CWRU/UH AIDS Clinical Research Site
AIDS Clinical Trials Group Study A5359
Provider Summary

A phase III randomized, cross-over study to evaluate long-acting, injectable antiretroviral therapy for people living with HIV who have not been adherent to their antiretroviral therapy

Brief Description: This 4 step study compares long-acting (LA) injectable antiretroviral therapy (ART) to standard of care (SOC) oral ART in previously non-adherent individuals.

Step 1 is the induction phase and all participants receive study provided SOC oral ART. Participants receive financial incentives for meeting study specified goals. In order to continue to Step 2, participants must achieve viral load suppression during this step (HIV RNA<50 copies/mL).
Step 2 is the randomization phase and participants are randomized 1:1 to receive LA ART or continue on SOC for 52 weeks.
Step 3 is the crossover/continuation phase. Participants randomized to LA ART will continue that therapy and eligible SOC participants will crossover to receive LA ART for 52 weeks.
Step 4 is the observational phase that switches participants who received at least one LA ART injection and are no longer eligible for injections back to locally-sourced oral SOC ART for 52 weeks.

Objectives: To compare regimen success of LA ART (using RPV-LA and CAB-LA) to Standard of Care (SOC) in previously non-adherent, HIV-infected individuals by 48 weeks of follow-up after an incentivized oral induction period.

Key Inclusion Criteria:

- HIV-1 infected individuals who are 18 years of age or older.
- Prescribed ART for at least 6 months.
- Screening HIV RNA is greater than 200 copies/mL.
- Women must not be pregnant, planning to become pregnant, or breastfeeding. Women who can become pregnant must agree to use 1 form of effective birth control.
- Evidence of non-adherence to their HIV medications.

Non-adherence to HIV medications will be defined as having <u>one</u> of the two criteria below:

1. Poor virologic response within the last 18 months (defined as <1 $\log_{10}$ decrease in HIV-1 RNA from the participant's historical baseline value <u>or</u> HIV-1 RNA >200 copies/mL at two time points at least 4 weeks apart) in individuals who have been prescribed ART for at <u>least</u> 6 consecutive months.

2. Lost to clinical follow-up within the last 18 months with ART non-adherence for ≥6 consecutive months. Lost to clinical follow-up is defined as either no contact with provider or missed 2 or more appointments in a 6-month period. ART non-adherence is defined as a lapse in ART ≥7 days (consecutive or non-consecutive), in the 6-month period where they were lost to clinical follow-up per participant report.

Key Exclusion Criteria:

- Previous use of rilpivirine or cabotegravir.
- Uncontrolled seizures.
- Advanced liver disease.
- Unwilling to receive injections in the buttocks.
- Chronic Hepatitis C with anticipated use of anti-HCV therapy prior to the completion of step 2.
- Active Hepatitis B infection.

Treatment:

Step 1: The first 24 weeks of treatment will consist of at least 3 HIV medications, in a regimen selected by personal physician. Must include a protease inhibitor or an integrase inhibitor. Viral suppression (VL RNA<50 copies m/L) must be achieved during Step 1 in order to proceed to Step 2.

Step 2: LA ART Arm:
Weeks 0-4: Oral cabotegravir 30 mg and rilpivirine 25mg daily
Weeks 4-52: LA Injectable cabotegravir and rilpivirine every 4 weeks for 48 weeks.

SOC arm: Participants will continue their oral ART regimen from Step 1 for 52 weeks.

Step 3: LA ART Arm:
Participants continue LA Injectable cabotegravir and rilpivirine every 4 weeks for 52 weeks.

Crossover arm:
Participants with an HIV RNA <50 copies cross-over to the LA regimen.
Weeks 0-4: Oral cabotegravir 30 mg and rilpivirine 25mg daily
Weeks 4-52: LA Injectable cabotegravir and rilpivirine every 4 weeks.

Step 4: Participants who received at least one injection and transitioned off LA injectable before the end of Step 3 will enter step 4. Participants will take oral ART locally sourced.

Duration of Study:
Steps 1-3 combined are a total of 128 weeks. Step 4 lasts 52 weeks. The study provides ART in steps 1-3 and participants will transition to locally sourced ART for step 4.

Compensation Provided

For more information on this study at CWRU/UH AIDS Clinical Research Site please contact:

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