Lenacapavir for Persons with Multidrug-Resistant HIV

CAPELLA

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

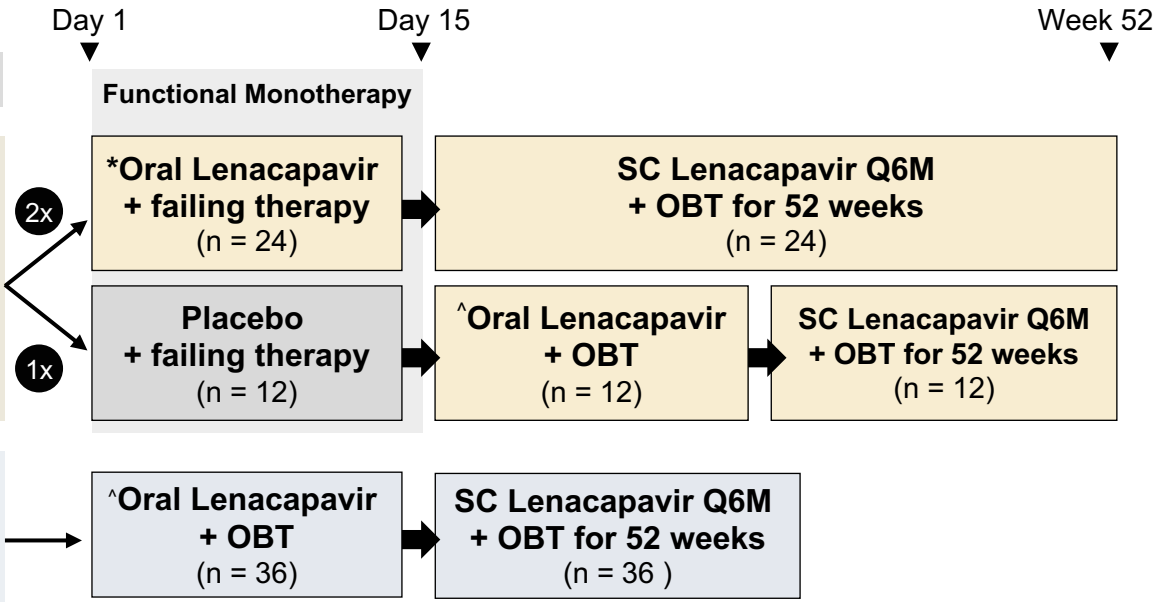
Study Cohorts

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



