZAB[b] are broadly neutralizing antibodies (bNAbs) which can be dosed twice yearly[6]
  - TAB targets the CD4-binding site of gp120 and ZAB targets the V3 glycan on the HIV-1 envelope
- At Weeks 26 and 52 in a Phase 2 study (NCT05729568), switching to twice-yearly LEN + TAB + ZAB exhibited similar efficacy and safety to continuing an oral stable baseline regimen (SBR)[7,8]

Objective: To evaluate the Week 104 efficacy and safety of switching to twice-yearly LEN + TAB + ZAB

[a]3BNC117-LS. [b]10-1074-LS.

ART, antiretroviral therapy; **bNAb,** broadly neutralizing antibody; **LEN,** lenacapavir; **PWH**, people with HIV-1; **SBR**, stable baseline regimen; **TAB**, teropavimab; **ZAB,** zinlirvimab.

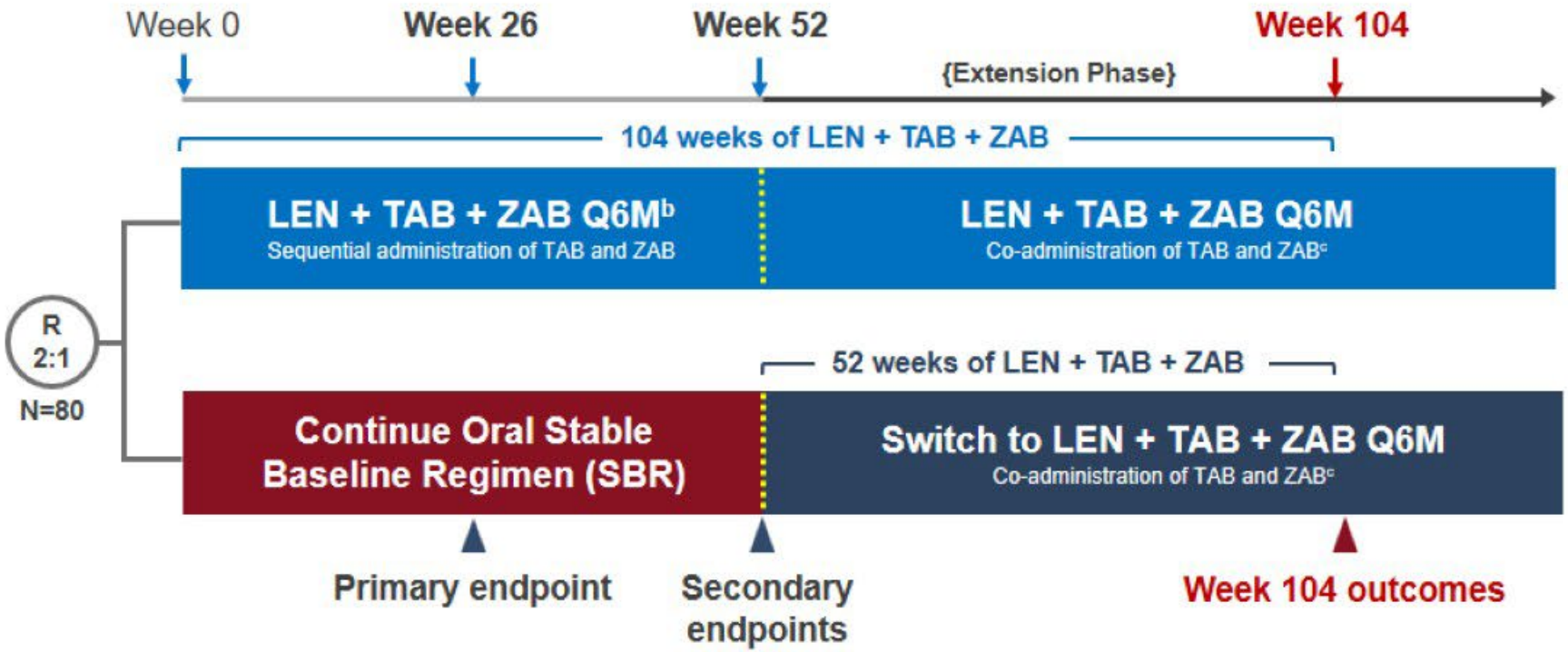
1. Claborn KR, et al. *Psychol Health Med* 2015; 20(3): 255–65. **2.** Sunlenca® EU Summary of Product Characteristics, available at https://www.ema.europa.eu/en/documents/product-information/sunlenca-epar-product-information_en.pdf [Accessed July 2026]. **3.** Sunlenca® US Prescribing Information, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215973s000lbl.pdf [Accessed July 2026]. **4.** Yeytuo EU Summary of Product Characteristics, available at https://www.ema.europa.eu/en/documents/product-information/yeytuo-epar-product-information_en.pdf [accessed July 2026]. **5.** Yeztugo® US Prescribing Information. Available at https://www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.pdf [Accessed July 2026]. **6.** Gautam R, et al. *Nat Med*. 2018;24:610–6. **7.** Ogbuagu O, et al. *Lancet Microbe* 2026;7(3):101283. **8.** Ogbuagu O, et al. EACS 2025. Presentation #PS09.2.

