National HIV Curriculum

Lenacapavir (*Sunlenca*)

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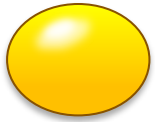
Last Updated: December 28, 2022

Lenacapavir

Oral Lenacapavir



300 mg tablets

Take with or without food

Subcutaneous Lenacapavir

Each 1.5 mL vial = 463.5 mg

Administer as Subcutaneous Injection

Lenacapavir

- **Type of Medication**
  - HIV capsid inhibitor
- **Indication**
  - Treatment of HIV-1 in combination with other antiretroviral medications in heavily treatment-experienced adults with multidrug resistant HIV
- **Preparations**
  - Oral: 300 mg tablets
  - Subcutaneous injection: 463.5 mg/1.5 mL vial
- **Adverse Reactions**
  - Most common adverse effects are nausea and injection site reactions
- **Contraindications**
  - Contraindicated to give with strong CYP3A inducers

Source: Lenacapavir Prescribing Information.

Lenacapavir Dosing Schedule

Lenacapavir Dosing Schedule	
Initiation Option 1	
Day 1	927 mg by subcutaneous injection (2 x 1.5 mL injections) + 600 mg orally (2 x 300 mg tablets)
Day 2	600 mg orally (2 x 300 mg tablets)
Initiation Option 2	
Day 1	600 mg orally (2 x 300 mg tablets)
Day 2	600 mg orally (2 x 300 mg tablets)
Day 8	300 mg orally (1 x 300 mg tablets)
Day 15	927 mg by subcutaneous injection (2 x 1.5 mL injections)
Maintenance	
927 mg by subcutaneous injection (2 x 1.5 mL injections) every 6 months (26 weeks) from date of the last injection +/-2 weeks	
Missed dose: If more than 28 weeks since last injection and clinically appropriate to continue lenacapavir, restart initiation from Day 1, using either Option 1 or Option 2	

Source: Lenacapavir Prescribing Information

Lenacapavir Dosing: Initiation Option 1

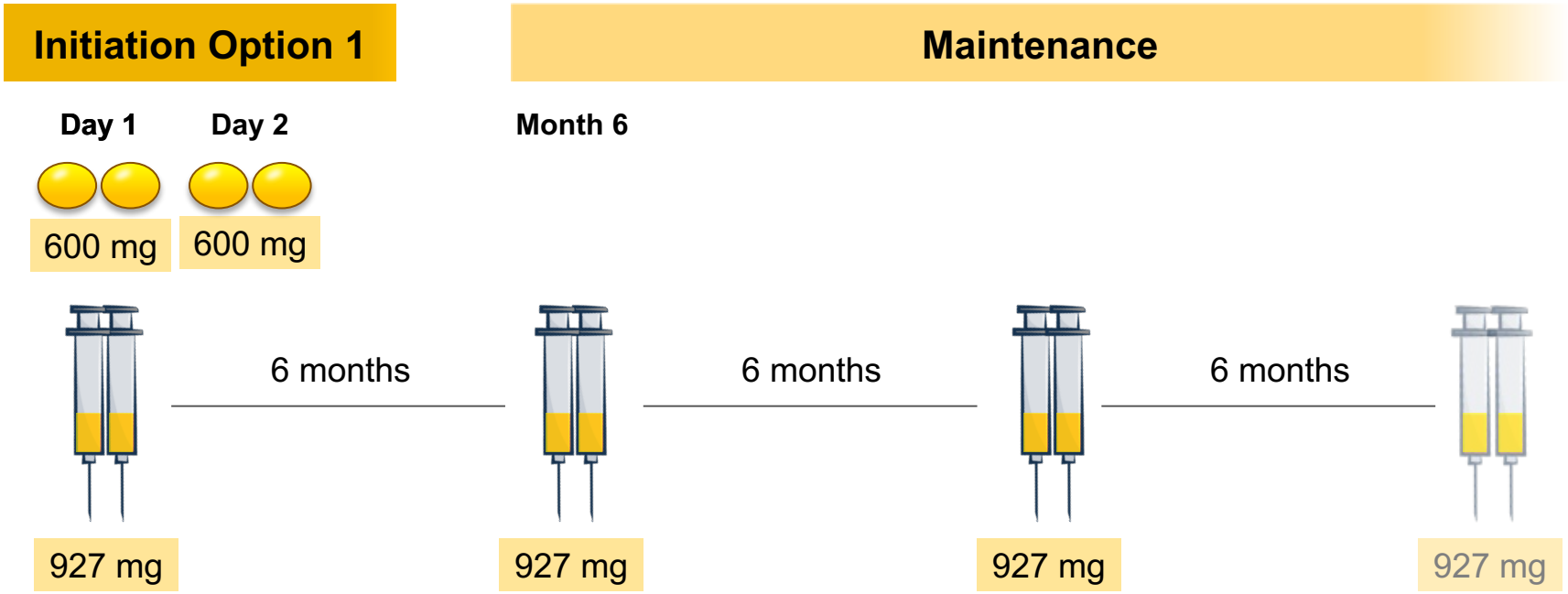


Illustration: David H. Spach, MD

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Lenacapavir Dosing: Initiation Option 2

