MHRP

RV397:
Therapeutic Efficacy of Broadly Neutralizing HIV-1 Specific Monoclonal Antibodies in Thai Patients who Initiated Antiretroviral Therapy During Early Acute HIV Infection

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.

MHRP
U.S. MILITARY HIV RESEARCH PROGRAM

MHRP

Rationale for this Study

- The main goal is to evaluate
  - Viremic control < 50 copies/ml after interruption of ART in early treated acutely infected patients
  - Potential endpoint--$VS_{LLD}OT_{weeks:}$ "Virologic Suppression Off Therapy" defined by lower limit of detection of assay for a duration of x weeks.
- Unique intervention
  - VRC01 broadly neutralizing antibody can suppress viremia
- Unique population
  - Early treated acutely infected subjects in the RV254/SEARCH010 study with extremely low HIV reservoir size

MHRP

Study Schema

Subjects treated with ART during
Fiebig I to III (neg HIV IgG) acute HIV, ART for ≥ 2 years,
HIV RNA < 50 (n=24)
ART interruption at week 0

VRC01 monoclonal antibody,
40mg/kg IV q 4 weeks
for 6 months (n=18)

Placebo IV q 4 weeks for 6
months (n=6)

Primary endpoints at week 24
Frequency of sustained viremic control ($VS_{50}OT_{24\ wks}$)
following ART interruption, safety of VRC01
FU to week 48

Objectives

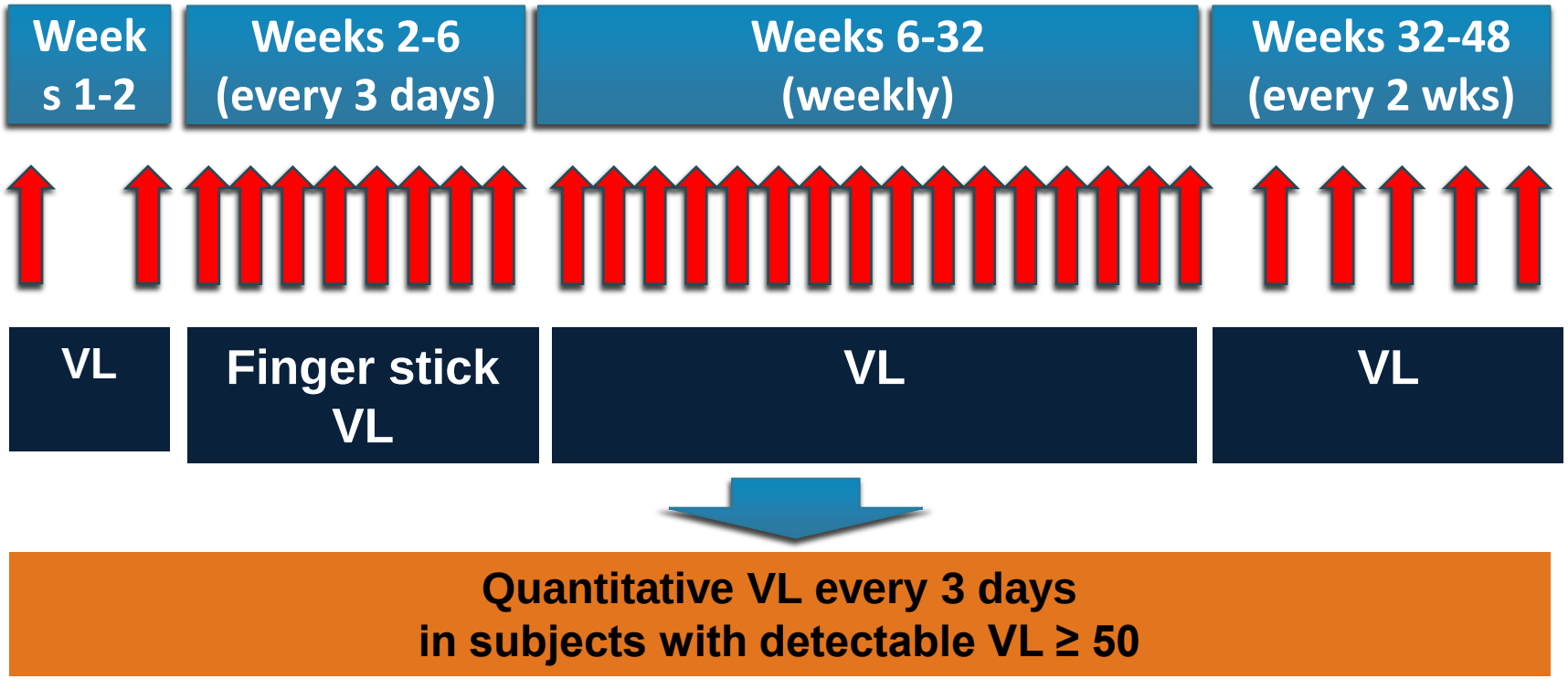
- Primary objectives
  - To evaluate the safety of VRC01 administration at the time of ATI.
  - To evaluate the efficacy of VRC01 in achieving sustained viremic control at 6 months following ATI.
- Secondary objectives: assess the impact of VRC01 on
  - Viral dynamics following ATI
  - Clinical characteristics of HIV infection following ATI
  - CD4 preservation following ATI
  - HIV reservoir replenishment and expression following ATI
  - Markers of immune activation following ATI

Population and Key Eligibility Criteria

- Recruited from the RV254 cohort at the Thai Red Cross in Bangkok, Thailand
  - 18-50 years old
  - Started on ART during AHI (Fiebig I-III)
  - Prescribed ART for ≥24 mo
  - HIV-1 RNA <50 copies/mL for ≥12 mo
  - Undetectable integrated HIV DNA in PBMCs in the last 6 months
  - CD4 >400 cells/mm^3
  - No HIV-related illness in last 6 months
- Exclusions: pregnancy, hepatitis B, hepatitis C, drug/alcohol abuse, psychiatric disorder

MHRP

Viral Load Monitoring during Treatment Interruption



Criteria for ART Resumption

- HIV-1 RNA >1,000 copies/mL on 2 consecutive determinations at least 3 days apart.
- HIV-1 RNA rise of ≥ 0.5 $\log_{10}$copies/ml per day (if last HIV-1 RNA is above 1000 copies/mL)
- Any HIV-1 RNA >10,000 copies/mL
- CD4 <350 cells/mm^3 twice over 2 weeks
- CD4 decline > 50% from baseline prior to ATI
- Clinical progression to CDC Category B or C disease
- Acute retroviral syndrome
- Pregnancy

Safety monitoring

- Study pause or termination
  - Automatic pause if one participant experiences a grade 5/probably or definitely related grade 4 event

- Protocol safety review team
  - Review all adverse events
  - Review aggregates of adverse events weekly

Justification for the Control Arm

- Blinded, randomized study design is required
  - Attribution of success due to VRC01 might be compromised
    - Enrolled subjects are early treated persons who have undetectable integrated HIV DNA; therefore, a likelihood of achieving viremic control following ART interruption regardless of intervention
- Analytic treatment interruptions can be performed safely
  - Close monitoring
  - Early resumption of ART