Phase 2 Study Design

— Randomized, open-label, active-controlled, multicenter study (NCT05729568)

Key inclusion criteria

- Age 18–65 years
- HIV-1 RNA <50 copies/mL for ≥12 months
- Highly susceptible to **both** bNAbs (IC_{90} ≤2 µg/mL)[a]



Week 104 Outcomes:

— HIV-1 RNA <50 copies/mL and ≥50 copies/mL by missing=excluded (M=E) analysis

— Change from baseline in CD4+ T-cell count; safety (adverse events); pharmacokinetics of LEN + TAB + ZAB; anti-drug antibodies (ADAs)

[a]By PhenoSense® mAb Assay (Monogram Biosciences). [b]Subcutaneous LEN 927 mg (+ oral 600 mg Days 1+2) with IV TAB 2550 mg and IV ZAB 2550 mg. [c]From Week 52, TAB and ZAB could be co-administered; prior to Week 52, TAB and ZAB were sequentially administered.
ADA, anti-drug antibody; **bNAb,** broadly neutralizing antibody; **IC_{90},** 90% inhibitory concentration; **IV,** intravenous; **LEN,** lenacapavir; **M**=E, missing=excluded; **Q6M,** every 6 months; **R,** randomized; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

Screening bNAb Susceptibility

— The screening population included participants from both the SBR and LEN + TAB + ZAB groups

Screened (N=241)

- *Assay failure (n=41)*

Susceptibility results available (n=200)

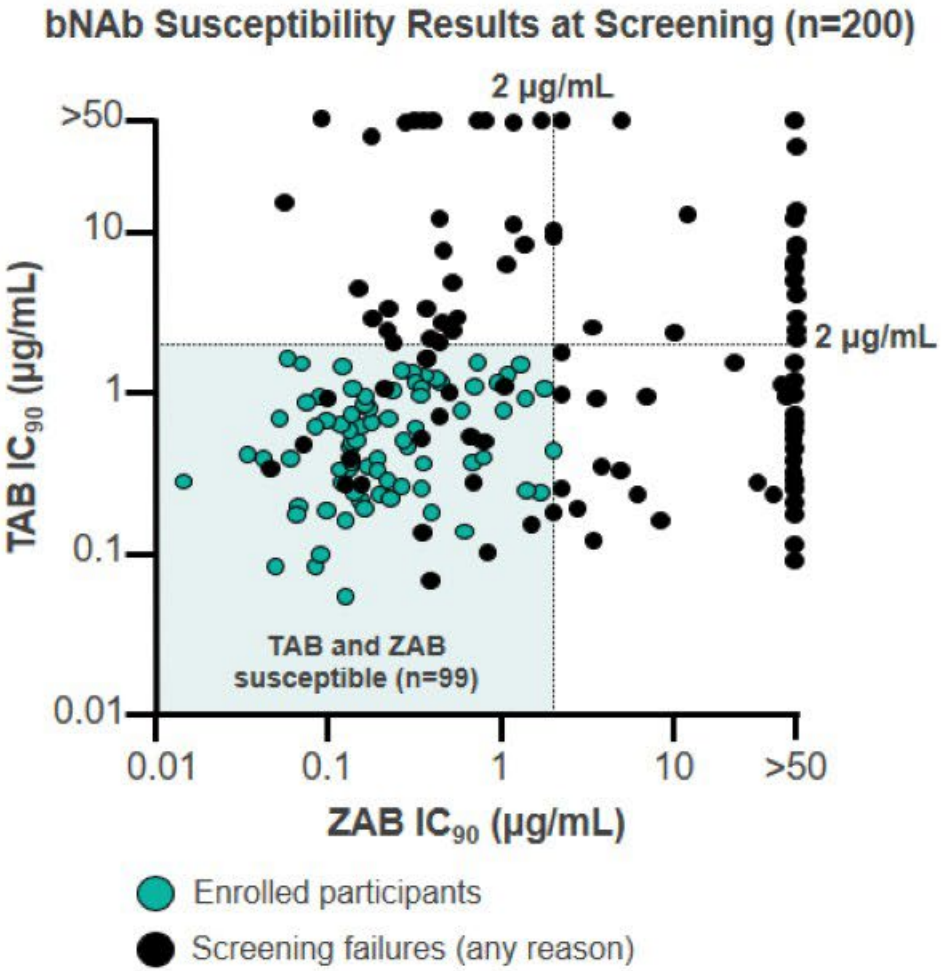
- *Not susceptible to both TAB and ZAB (n=101)[a]*