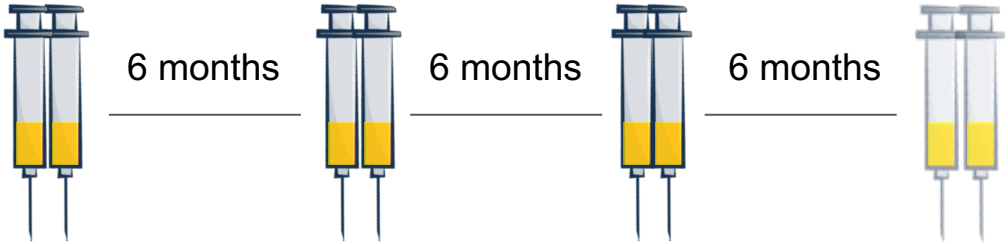
Initiation Option 2

Day 1 **Day 2** **Day 8**

600 mg | 600 mg | 300 mg

Maintenance

Day 15



927 mg | 927 mg | 927 mg | 927 mg

Oral lenacapavir 300 mg

Subcutaneous lenacapavir 463.5 mg

Illustration: David H. Spach, MD

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Lenacapavir for HIV Treatment
Summary of Key Phase 2 and 3 Studies

- **Salvage Therapy for Treatment-Experienced with Multidrug Resistance**
  - **CAPELLA (Phase 3): Lenacapavir plus Optimized Background Therapy**
- **Initial and Maintenance Therapy for Treatment-Naïve**
  - **CALIBRATE (Phase 2): Lenacapavir with Various ARV Combinations**

Lenacapavir for Persons with Multidrug-Resistant HIV

CAPELLA

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Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Background

- **Background**
  - Phase 3, randomized, trial with oral and subcutaneous lenacapavir, a first-in-class capsid inhibitor, versus optimized background therapy (OBT)
- **Enrollment Criteria:**
  - Age ≥12 years
  - Virologic failure on current ART
  - HIV RNA >400 copies/mL for ≥8 wks
  - Documented HIV drug resistance to at least 2 HIV medications from at least 3 of the 4 main classes
  - At least one fully active agent available for HIV treatment

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Study Design

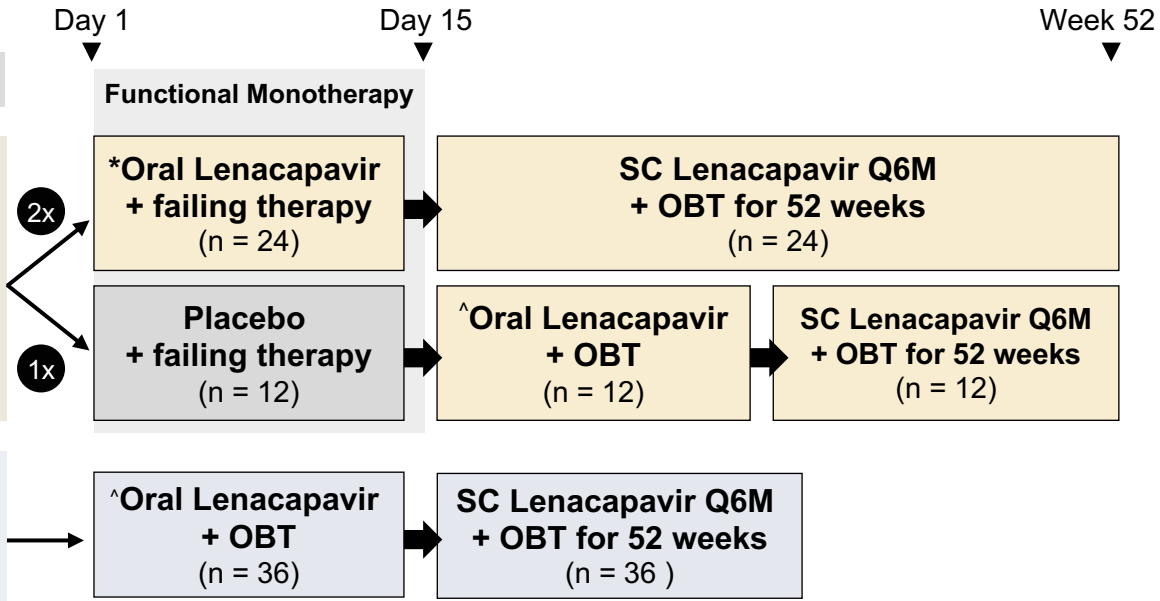
Study Cohorts

Cohort 1 (Randomized, Stable Viremia)

