Building on RV144: Large-Scale HIV Vaccine Trial to Go Forward in South Africa

On May 18—HIV Vaccine Awareness Day—NIAID announced that a follow-up efficacy study using a similar vaccine used in RV144 will move forward to efficacy testing in Southern Africa. This new study, called HVTN 702, will begin in late 2016 and will conclusively determine whether the regimen is safe and effective at preventing HIV infection among South African adults. The study will be the first large-scale clinical trial of an HIV vaccine in more than seven years.

MHRP is part of the leadership group that planned this study, called the Pox-Protein Public-Private Partnership, or the P5—a diverse set of public and private organizations, committed to building on the success of RV144. This group has worked to both improve and prolong the protective effect seen in the RV144 study by testing vaccine boosts and adjuvants to increase efficacy. MHRP has been conducting two smaller follow-up studies in Thailand—RV305 and RV306—that have informed the regimen that will be used in HVTN702.

This pivotal Phase 2b/3 trial sponsored by NIAID will enroll 5,400 HIV-uninfected men and women ages 18 to 35 years who are at risk for HIV infection. NIAID and the Bill & Melinda Gates Foundation will co-fund the study, and the NIAID-funded HIV Vaccine Trials Network will conduct it. Results are expected in late 2020.

The HVTN 702 vaccine regimen includes a canarypox-based vaccine called ALVAC-HIV and a bivalent gp120 protein subunit vaccine. Both ALVAC-HIV (supplied by Sanofi Pasteur) and the protein vaccine (supplied by GlaxoSmithKline Biologicals) have been modified from RV144 to be specific to HIV subtype C, the predominant HIV subtype in southern Africa. In addition, the protein vaccine in HVTN 702 is combined with a different adjuvant than the one in RV144 in the hope of generating a more robust immune response. Finally, the HVTN 702 vaccine regimen will include booster shots at the one-year mark in an effort to prolong the early protective effect observed in RV144.

RV217 Allows for Characterization of Acute HIV Infection

In a study by MHRP, published in The New England Journal of Medicine, scientists enrolled and intensively followed a cohort of high-risk individuals, tracking their HIV status and characterizing the disease through the acute stages of HIV infection.

This landmark study (RV217) is a prospective cohort of individuals from East Africa and Thailand at high risk for HIV infection, who had blood drawn twice weekly for qualitative plasma HIV RNA nucleic acid testing (NAT), a highly sensitive assay that allows for early detection of the virus. This is the first study to characterize the evolution of symptoms and signs prospectively in a large number of persons with acute infection.

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Early Capture HIV Cohort (ECHO) Study Site Recognized as Official AFRIMS Annex

On March 16, Major General Sayan Sawatsri, Director General of Royal Thai Army AFRIMS, hosted a ceremony recognizing the recent designation of the Early Capture HIV Cohort (ECHO) study site as an official annex of AFRIMS, formally named the “Armed Forces Research Institute of Medical Sciences; Pattaya Annex.”

AFRIMS Director COL Solits and the President of the Senate of Pattaya were on hand at the ECHO Center ceremony, along with representatives from nearly all NGO and HIV/AIDS care providing organizations in the Pattaya area.

MHRP Begins VRC01 Therapy Study in Acutely Infected Volunteers

In April, MHRP initiated a phase 1 clinical trial to evaluate the safety and impact of a novel therapeutic strategy using broadly neutralizing human monoclonal antibodies (mAb) administered during acute HIV infection.

Broadly neutralizing monoclonal antibodies have the potential to treat HIV by reducing virus particles’ ability to cause infection and by mediating the destruction of virus-producing cells. This placebo-controlled proof of concept study will evaluate the impact of VRC-HIVMABo60-00-AB (VRC01), a broadly neutralizing human mAb that targets the HIV-1 virus.

The study will be carried out at sites in Kenya, Thailand, Tanzania and Uganda. VRC01 or a placebo will be administered to 24 volunteers who are in the early acute stage of HIV infection, within 21 days of contracting the virus. The main objectives of the trial will be to determine the safety of VRC01 in individuals with acute HIV infection and to examine whether VRC01 has an impact on plasma viremia compared to the use of antiretroviral therapy (ART) alone.

MHRP’s previous studies of acute infection have shown that during these earliest stages of infection, the viral load set point is established, which determines how fast the disease progresses. To achieve HIV remission, this may be a critical opportunity to intervene.
Joint West Africa Research Group to Foster Biopreparedness

The West African Ebola outbreak highlighted gaps in global public health response and a lack of countermeasures. The DoD invested in a strategic initiative called the Join West Africa Research Group (JWARG) to leverage existing research platforms and relationships to improve biopreparedness in the region.

This new program is a collaboration between MHRP/WRAIR, Naval Medical Research Unit 3-Ghana Detachment and the Austere Environment Consortium for Enhanced Sepsis Outcome. Partners will build upon existing programs in Nigeria, Ghana and Liberia with initiatives focused on lab strengthening, bio-surveillance and countermeasure development.

The goal of the collaboration will be to conduct research that builds capabilities complementary to the work of USG partners that will contribute to health diplomacy in the region, engage key community stakeholders and encourage adherence to Good Participatory Practices.

MHRP has been developing research infrastructure and capability in Nigeria for the last 10 years. The Walter Reed Program-Nigeria began an Ebola vaccine study in 2015 and will begin another (RV456) in 2016.