Susceptible to TAB and ZAB (n=99)

Met all eligibility criteria (n=84)

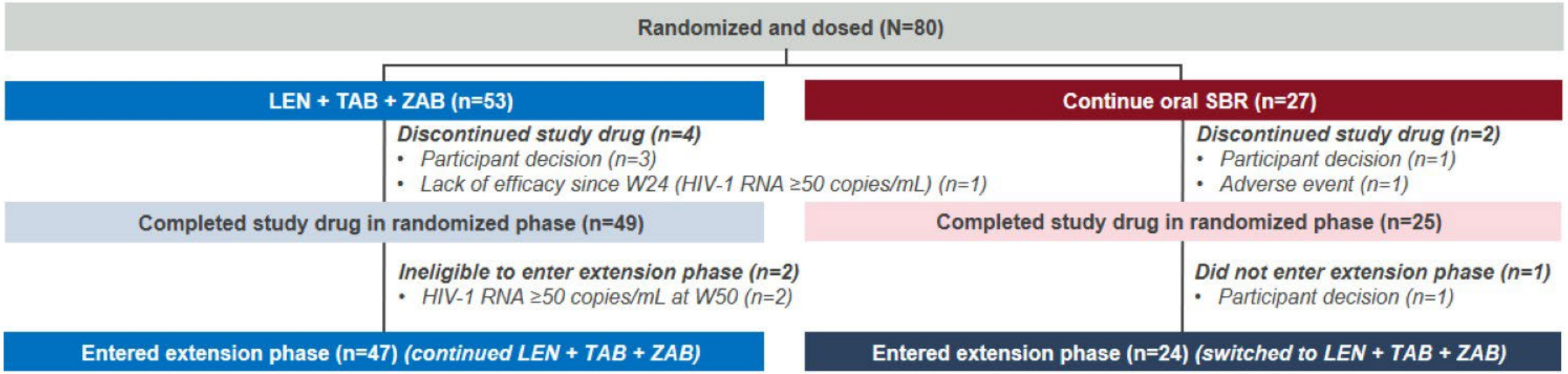
- *Not randomized (n=1)[b]*
- *Randomized but not dosed (n=3)[b]*

Randomized and dosed (N=80)



[a]Susceptibility:TAB only: 47 (24%); ZAB only: 31 (16%); neither: 23 (12%). [b]Participant decision.
bNAb, broadly neutralizing antibody; **IC_{50},** 90% inhibitory concentration; **LEN,** lenacapavir; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