- First 36 participants with:
  - HIV RNA decrease <0.5 log between the screening and cohort-selection visits
    and
  - HIV-1 RNA ≥ 400 copies/mL during screening

Cohort 2 (Nonrandomized, Reduced Viremia)

- Participants with:
  - HIV RNA decrease ≥0.5 log between the screening and cohort-selection visits
    or
  - HIV-1 RNA <400 copies/mL during screening



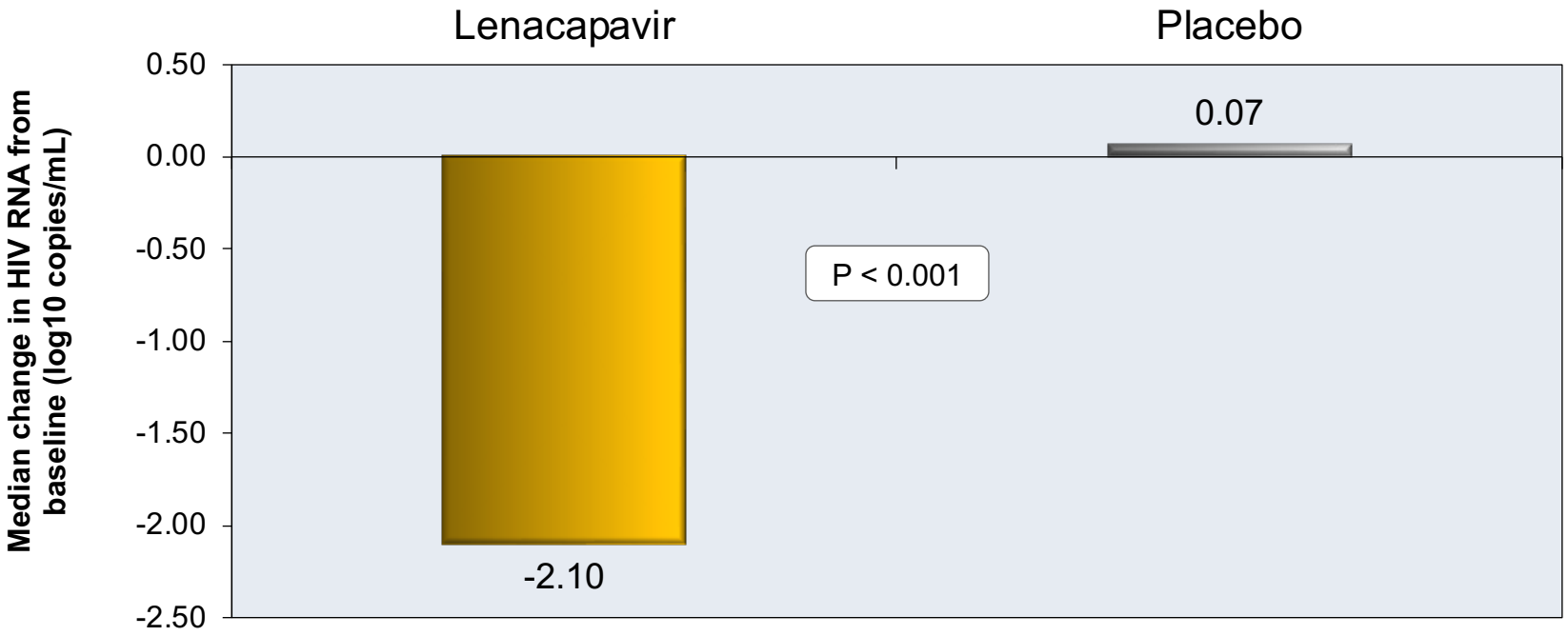
OBT = optimized background regimen

*Oral lenacapavir = 600 mg days 1 and 2, 300 mg day 8
^Oral lenacapavir = 600 mg days 15 and 16, 300 mg day 22
SC Lenacapavir = 927 mg every 6 months