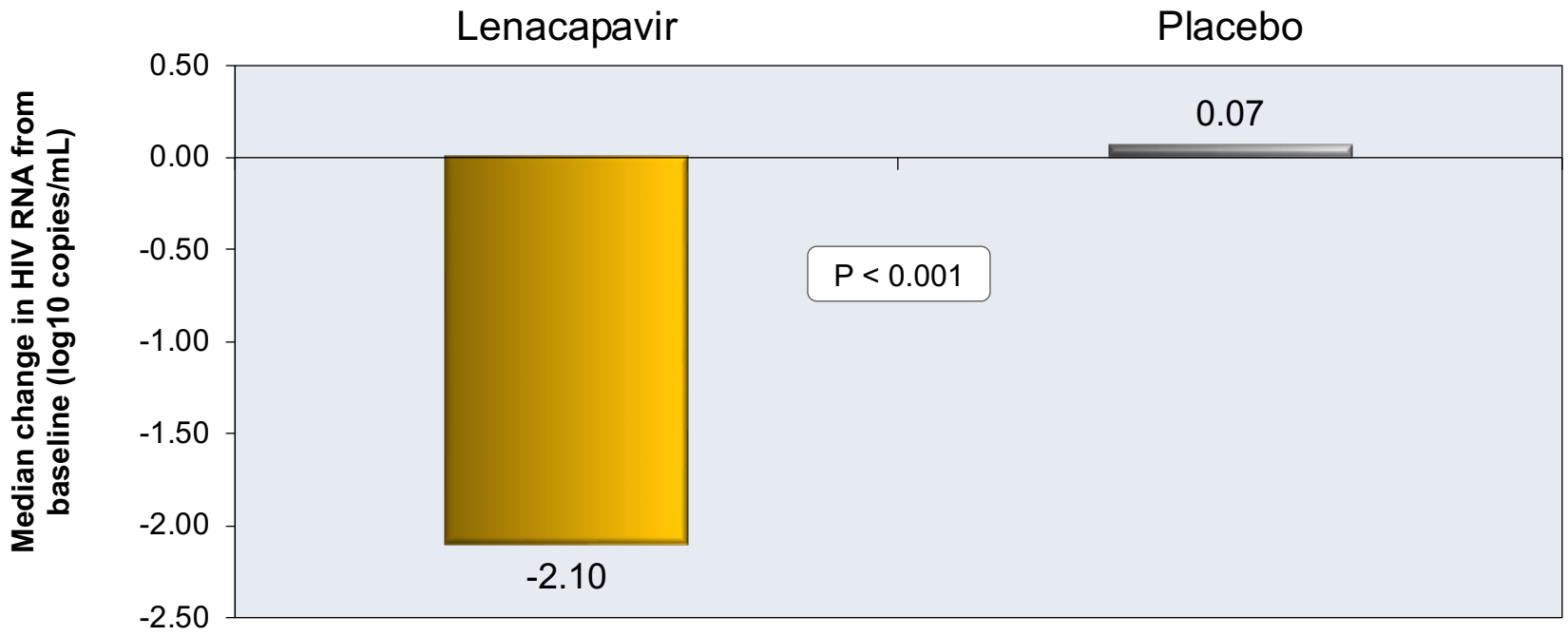
OBT = optimized background regimen

*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

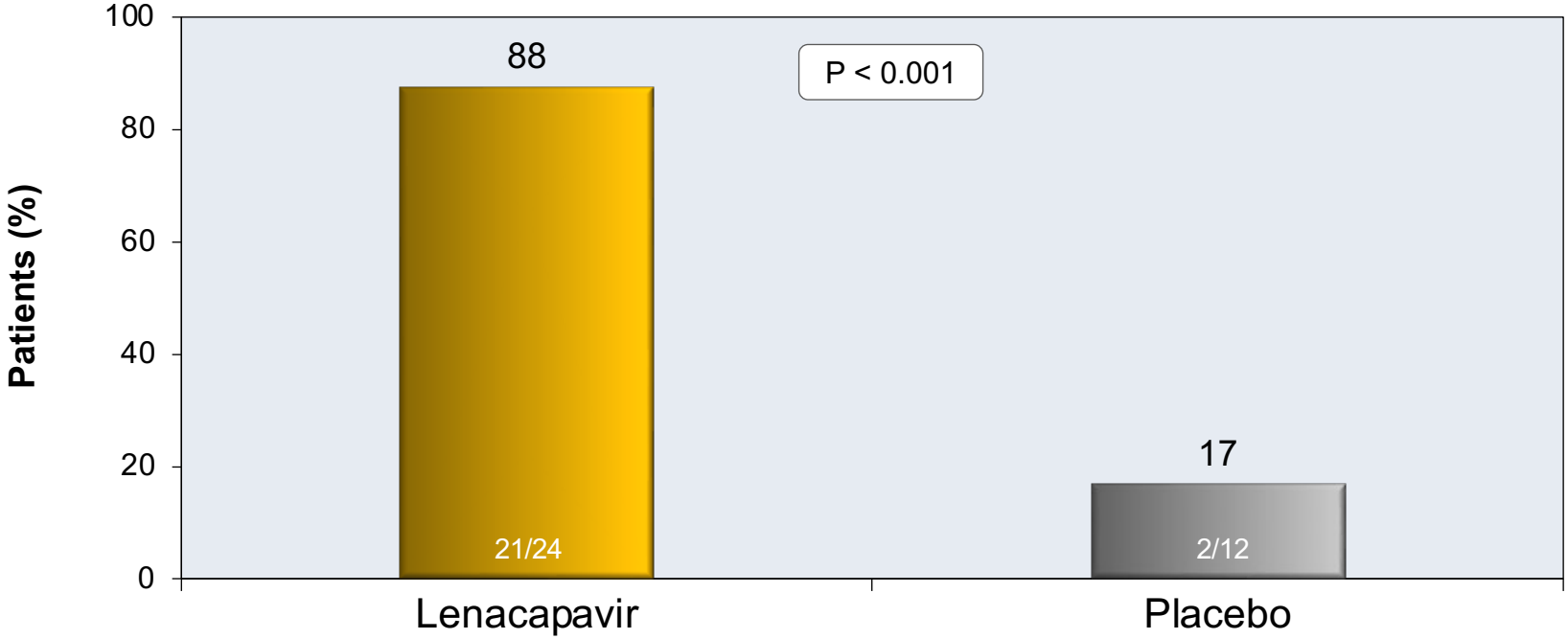
Baseline to Day 15 Change in HIV RNA Level (Functional Monotherapy in Randomized Cohort)



