The acute, or first stage of HIV infection immediately follows exposure to the virus and occurs before common tests to diagnosis HIV are able to identify infection. It is during this stage that the virus begins to replicate and invade the immune system.

In order to better understand how the immune system responds during the critical moments of early infection, MHRP launched two innovative cohort studies in Thailand and East Africa, RV217 and RV254.

**RV217/Early Capture HIV Cohort Study (ECHO)**

Since 2009, MHRP has led an ambitious multi-site study in East Africa and Thailand that follows a group of high-risk volunteers, tracking their HIV status and characterizing their progression through the acute stages of HIV infection. This prospective study has captured samples from some of the earliest stages of HIV infection – in some cases within days – along with blood samples before infection. As of mid 2016, more than 2,000 volunteers have been enrolled in RV217 in East Africa and Thailand and 121 incident cases have been observed.

The study, published in *The New England Journal of Medicine* in May, 2016, found that early events in HIV infection impact future course of the disease in individuals. Specifically, viral load set-point is established at resolution of acute viremia, within 18-42 days after infection. Researchers also found that clinical presentation of HIV infection was less symptomatic than previously believed. The Protocol Chair for this study is Merlin Robb, MD, MHRP’s Deputy Director for Clinical Research. RV217 is funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. NIH, and conducted at four MHRP sites in East Africa and Thailand.

**Functional Cure Studies**

MHRP is launching “cure” studies within these cohorts. These small studies will evaluate strategies aimed at inducing HIV remission (controlling virus without the need for long term anti-retroviral treatment). Examples of the interventions are giving HIV vaccines or antibody against HIV. In order to provide maximum safety to the volunteers who come off ART, researchers will screen for viral load every 3-7 days and will immediately resume ART if volunteers do not control the virus.

In late 2016, MHRP will evaluate the safety and impact of a novel therapeutic strategy using broadly neutralizing human monoclonal antibodies (mAb) administered to volunteers in both of these acute cohorts. These studies will be testing (VRC01), a broadly neutralizing human mAb developed at the VRC, NIH that targets the HIV-1 virus. Plans are also underway to test a vaccine candidate in the RV254 cohort.

“**It is important to us to capture people with acute infection because if we want to cure people, this may be our point of opportunity to intervene.**”

Dr. Merlin Robb
RV217 Protocol Chair
In Thailand, MHRP researchers collaborate with the Thai Red Cross AIDS Research Center to identify acutely infected individuals and place them onto ART immediately. Researchers have found that this very early initiation of ART results in immune restoration and a very small or undetectable reservoir of HIV DNA, very similar characteristics to “elite” HIV controllers.

Samples from more than 170,000 individuals have been collected from voluntary testing and counseling clinics in Bangkok. Samples found to be negative with routine testing then underwent a Nucleic Acid Test (NAT). So far, 390 people found to be acutely infected have been enrolled in this cohort, and nearly all of them opted to start ART within days of discovering their status. The Protocol Chair for this study is Jintanat Ananworanich, MD, PhD, MHRP’s Associate Director for Therapeutics Research.

RV254/SEARCH is a collaboration between the Thai Red Cross AIDS Research Centre, the University of California San Francisco, and the Department of Retrovirology, US Army Medical Component, Armed Forces Research Institute of Medical Sciences (USAMC-AFRIMS).

“By focusing on the earliest stages of infection, scientists hope to understand what’s needed to create an effective HIV vaccine and inform research towards a functional cure.”

COL Nelson Michael
MHRP Director

Earliest Stages of HIV Provides Critical Information

MHRP researchers are exploring immune responses during this early phase of infection, along with genetic changes in the virus. They also work with leading HIV researchers to analyze data from the two cohorts and identify additional research questions that the cohorts can help answer.