

RV 397 Statistical Analysis Plan

Safety and Therapeutic Efficacy of the Broadly Neutralizing HIV-1 Specific Monoclonal Antibody VRC01 during Analytic Treatment Interruption in Patients who Initiated Antiretroviral Therapy During Early Acute HIV Infection

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In Collaboration with
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STATISTICAL ANALYSIS PLAN

Baseline characteristics including demographics and laboratory measurements will be summarized using descriptive statistics.

The analysis of study data will be primarily descriptive, with emphasis on tabular and graphical displays. Summary statistics will be calculated, along with point and interval estimates of solicited and unsolicited adverse event and immune response rates. This study is exploratory, and any statistical inferences will be hypothesis generating, and not confirming.

1 Primary Endpoints

The primary efficacy endpoint is sustained virologic control (HIV RNA <50 copies/mL) at 24 weeks after ATI. The rate of virologic control will be compared between treatment groups using a two-sided exact unconditional test with a significance level of 0.05.

To assess safety, summaries of the number and percentage of subjects experiencing any SAE, AE, or reactogenicity will be tallied by treatment group and presented along with two-sided exact 95% confidence intervals for the proportion.

For solicited AEs/reactogenicity, number and percentage of subjects experiencing each type of solicited sign or symptom will be tabulated by severity. For a given sign or symptom, each subject's solicited AEs will be counted once under the maximum severity for all assessments.

For unsolicited AEs, number and percentages of participants experiencing each specific adverse event will be tabulated by severity and relationship to treatment. For the calculations in these tables, each participant's adverse experience will be counted once under the maximum severity or strongest recorded causal relationship to treatment.

Further, frequency of solicited and unsolicited adverse events will be reported (together and separately) by system organ class, preferred term, and treatment group overall and at various timepoints throughout the study.

A complete listing of adverse experiences for each participant will provide details including severity, relationship to treatment type, onset, duration and outcome.

2 Secondary Endpoints

1. Time to viral rebound and level of rebound viremia after cessation of ART.

Time to viral load rebound will be described using a Kaplan-Meier estimator to account for possible censoring and compared between treatment groups using an exact log-rank test. Number of HIV RNA copies at the time of rebound viremia will be described using medians and range and compared between treatment groups using a Wilcoxon-Rank Sum test.

2. Time to ART resumption for any reason after cessation of ART

Time to ART resumption will be described using a Kaplan-Meier estimator to account for possible censoring and compared between treatment groups using an exact log-rank test.

3. Detectable HIV RNA via single copy assay at various timepoints, such as weeks 24 and 48, as compared to baseline at week 0.

Number of HIV RNA copies will be described using medians and range at baseline, week 24, and week 48 for subjects with HIV RNA <50 copies/mL by standard PCR. Change from baseline at week 24 and week 48 will be compared between treatment groups using a Wilcoxon-Rank Sum test.

4. CD4+ T cell count various timepoints, such as weeks 24 and 48, as compared to baseline at week 0. CD4+ T cell counts will be described using medians and range at baseline, week 24, and week 48. Change from baseline at week 24 and week 48 will be compared between treatment groups using a Wilcoxon-Rank Sum test.

5. Cell-associated HIV RNA and DNA in the peripheral compartment various timepoints, such as weeks 24 and 48, as compared to baseline at week 0. Cell-associated HIV RNA and DNA in the peripheral compartment will be described using medians and range at baseline, week 24, and week 48. Change from baseline at week 24 and week 48 will be compared between treatment groups using a Wilcoxon-Rank Sum test.

6. Neuropsychological battery performance at weeks 24 and 48, as compared to baseline at week 0. Neuropsychological data will be summarized using z-scores based on age-matched normative data when such data is available or as raw scores when not available. With either approach, individual performance can be compared longitudinally to determine the impact of the intervention on cognitive performance, the primary interest of the neuropsychological testing portion of this study.

7. Frequency of hospitalization and incidence of non-AIDS related conditions.

Frequency of hospitalizations will be summarized and described by treatment group, Number of hospitalizations can be compared between groups using a Wilcoxon-Rank Sum test and proportion of subjects experiencing a hospitalization will be compared using an exact unconditional test. Incidence of non-AIDS related conditions will be compared in a similar fashion.

Exploratory objectives will be analyzed in a similar fashion to primary and secondary objectives although if the rate of consent for invasive procedures is low then analyses may be primarily descriptive. Continuous variables will be described at each timepoint using medians and range. Change from baseline will be compared between treatment groups at weeks 24 and 48 using Wilcoxon-Rank Sum tests. If possible repeated measures models will be fit to account for within subject correlation and assess a treatment group effect. Binary endpoints will be compared between treatment groups using exact unconditional tests. Clinical characteristics will be summarized and described by treatment groups. Significance will be assessed using two-sided testing at the 0.05 level. Given the size and exploratory nature of the trial, adjustments for multiple comparisons will not be made.