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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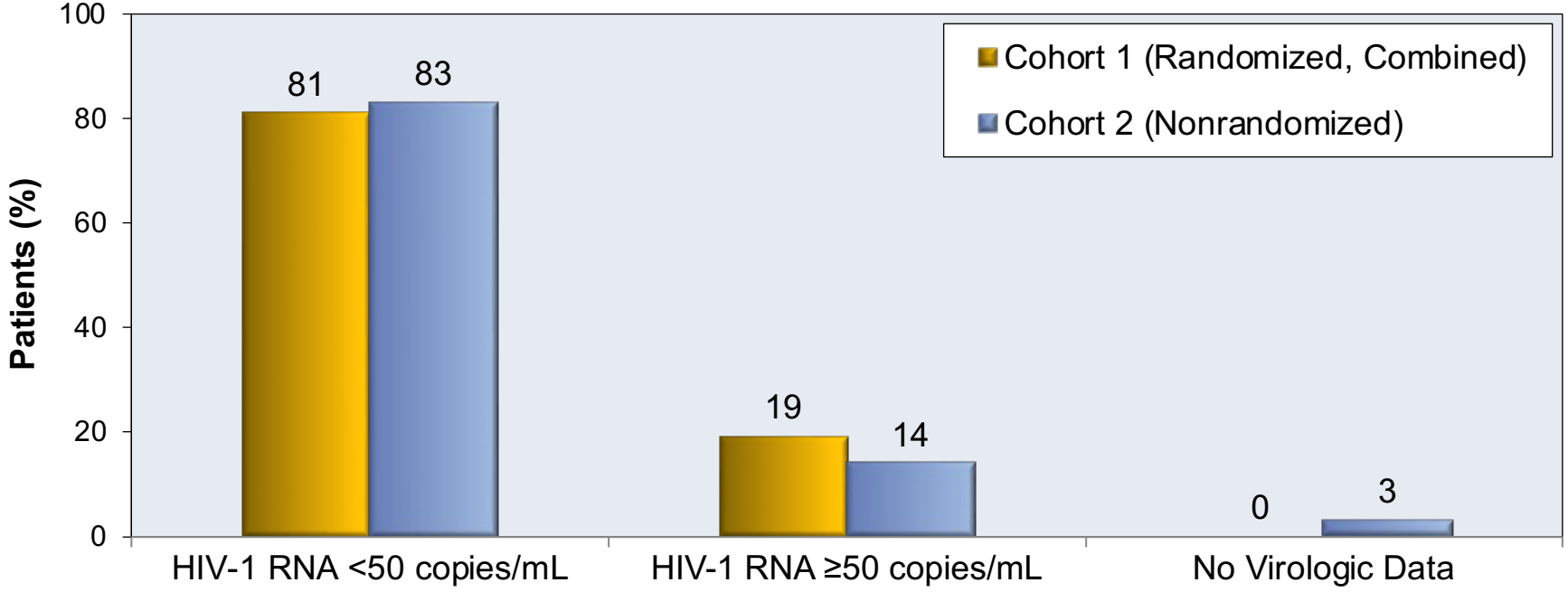
Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

