CWRU/UH AIDS Clinical Research Site
AIDS Clinical Trials Group Study #5377 (TRIO)
Provider Summary

A Phase I, First-in-Human, Ascending Dose Study of SAR441236, a Tri-specific Broadly Neutralizing Antibody, in Participants with HIV

Version 2.0 w/LOA#1

Brief Summary: A5377 is a phase I, first-in-human, two-arm, ascending dose study of SAR441236. SAR441236, a tri-specific broadly neutralizing antibody (bNAb), has been engineered to recognize three parts of the HIV virus in one antibody and to neutralize the ability of the virus to infect cells. In Arm A, three successive dosing groups of antiretroviral-treated, virologically suppressed participants will each be randomized to receive a single intravenous dose of SAR441236 or placebo. A fourth cohort will receive multiple (four) infusions. In Arm B, four to five successive escalating dosing cohorts of antiretroviral naïve, viremic participants will each receive a single intravenous dose of SAR441236.

Objectives:

- To evaluate the safety and tolerability of single ascending doses of SAR441236 in virologically suppressed participants and in treatment naïve viremic participants, and of multiple doses in virologically suppressed participants.

- To evaluate the PK of single ascending doses of SAR441236 in virologically suppressed participants and in treatment naïve, viremic participants, and of multiple doses in virologically suppressed participants.

- To evaluate the antiviral activity of a single dose of SAR441236 in treatment-naïve, viremic participants with HIV.

Inclusion/Exclusion Criteria:

Adults living with HIV, 18 to 70 years of age
Negative active hepatitis C infection and negative hepatitis B surface antigen

Arm A: **(Enrollment completed)**

- Receiving combination (three-drug) antiretroviral treatment (ART) for at least 12 months, with no changes in ART regimen within the 12 weeks prior to entry.
- Within 12 months prior to study entry and before screening, at least one plasma HIV-1 RNA below the limit of quantification
- A single HIV-1 RNA $\geq$ 50 but < 200 at least 6 months prior to screening is permitted if followed within 2 months by an HIV-1 RNA < 50.
- HIV-1 RNA below the limit of quantification of any assay within 45 days of entry
- CD4+ count of ≥200 cells/mm^3

Arm B: **(Currently enrolling)**

- No prior use of ART, including pre-exposure prophylaxis (PrEP) at any time.
- HIV-1 RNA >5000 and <200,000 copies/mL
- CD4+ cell count of ≥350 cells/mm^3
- Willing and able to start ART by Day 28 of the study

Treatment:

Arm A**:** ART-treated, virologically suppressed participants will be assigned sequentially to one of four Dosing Groups and will be randomized 2:1 in a double-blind fashion to receive either SAR441236 or placebo.

The Arm A Dosing Groups are:

- Dosing Group 1: 1 mg/kg SAR441236 or placebo (one infusion)
- Dosing Group 2: 3 mg/kg SAR441236 or placebo (one infusion)
- Dosing Group 3: 10 mg/kg SAR441236 or placebo (one infusion)
- Dosing Group 4: 30 mg/kg SAR441236 or placebo (four infusions, one every 12 weeks)

Participants in Arm A will continue to take their non-study-provided anti-HIV medications throughout the study.

Arm B: ART-naïve, HIV viremic participants will be assigned sequentially to one of the Dosing Groups and will receive one open-label infusion of SAR441236.

The Arm B Dosing Groups are:

Dosing Group 5: 1 mg/kg SAR441236
Dosing Group 6: 3 mg/kg SAR441236
Dosing Group 7: 10 mg/kg SAR441236
Dosing Group 8: 30 mg/kg SAR441236
(Dosing Group 9: 0.3 mg/kg SAR441236, only if testing a lower dose is warranted)

Participants in Arm B will initiate non-study-provided ART on Day 28 or earlier if an ART initiation criterion is met.

For Arms A and B, SAR441236 or placebo will be given as an intravenous infusion over 30 or 60 minutes.

On the day of the infusion, blood will be collected over 24 hours, so participants may need to stay in the clinic overnight.

Duration of Study:

Participants will be followed on study for 24 weeks, with the exception of participants in Arm A Dosing Cohort 4 who will be on study for 72 weeks.

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

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