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

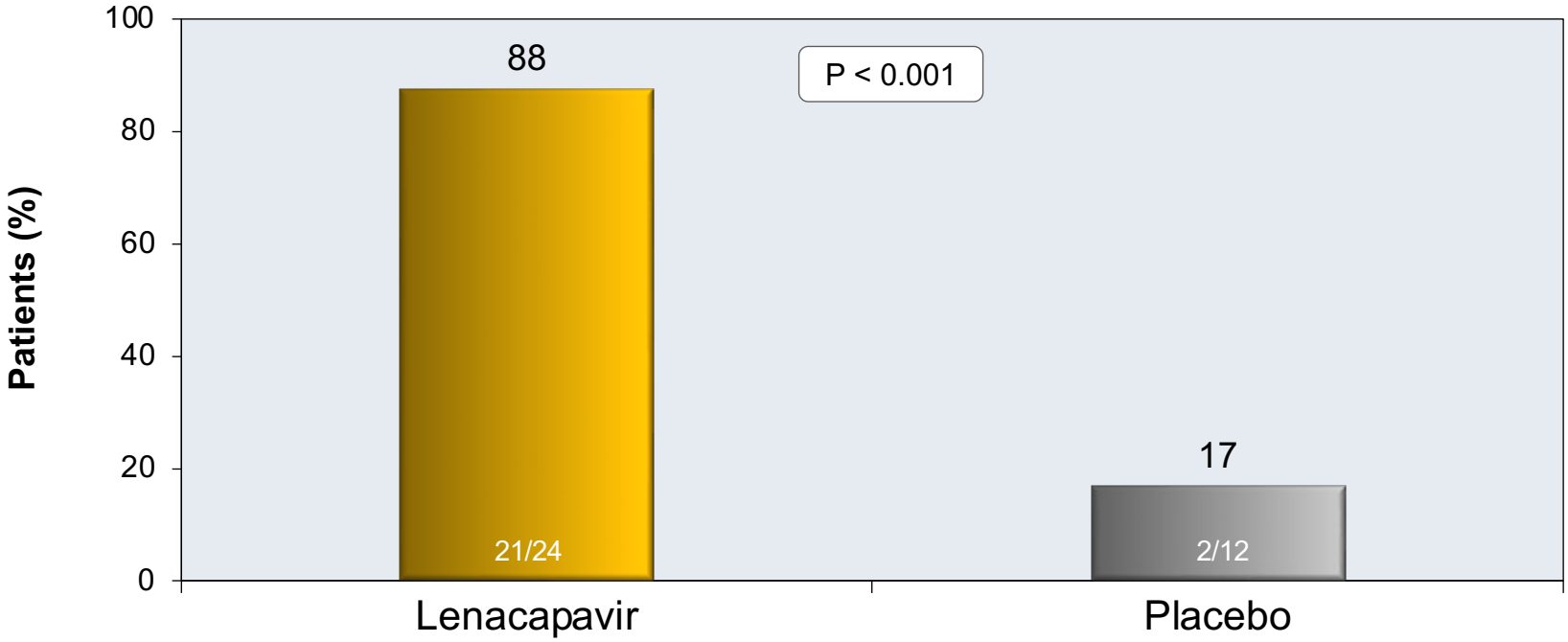
Baseline to Day 15 Change in HIV RNA Level (Functional Monotherapy in Randomized Cohort)



Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

Decrease in HIV RNA Level of ≥0.5 log at Day 15 (Functional Monotherapy in Randomized Cohort)



Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

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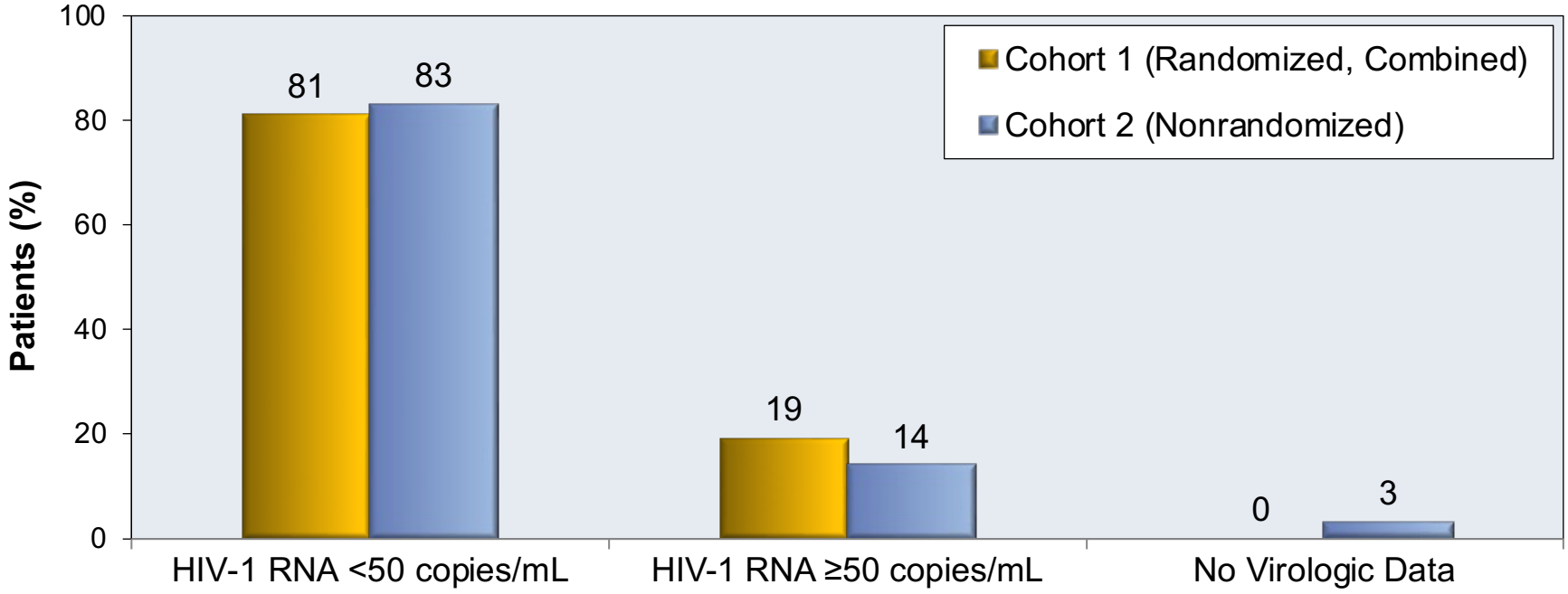
Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

Virologic Responses at 26 Weeks



Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Capsid Inhibitor Resistance

Lenacapavir-related capsid substitutions developed in 8 participants

- 5 with M66I (alone)
- 1 with M66I + N74D
- 1 with Q67H + K70R
- 1 with K70H (alone)

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Capsid Inhibitor Resistance

Mutations and median change in lenacapavir susceptibility

- M66I: 234-fold decrease
- 1 with Q67H + K70R: 15-fold decrease
- 1 with K70H: 265-fold decrease

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Conclusions

Conclusions: “In patients with multidrug-resistant HIV-1 infection, those who received lenacapavir had a greater reduction from baseline in viral load than those who received placebo.”

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir for Treatment-Naïve Persons with HIV

CALIBRATE

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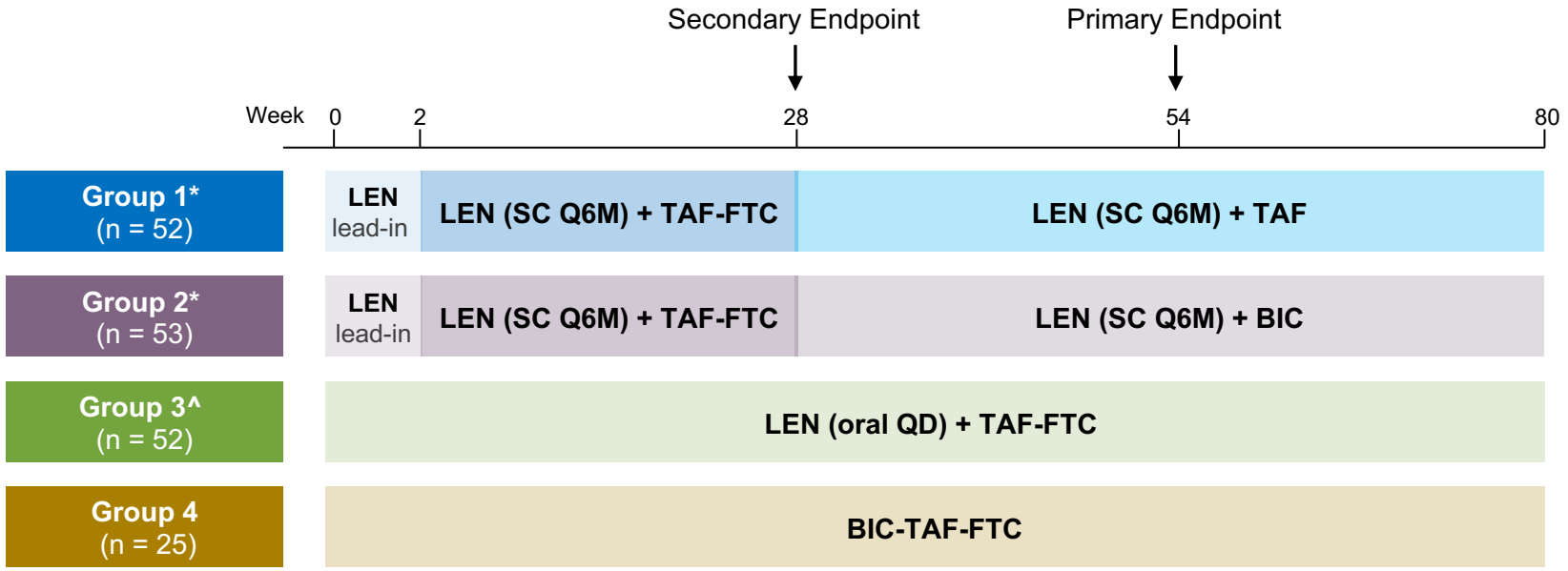
Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Background