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

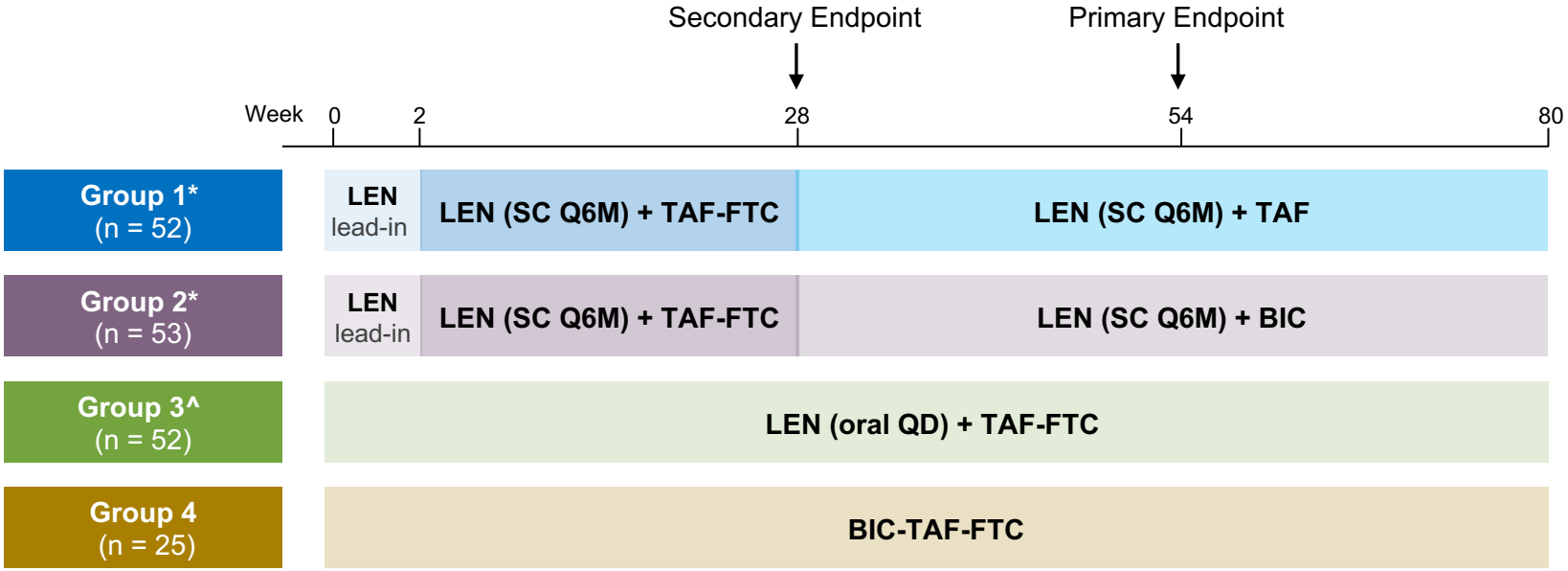
CALIBRATE

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



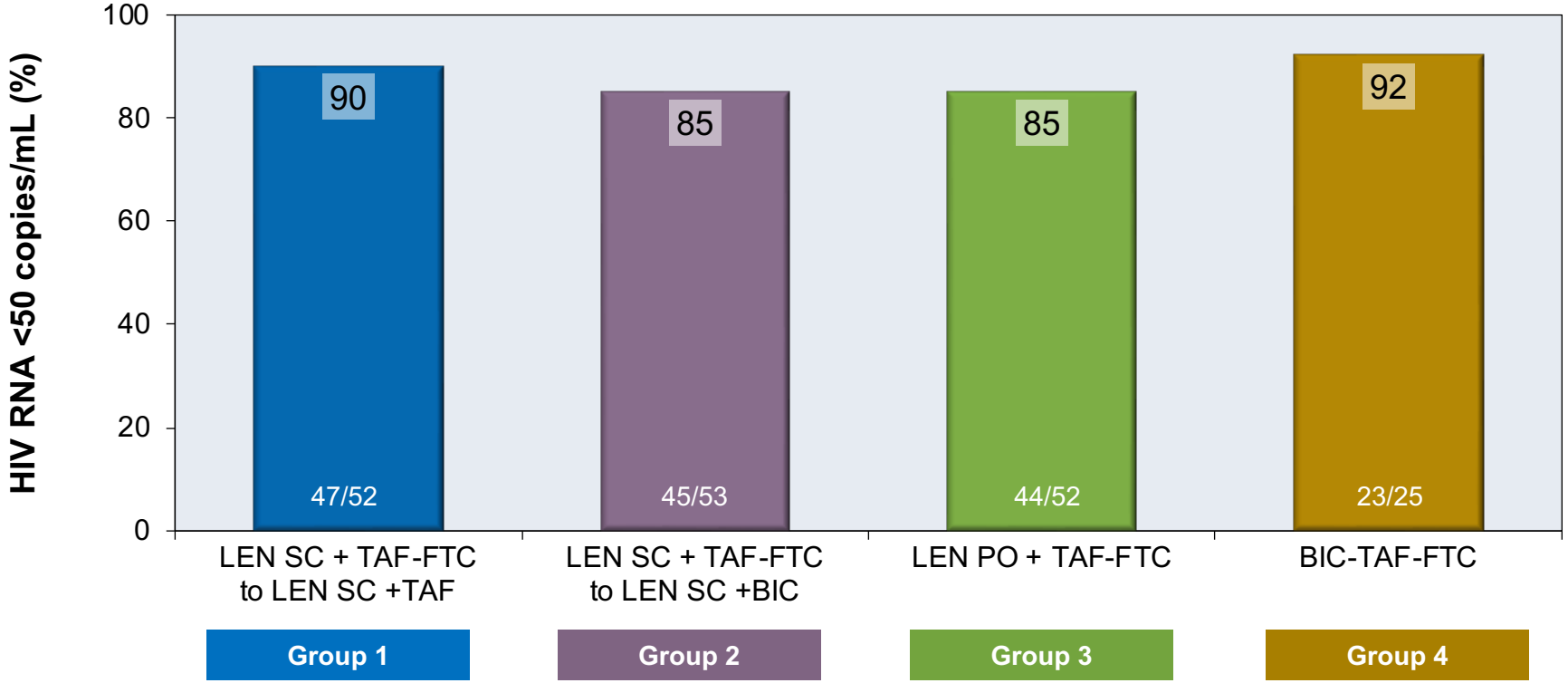
*Groups 1 and 2: LEN Oral lead in = 600 mg days 1 and 2, 300 mg day 8; first dose LEN SC = 927 mg on day 15; requires HIV RNA <50 copies/mL on weeks 16 and 22 to change to 2-drug regimen