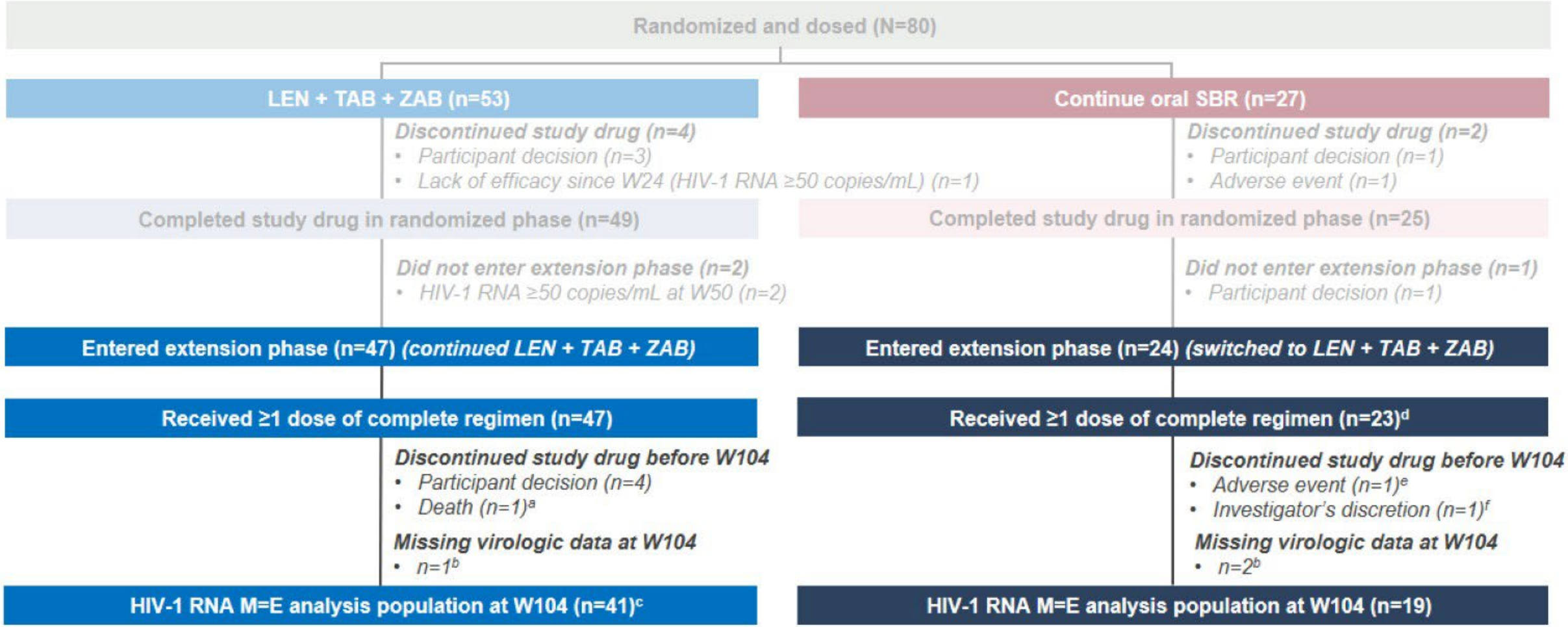
Participant Disposition



Overall, 71/72 (99%) eligible participants chose to enter the extension phase

LEN, lenacapavir; **SBR,** stable baseline regimen; **TAB,** teropavimab; **W**, week; **ZAB,** zinlirvimab.

Participant Disposition



[a]Cardiac arrest unrelated to study treatment (methamphetamine/amphetamine intoxication). [b]Remained on treatment but was missing virologic data at Week 104, with HIV-1 RNA <50 copies/mL at next visit. [c]One participant met criteria for confirmed virologic rebound at Week 104 and discontinued due to lack of efficacy. [d]One participant received oral LEN and one of the two subcutaneous LEN doses only; excluded from efficacy analyses. [e]LEN injection site nodule. [f]Detailed on 'virologic outcomes' slide.

LEN, lenacapavir; **M=E**, missing=excluded; **SBR,** stable baseline regimen; **TAB,** teropavimab; **W,** week; **ZAB,** zinlirvimab.

