

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

Lenacapavir in Multidrug Resistant HIV

CAPELLA Study: Study Design

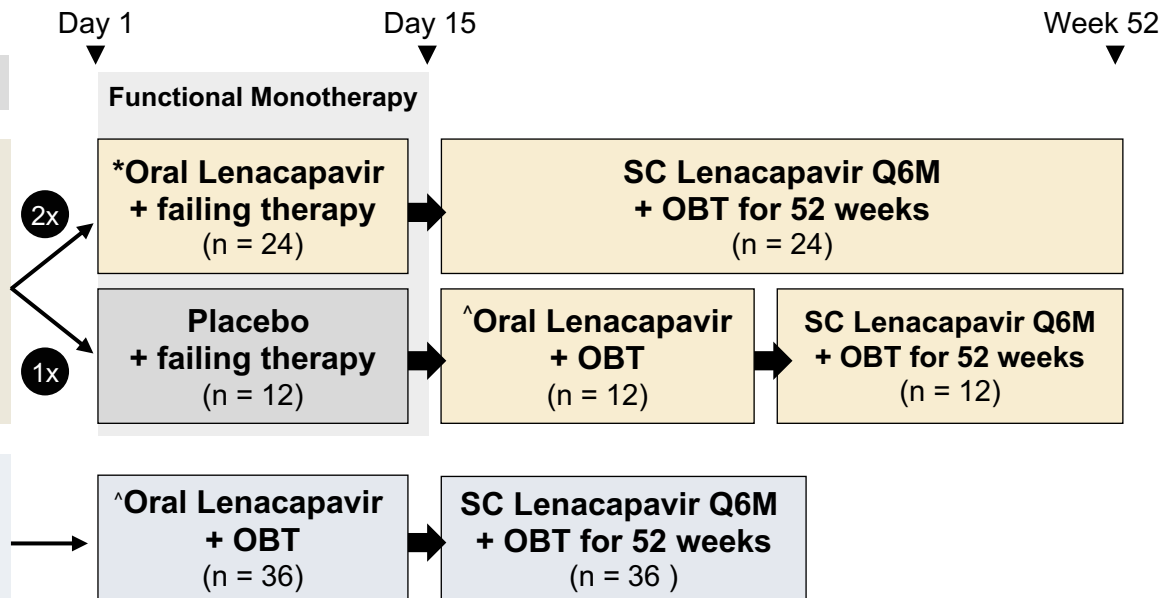
Study Cohorts

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

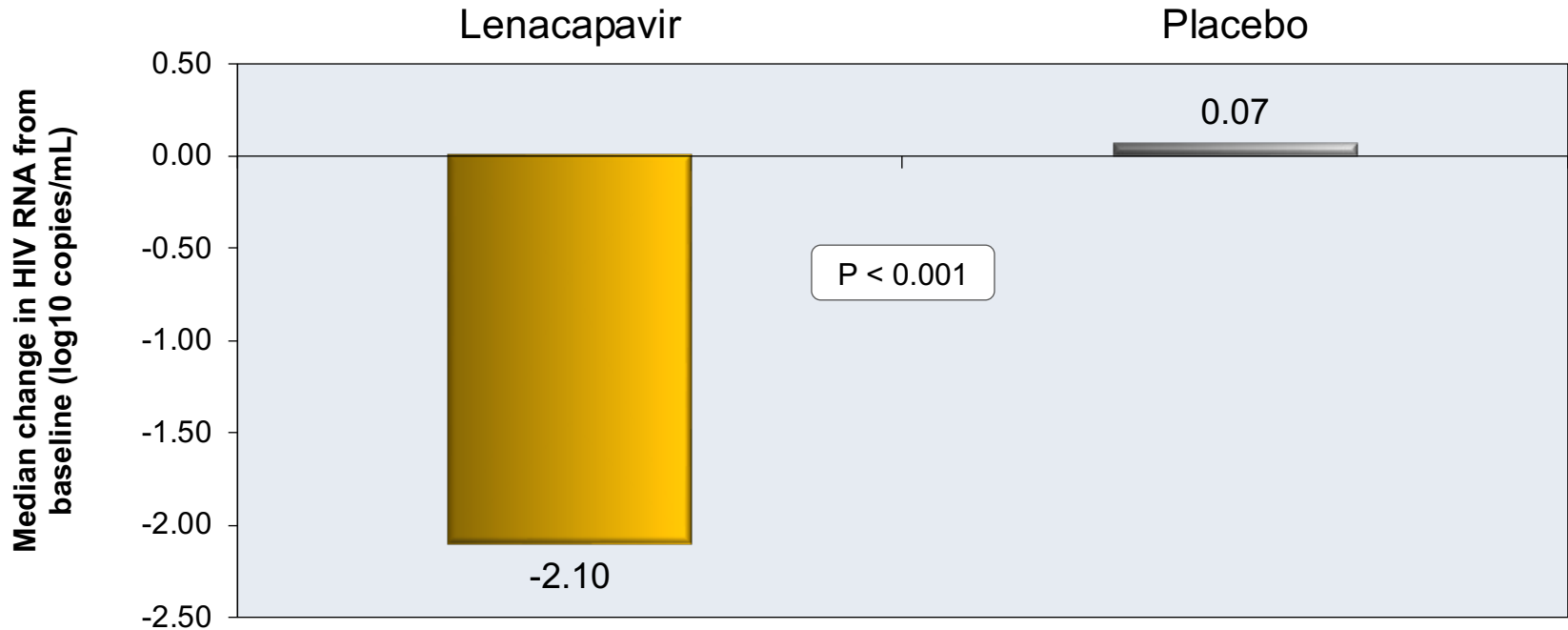
^Oral lenacapavir = 600 mg days 15 and 16, 300 mg day 22