^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



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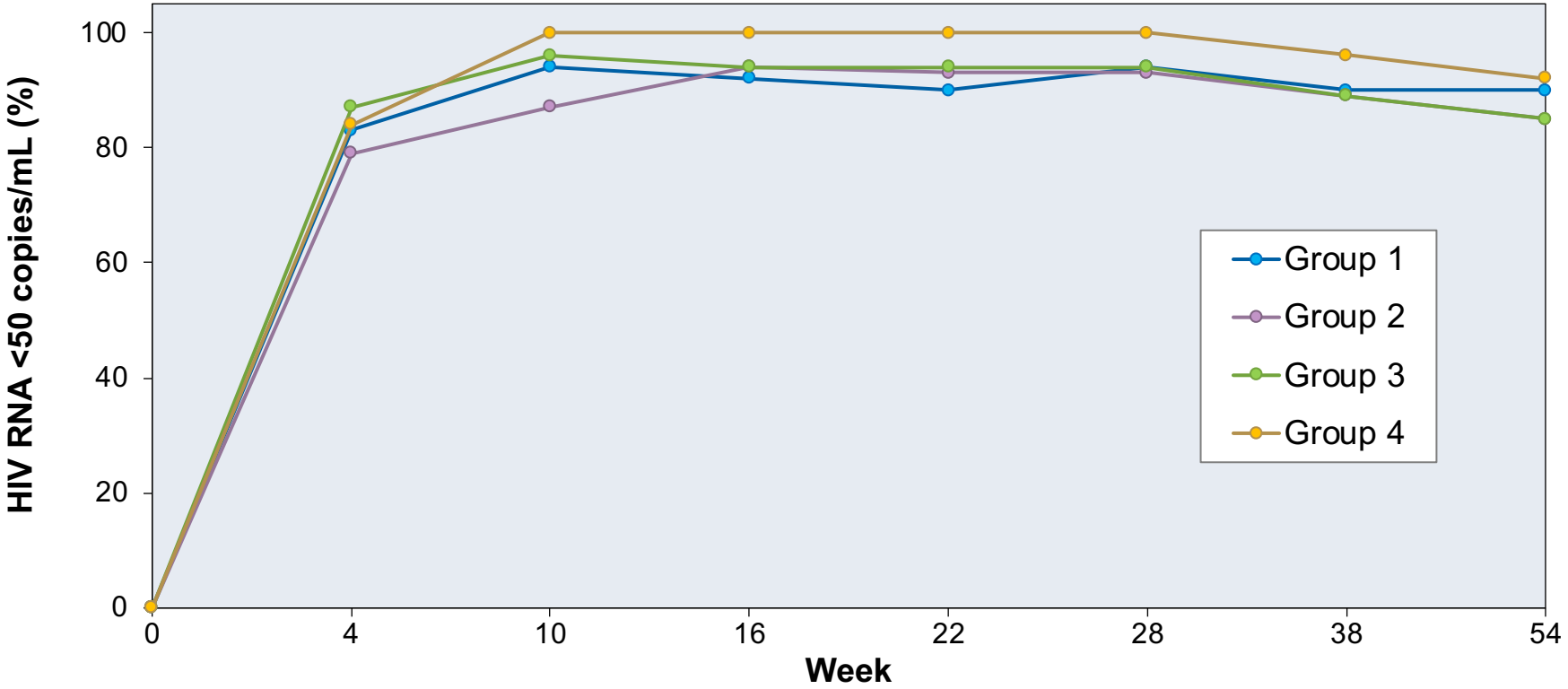
Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results