Baseline Characteristics

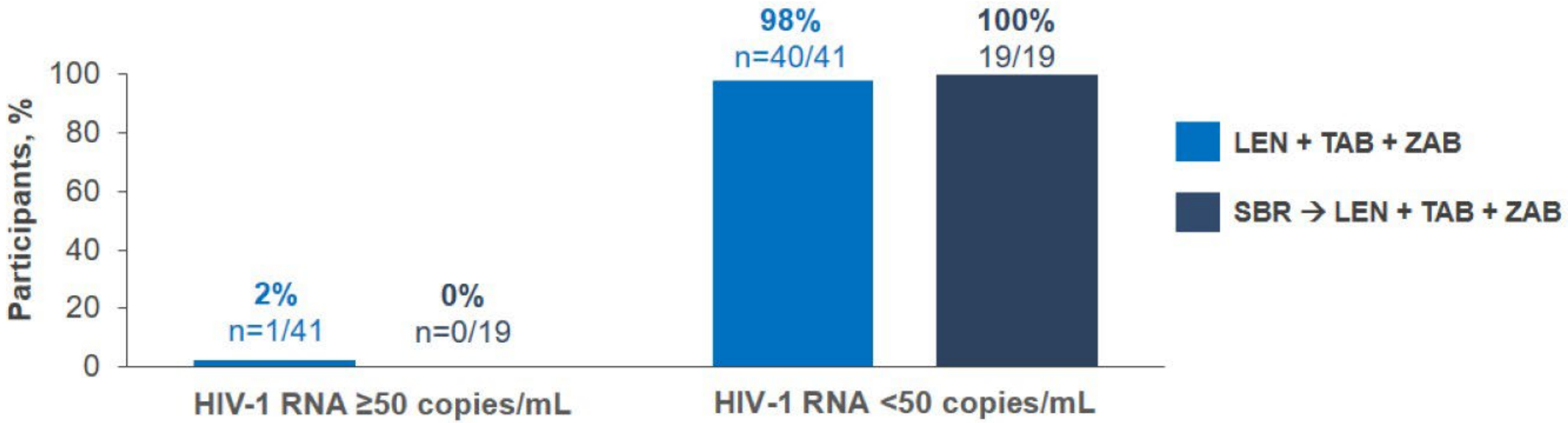
	LEN + TAB + ZAB n=53	SBR → LEN + TAB + ZAB n=24
Median (range) age, years	46 (20–65)	56 (30–65)
Female sex at birth, n (%)	8 (15)	4 (17)
Race, n (%)		
Asian	1 (2)	1 (4)
Black	21 (40)	8 (33)
White	28 (53)	13 (54)
Other	3 (6)	2 (8)
Hispanic or Latine ethnicity, n (%)	13 (25)	6 (25)
Median (range) weight, kg	93 (56–156)	85 (59–162)
Median (range) BMI, kg/m²	29.2 (20.4–48.9)	27.6 (19.3–49.1)
BMI ≥30 kg/m², n (%)	23 (43)	5 (21)
Median (IQR) CD4+ T-cell count, cells/μL	710 (552–895)	734 (595–941)
Baseline ARV containing INSTI + NRTI(s), n (%)	42 (79)	21 (88)
USA region,[a] n (%)	48 (91)	17 (71)

Baseline characteristics are reported for the safety analysis set, which includes all participants who received LEN, TAB, or ZAB at any point in the study. Baseline values were defined as the last non-missing value obtained on or prior to the first dose of LEN + TAB + ZAB.

[a]Ex-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; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB**, zinlirvimab.

Week 104 Virologic Outcomes (Missing=Excluded)