SC Lenacapavir = 927 mg every 6 months

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CAPELLA Study: Results

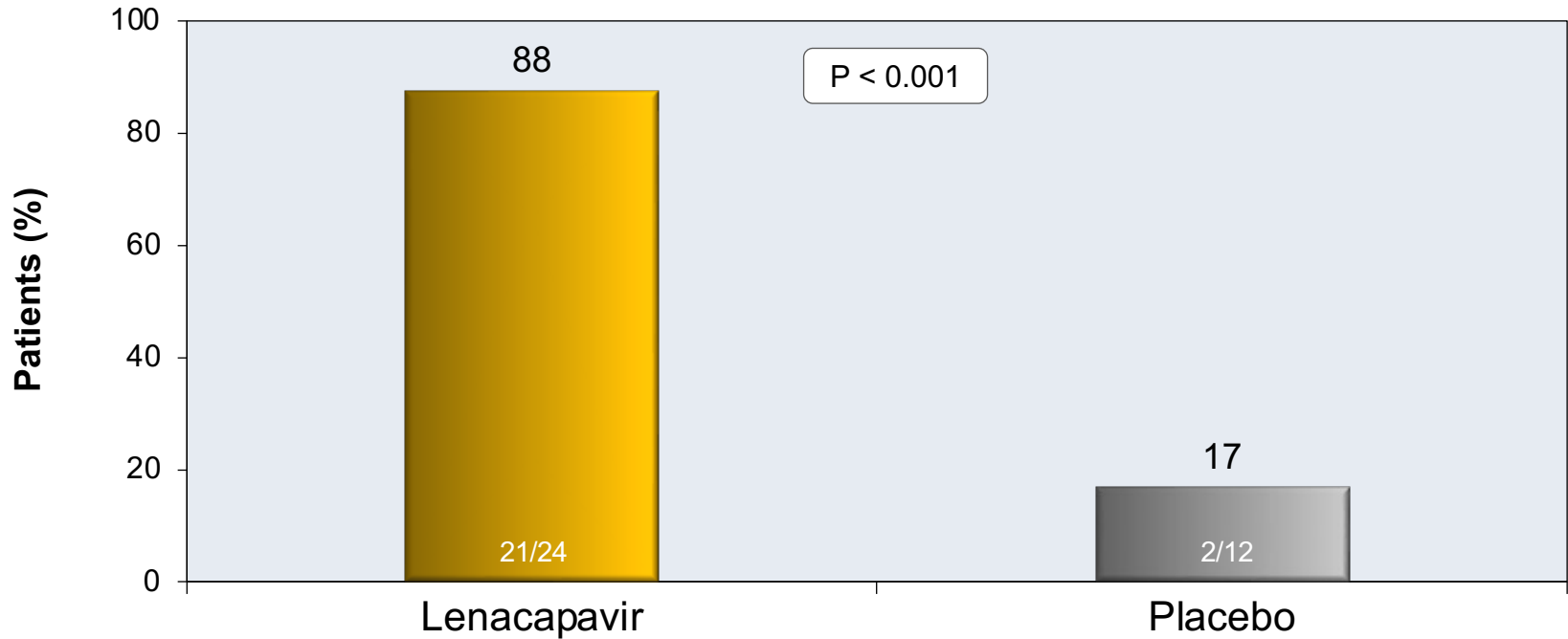
Baseline to Day 15 Change in HIV RNA Level (Functional Monotherapy in Randomized Cohort)



