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
  - 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
  - HIV-1 RNA <400 copies/mL during screening

**Functional Monotherapy**

- Day 1
  - *Oral Lenacapavir + failing therapy* (n = 24)
  - Placebo + failing therapy (n = 12)

- Day 15
  - SC Lenacapavir Q6M + OBT for 52 weeks (n = 24)
  - ^Oral Lenacapavir + OBT (n = 12)

- Week 52
  - SC Lenacapavir Q6M + OBT for 52 weeks (n = 12)
  - SC Lenacapavir Q6M + OBT for 52 weeks (n = 36)

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

OBT = optimized background regimen

Lenacapavir in Multidrug Resistant HIV
CAPELLA Study: Results

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

![Graph showing median change in HIV RNA from baseline (log10 copies/mL)]

- Median change in HIV RNA from baseline (log10 copies/mL):
  - Lenacapavir: -2.10
  - Placebo: 0.07

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)

Lenacapavir in Multidrug Resistant HIV CAPELLA Study: Results

Virologic Responses at 26 Weeks

Lenacapavir-related capsid substitutions developed in 8 participants

- 5 with M66I (alone)
- 1 with M66I + N74D
- 1 with Q67H + K70R
- 1 with K70H (alone)
Mutations and median change in lenacapavir susceptibility

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

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.”
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