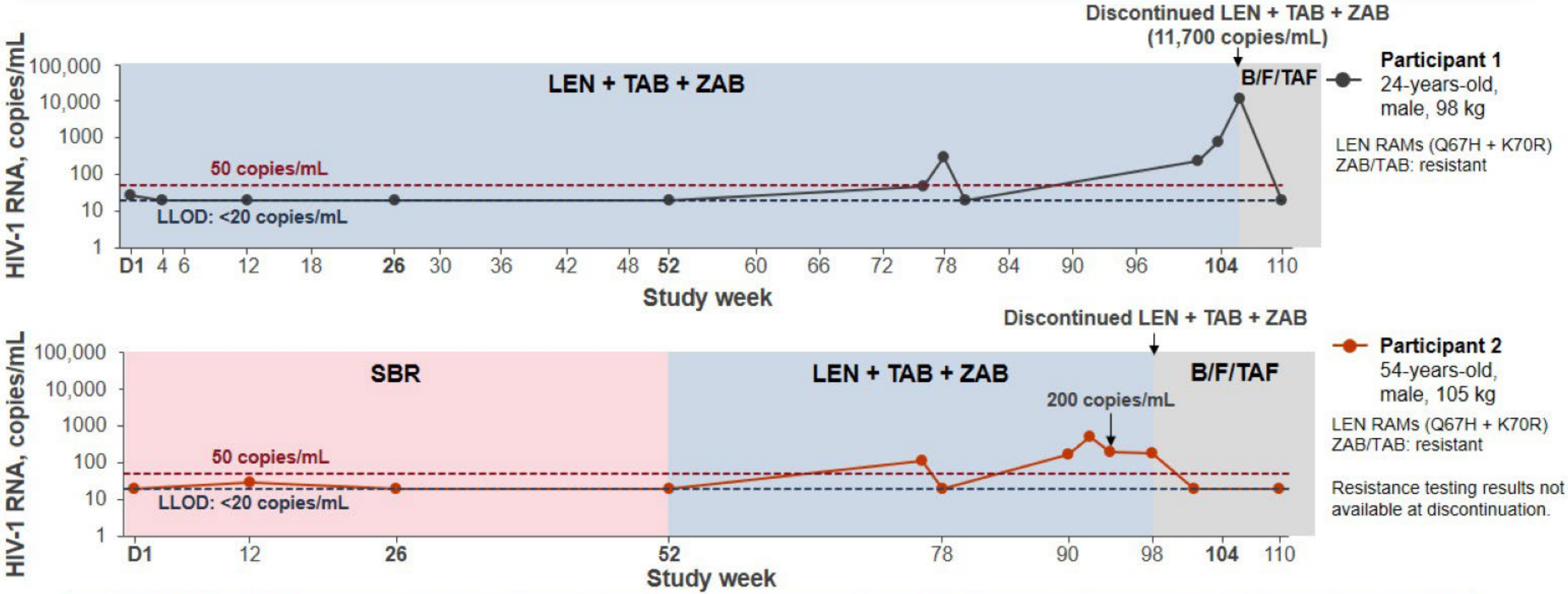
- One participant in the LEN + TAB + ZAB group met criteria for confirmed virologic rebound at Week 104 and discontinued due to lack of efficacy
- One participant in the SBR → LEN + TAB + ZAB group met criteria for confirmed virologic rebound at Week 90
  - Discontinued study treatment prior to Week 104 (investigator's discretion): Week 104 data are 'missing' and excluded from M=E analysis

Median (IQR) CD4+ T-cell count changes from baseline at Week 104:

- **+34 (–71 to 111) cells/µl** in the LEN + TAB + ZAB group
- **–38 (–159 to +40) cells/µl** in the SBR → LEN + TAB + ZAB group

On-treatment efficacy data are summarized.
IQR, interquartile range; **LEN,** lenacapavir; **M=E**, missing=excluded; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

Participants with Virologic Rebound



- PK of TAB and ZAB were consistent with the median of the respective group; trough LEN concentrations were below the median, but within the range observed in this and prior studies with LEN[1–3]
- No ADAs to TAB or ZAB were detected in either participant

LEN + TAB + ZAB administration timepoints are indicated in bold.

ADA, antidrug antibody; **B/F/TAF,** bictegravir/emtricitabine/tenofovir alafenamide; **LEN,** lenacapavir; **LLOD,** lower limit of detection; **PK,** pharmacokinetics; **RAM,** resistance-associated mutation; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

1. Ogbuagu O, et al. *Lancet Microbe* 2026;7(3):101283. **2.** Eron JJ, et al. *Lancet HIV* 2024;11(3):e146–e155. **3.** Kelley CF, et al. *N Engl J Med* 2025; 392:1261–1276.