Laboratory training began in May, and clinical training will take place in June. The trainings will focus on skills needed to execute the upcoming JWARG biosurveillance protocol.

HIV Infant Tracking System to Improve Outcomes for HIV-Exposed Infants in Tanzania

There have been significant advances in the management of HIV/AIDS over the years. However, managing HIV-exposed infants has been hampered by challenges of tracking the testing process and communicating results to the mothers for initiation of care in a timely manner. Early infant diagnosis (EID) of HIV infection is essential to ensure timely initiation of ART and reduce the high morbidity and mortality that occurs among HIV-infected infants.

The HIV infant tracking system (HITSystem) is a web-based mHealth intervention developed by Global Health Innovations (GHI) that seeks to improve EID outcomes. Since 2013, MHRP’s PEPFAR program in Tanzania in collaboration with GHI has been piloting the HITSystem in the Southern Highlands.

Once entering the HITSystem, an infant is tracked up to 18 months of age. The system is able to communicate with the mother/healthcare worker via a mobile phone message notifying her to go to the clinic once test results are ready for pick-up. If an intervention is skipped, HITSystem utilizes automated alerts to ensure prompt action from PMTCT providers and laboratory technicians using a computer installed at the sites and at the main PCR laboratory.

Since the initiation of the HITSystem in Tanzania’s Southern Highlands in 2013, it has been piloted in over 100 Health facilities offering EID services for more than 6,000 infants with very promising outcomes.

The programmatic turnaround time from sample collection to reporting results to the healthcare worker and mother has reduced drastically from over 2 months to 3 weeks on average and more than 91% of the mothers have been notified of their infants test results.

Based on these highly positive outcomes, there are plans to roll out the HITSystem to all EID facilities in the Southern Highlands of Tanzania and to improve follow-up testing at 13 and 18 months of age for the infants who were negative at the initial test.
MUWRP Research Associate Awarded Fulbright Scholarship

Allan Omalla, a research associate at Uganda’s Makerere University Walter Reed Project (MUWRP), has been awarded a 2016 Fulbright Junior Staff Development grant to pursue a Ph.D. in immunology, pathology and infectious diseases at the University of Nebraska Medical Center, Omaha.

The Fulbright scholarship is for 2 years and the remaining years will be supported through a fellowship awarded by the lab he where he will conduct his research.

“I do anticipate that I will now be better positioned to carry out next phases of my research that were limited probably due to unavailable instrumentation and in some instances lack of suitable experience,” said Omalla. “Under the tutelage of established researchers from UNMC, continued collaboration with my mentors from MUWRP, Makerere University and MHRP; I believe we will now be better placed to develop and test new basic science concepts that seek to address crucial health problems in Sub-Saharan Africa.”

Omalla’s research interests lie in understanding the overall impact of chronic immune activation on HIV-1 pathogenesis, especially as it relates to the unique immune activation profile observed in most Sub-Saharan Africans. He was recently awarded $100,000 by GlaxoSmithKline to study the effects of plants commonly used by HIV-1 patients in Uganda on HIV-1 T cell immune activation. He is currently working on this research and hopes to finalize it prior to leaving the MUWRP labs for Omaha.

MHRP Research Physician Examines Overlap in HIV and Tuberculosis

Tuberculosis recently overtook HIV as the top infectious disease killer worldwide, and in 2015, 1 in 3 HIV deaths were due to TB. With a research background in multi-drug resistant tuberculosis, MHRP research physician Dr. Elizabeth Harausz is well positioned to battle these entangled epidemics.

In November, Dr. Harausz traveled to Geneva, Switzerland, to advise the World Health Organization on their guidelines for the treatment of drug-resistant tuberculosis in children.

“Until now, the pediatric recommendations have been based on data from adults,” said Dr. Harausz. “Kids have been ignored in treatment and diagnostics, and they need their own guidelines because they get different types of the disease and need different doses of medicines.”

Dr. Harausz’s research interest in tuberculosis stems from the infectious disease fellowship she completed at Case Western Reserve University, where she worked alongside some of the leading researchers in adult and pediatric TB.

Following her infectious disease fellowship, Dr. Harausz worked for the Desmond Tutu TB Centre in Cape Town, South Africa, where she managed an ambitious meta-analysis project examining treatment and outcomes of more than one thousand pediatric patients with multi-drug resistant tuberculosis. She is currently working on the first paper to come from that analysis.

Dr. Harausz joined MHRP in August of 2015 and will expand the program’s portfolio of tuberculosis research. Some of her upcoming work will include a protocol examining novel methods to screen HIV positive people for TB and an evaluation of the TB treatment program at MHRP’s Nigeria site.

MHRP Welcomes...

Dr. Farrukh Rizvi joined MHRP as HIV Research Chief of Staff in January. Dr. Rizvi comes to MHRP after working at Sanofi and MRMC, and he has more than 25 years of academic and industry experience in microbiology, vaccinology, immunology, and infectious diseases.

Dr. David Brett-Major officially joined MHRP in April as Network Associate Director for Clinical Research. An internal medicine and infectious diseases physician, Dr. Brett-Major worked on the ground in West Africa during the Ebola outbreak and most recently published a paper on taking lessons from previous Zika outbreaks to respond to its current re-emergence.

Dr. David Elkins is MHRP’s new Executive Director of Global Health Programs in Tanzania. He has 16 years of experience with USAID, DFID and AusAID and most recently served as team lead of the Fiji Health Sector Support Program.