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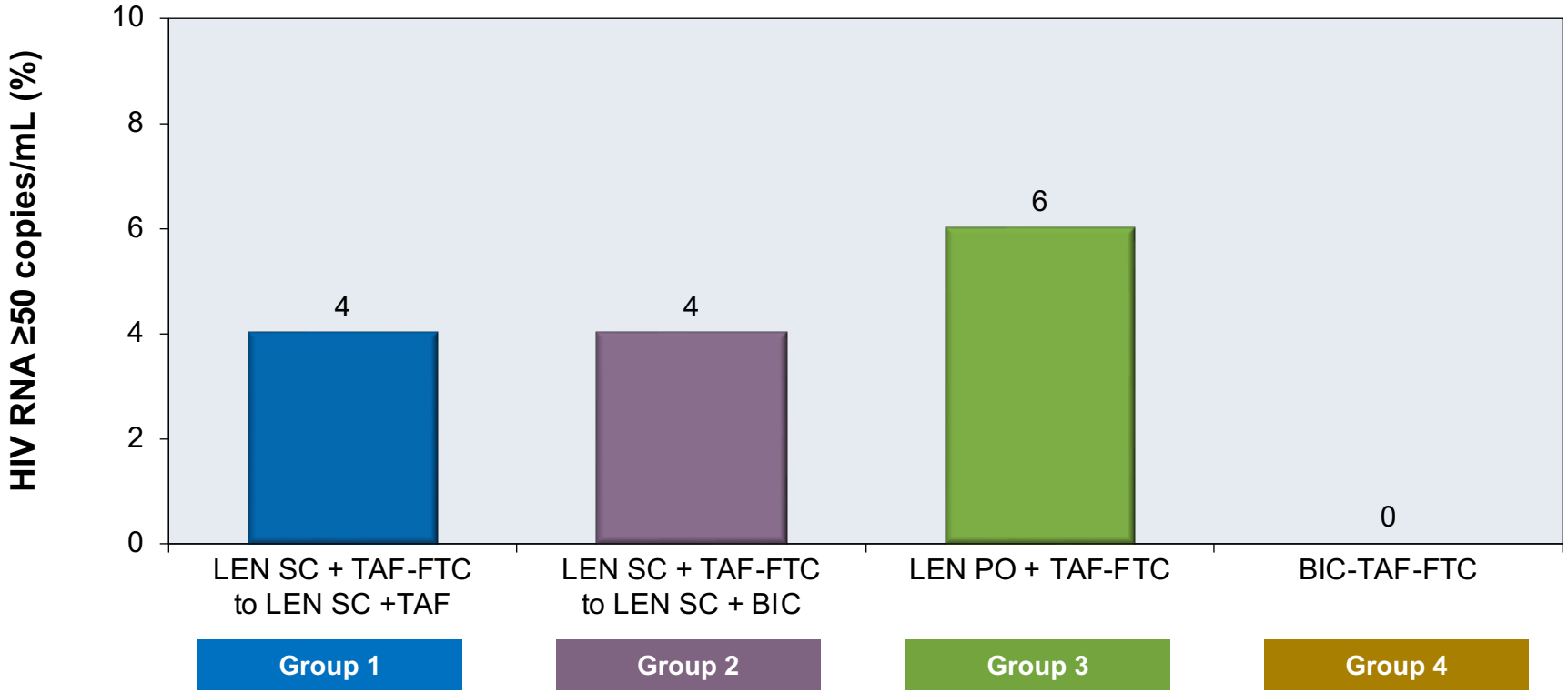
Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: Results



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

Lenacapavir in Treatment-Naïve Persons with HIV
CALIBRATE: 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

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AETC AIDS Education & Training Center Program

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