Pharmacokinetics and Anti-Drug Antibodies (ADA)

— Therapeutic concentrations of LEN + TAB + ZAB were maintained at Week 104 in both treatment groups, consistent with prior presentation[1]

Validated three-tiered ADA assay per monoclonal antibody (mAb) development standards (completed at all visits baseline–Week 104)

↓

When ADA was detected, it's impact on PK and safety was assessed

— **Participants with treatment-emergent ADAs detected in the two treatment groups combined:**

- TAB: 10/76 (13%)[a]
- ZAB: 18/76 (24%)[b]

— **When detected, ADA titers were low[c]**

— In the LEN + TAB + ZAB group, no participants had newly detected treatment-emergent ADAs after Week 52; the proportion of participants with detectable ADAs declined in the second year

- At Week 104 only 1/40 participants had detectable ADA to TAB and 1/40 participants had detectable ADA to ZAB

— No ADA impact on PK or safety was observed up to Week 104

Across both groups, a total of 76 participants were evaluable for ADA incidence. Six (8%) participants had treatment-emergent ADAs to both bNAbs[1] [a]Transient positive, n=7 (9%); persistent positive, n=3 (4%). [b]Transient positive, n=7 (9%); persistent positive, n=11 (14%). [c]Anti-TAB ADA titer range: <10–1,280; anti-ZAB ADA titer range: <10–160. Titer is defined as the highest dilution of the blood serum where ADAs are still detectable.
ADA, anti-drug antibody; **bNAb**, broadly neutralizing antibody; **LEN,** lenacapavir; **mAb**, monoclonal antibody; **PK,** pharmacokinetic; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

1. Ogbuagu O, et al. EACS 2025. Presentation #PS09.2.

Safety Overview (Excluding SC LEN-Related injection Site Reactions)

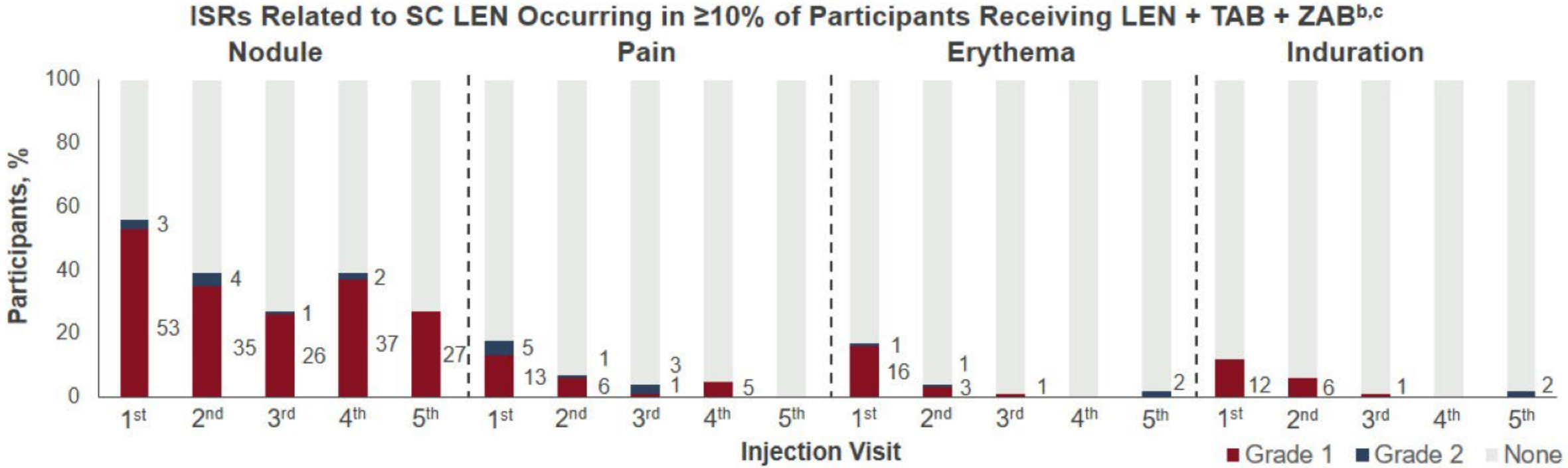
Participants, n (%)	LEN + TAB + ZAB (Any exposure up to 104 weeks of LEN + TAB + ZAB) n=53	SBR → LEN + TAB + ZAB (Any exposure up to 52 weeks of LEN + TAB + ZAB) n=24[a]
AEs	49 (92)	18 (75)
Grade ≥3	7 (13)	0
Treatment-related AEs	7 (13)	3 (13)
Grade ≥3	0	0
Serious AEs	5 (9)	0
Related to treatment	0	0
AEs leading to study treatment discontinuation	0	0
Deaths	1 (2)[b]	0
Related to treatment	0	0