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CAPELLA Study: Results

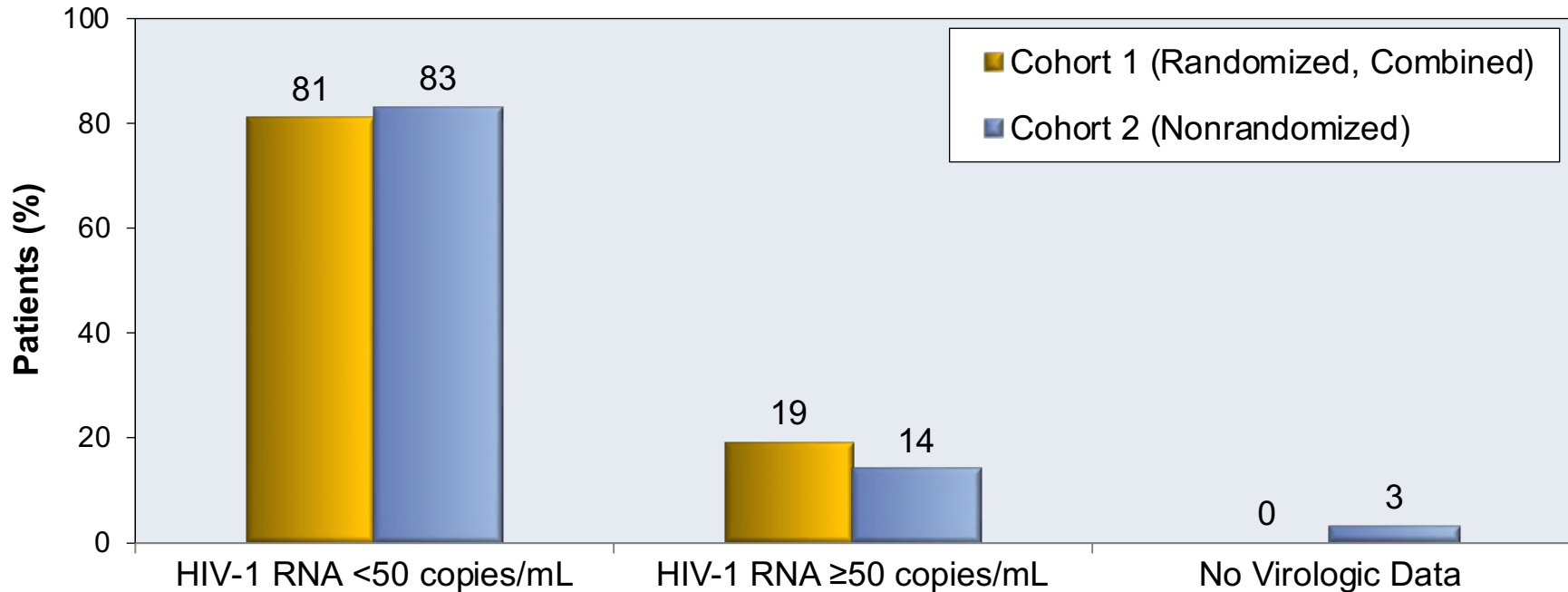
Decrease in HIV RNA Level of ≥ 0.5 log at Day 15 (Functional Monotherapy in Randomized Cohort)



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CAPELLA Study: Results

Virologic Responses at 26 Weeks



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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)

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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

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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.”

Acknowledgments

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