- **Background**
  - Phase 2 randomized, open-label trial in United States and Dominican Republic evaluating the efficacy of lenacapavir in various combinations as initial and maintenance antiretroviral therapy in persons with HIV
- **Enrollment Criteria:**
  - Age ≥18 years
  - Antiretroviral naïve
  - HIV RNA ≥200 copies/mL
  - CD4 count ≥200 cells/mm^3
  - Negative pregnancy test for women
  - Exclusions: hepatitis B, hepatitis C, or any active opportunistic infection

Source: Gupta SK, et al. Lancet HIV. 2023;10:e15-e23.

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Background



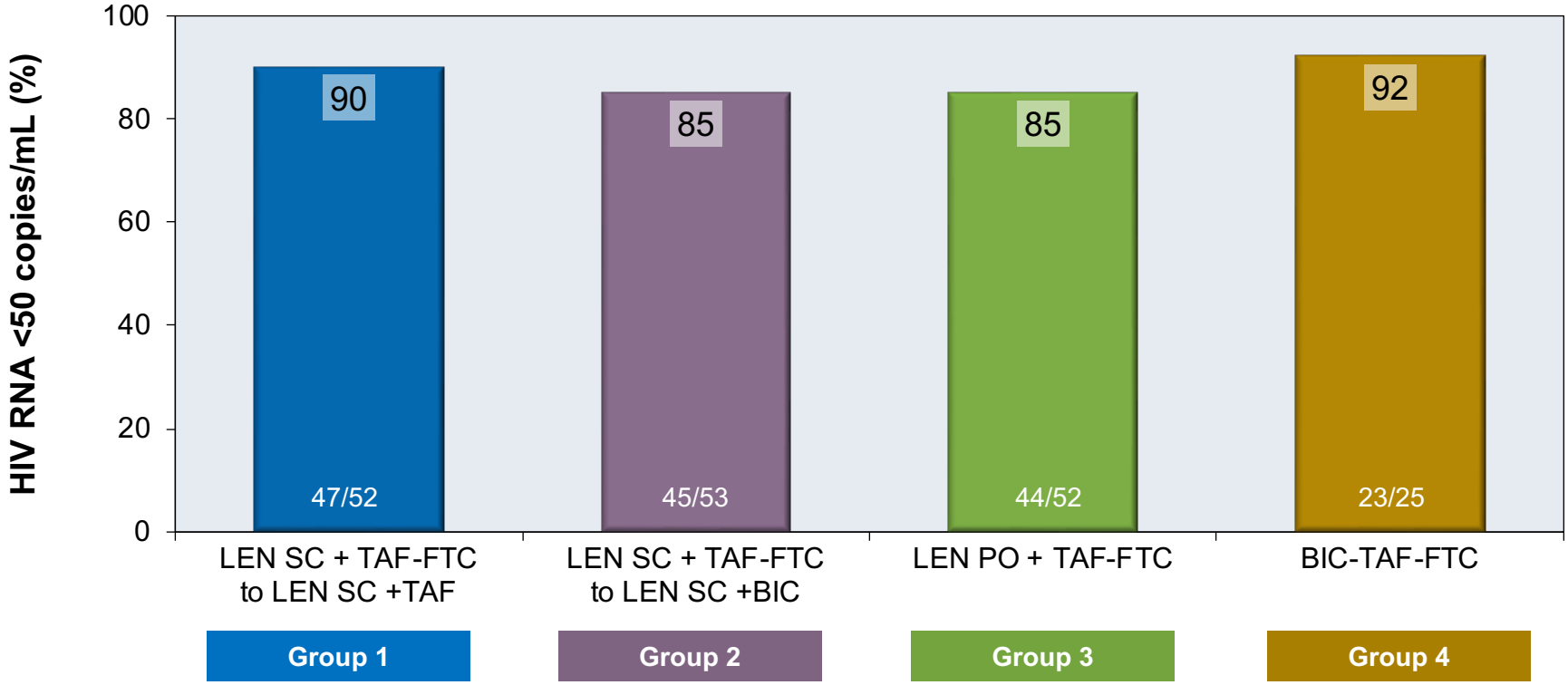
*Groups 1 and 2: LEN Oral lead in = 600 mg days 1 and 2, 300 mg day 8; first dose LEN SC = 927 mg on day 15; requires HIV RNA <50 copies/mL on weeks 16 and 22 to change to 2-drug regimen