— No treatment-related AEs were reported in more than one participant in either group

Safety data through the W104 data cut (up to last participant W104 visit) were included, and includes all participants who received ≥1 dose of LEN, TAB, or ZAB during the study.
[a]Twenty-four SBR→LEN + TAB + ZAB participants entered the extension phase; one participant received oral LEN and one of the two SC LEN doses only with no TAB and ZAB and is included in safety analyses.
[b]Cardiac arrest unrelated to study treatment (methamphetamine/amphetamine intoxication).
AE, adverse event; **ISR,** injection site reaction; **LEN**, lenacapavir; **SBR,** stable baseline regimen; **SC,** subcutaneous; **TAB,** teropavimab; **W,** week; **ZAB,** zinlirvimab.

Injection Site Reactions and Infusion-Related Reactions

— The most common AEs were ISRs related to SC LEN in 37 (70%) LEN + TAB + ZAB participants and in 20 (83%) SBR → LEN + TAB + ZAB participants[a]



One participant (SBR → LEN + TAB + ZAB group) had an infusion-related reaction (IRR) to TAB and ZAB

- Week 78 (2nd study drug administration): Grade 2 hypotension, Grade 1 back pain; Week 104 (3rd study drug administration): Grade 2 back pain
- In both cases, infusion was paused after which IRRs resolved; infusions restarted at a slower rate and TAB/ZAB dosing was completed
- Participant remains in the study on LEN + TAB + ZAB

[a]Two participants in the SBR→LEN + TAB + ZAB group had ISRs related to SC LEN leading to treatment discontinuation: injection site nodule in one participant; injection site necrosis, erythema, induration, and pain in one participant. [b]In total, n=77, n=71, n=68, n=43, and n=41 received an SC LEN injection at the first, second, third, fourth, and fifth injection visits, respectively. [c]From Week 52, TAB and ZAB were co-administered over 30–60 minutes or administered sequentially (30 minutes/bNAb); prior to Week 52, TAB and ZAB were only sequentially administered (30 minutes/bNAb).

AE, adverse event; **bNAb,** broadly neutralizing antibody; **IRR,** infusion-related reaction; **ISR,** injection site reaction; **LEN,** lenacapavir; **SBR,** stable baseline regimen; **SC,** subcutaneous; **TAB,** teropavimab; **ZAB,** zinlirvimab.

Conclusions

- Twice-yearly LEN + TAB + ZAB maintained high rates of virologic suppression through 104 weeks of treatment in the LEN + TAB + ZAB group and demonstrated a favorable safety profile
  - These constitute the longest follow-up for any bNAb-containing treatment combination, demonstrating durable maintenance of virologic suppression with this regimen
  - The SBR→LEN + TAB + ZAB group also maintained high rates of virologic suppression after 52 weeks of LEN + TAB + ZAB
  - The two cases of virologic rebound with resistance in the extension phase resuppressed after restarting B/F/TAF
- ISRs decreased in frequency over time, consistent with prior LEN data[1]
- No impact of ADA on the PK of TAB or ZAB was observed through Week 104, with declining prevalence of ADA in the second year of treatment
- These data support LEN + TAB + ZAB as the first potential complete twice-yearly combination treatment for PWH, and is under further investigation in Phase 3 studies (NCT07682961; NCT07683000)

ADA, anti-drug antibody; **bNAb,** broadly neutralizing antibody; **ISR**, injection site reaction; **LEN,** lenacapavir; **PK,** pharmacokinetics; **PWH**, people with HIV-1; **SBR,** stable baseline regimen; **TAB,** teropavimab; **ZAB,** zinlirvimab.

1. Ogbuagu O, et al. *Clin Infect Dis*. 2025;80(3):566–74.

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- A plain language summary of this presentation is available by scanning the QR code

ADA, anti-drug antibody; **PK,** pharmacokinetics.