^Group 3: LEN oral 600 mg days 1 and 2, followed by 50 mg daily

Abbreviations: LEN = lenacapavir; SC = subcutaneous; TAF-FTC = tenofovir alafenamide-emtricitabine; TAF = tenofovir alafenamide; BIC = bictegravir: BIC-TAF-FTC = bictegravir-tenofovir alafenamide-emtricitabine

Source: Gupta SK, et al. Lancet HIV. 2023;10:e15-e23.

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results



Source: Gupta SK, et al. Lancet HIV. 2023;10:e15-e23.

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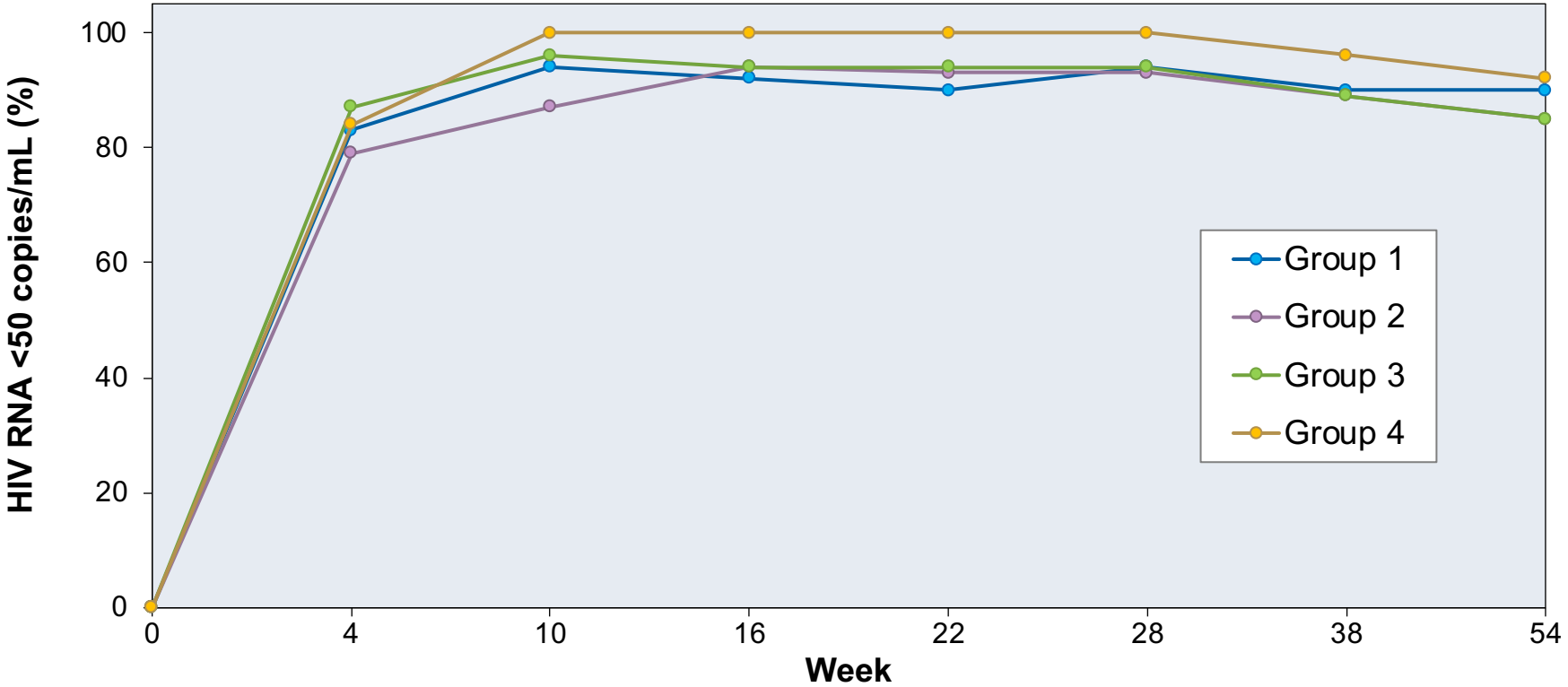
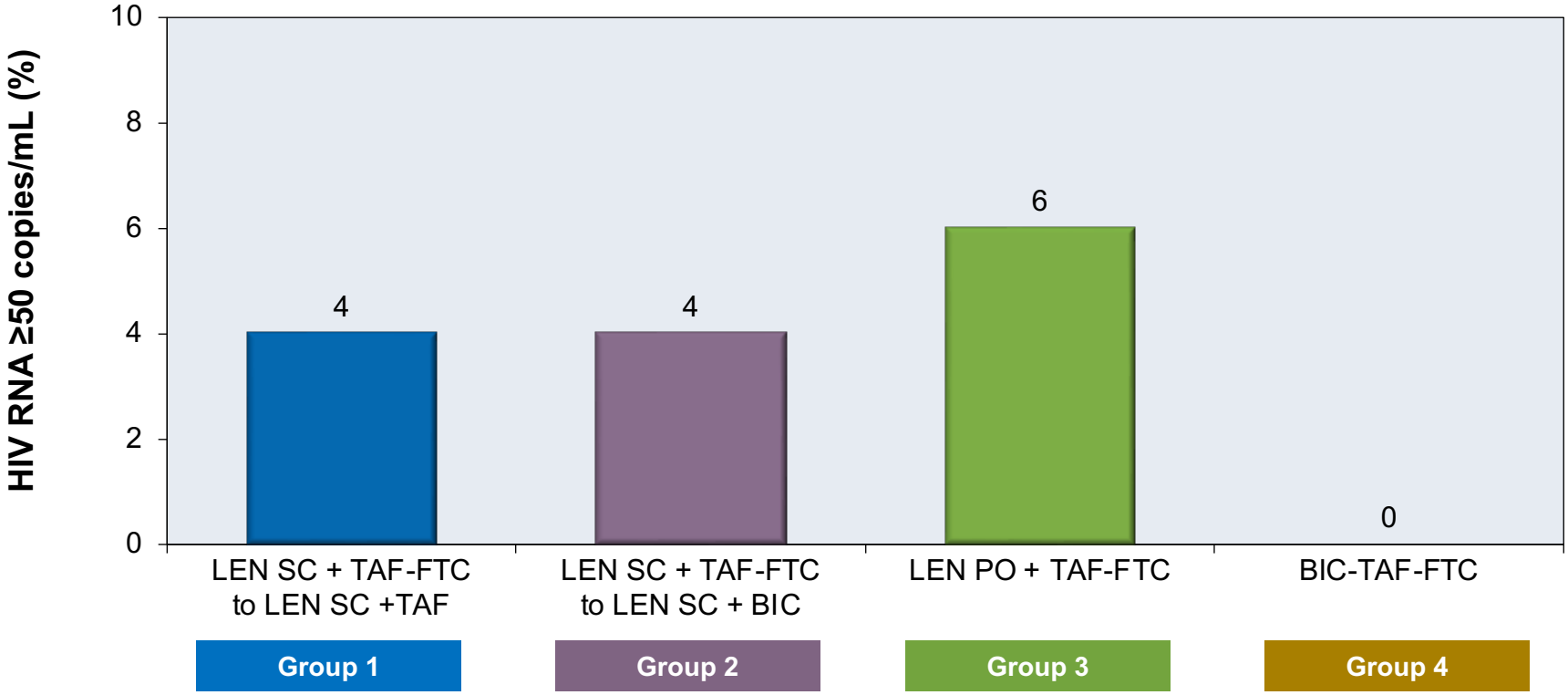
Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results



Source: Gupta SK, et al. Lancet HIV. 2023;10:e15-e23.

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results



Source: Gupta SK, et al. Lancet HIV. 2023;10:e15-e23.

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Resistance

Lenacapavir-related capsid substitutions developed in 2 of 157 participants

- Group 2 participant: Q67H + K70R
- Group 3 participant: Q67H

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE Study: Results

Interpretation: “Lenacapavir warrants further investigation as a potential antiretroviral used orally and as injection in combination with other antiretroviral drugs.”

Source: Segal-Maurer S, et al. N Engl J Med. 2022;386:1793-1803.

Acknowledgments

The **National HIV Curriculum** is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,021,448 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

AETC AIDS Education & Training Center Program

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