

MHRP EXCHANGE

NEWS FROM THE U.S. MILITARY HIV RESEARCH PROGRAM
AT THE WALTER REED ARMY INSTITUTE OF RESEARCH



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New HIV Vaccine Trial to Test ALFQ Adjuvant, Fractional Dosing



MHRP and collaborators recently launched a Phase 1 trial in Thailand that will evaluate two HIV vaccine candidates with and without the Army's novel ALFQ adjuvant to gain insight into late boosting strategies and the effects of fractional dosing.

This study builds on an earlier MHRP trial, RV306, which administered an HIV vaccine regimen to participants and included a late boost at either month 12, 15 or 18. Results showed that longer intervals between the primary vaccination series and late boost improved immune responses.

The new trial, RV546, is a randomized double-blind study that is enrolling a total of 120 participants from the earlier RV306 study. The trial will test two different HIV protein boosts.

The vaccine candidate A244 is a protein vaccine provided by Duke University and is similar to the "E" component of the AIDSVAX®B/E vaccine that was safely administered to more than 9,000 participants in MHRP's RV144 Thai trial, the first human vaccine trial to demonstrate modest efficacy in preventing HIV-1 infection. IHV01 is an HIV-1 subtype B protein vaccine developed by the University of Maryland Institute of Human Virology and that was shown to be safe and to induce frequent immune responses in a previous Phase 1a trial.

Adjuvants are vaccine components that help activate the immune system and improve immune responses. The ALF family of adjuvants was developed by MHRP scientists at WRAIR, and preclinical studies have shown it to be a potent adjuvant. A leading formulation, ALFQ, is being used to enhance immune response with several vaccines in testing, including those for COVID-19 and malaria. This is the first use of ALFQ with a candidate HIV vaccine.

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Trial in Thailand Evaluates Gonococcal Vaccine

MHRP and collaborators at two sites in Thailand are participating in the MAGI study, a NIAID-sponsored Phase 2 trial of a meningococcal Group B vaccine, Bexsero, in preventing gonococcal infection. The vaccine is currently FDA-approved for prevention of bacterial meningitis, but data suggest it may also have activity against gonorrhea.

The Thai Red Cross AIDS Research Center and the Armed Forces Research Institute of Medical Sciences - Royal Thai Army Clinical Research Center are together expected to enroll approximately 1,000 participants who are at risk for gonorrhea.

Enrollment at the Thai sites has been successful despite recent challenges due to COVID-19 surges in the country. As of the beginning of April, 316 participants were enrolled from the two sites in Thailand out of a total of 475 enrolled across all eight active sites in the multinational study.

MHRP's participation in the MAGI trial is overseen by the program's Department of Epidemiology and Threat Assessment (DETA). DETA conducts epidemiologic studies that improve understanding of circulating infectious disease threats and facilitate site capacity and community engagement. DETA has a growing portfolio of interventional studies that enroll military and civilian populations, with an emphasis on testing novel strategies to prevent HIV and other sexually transmitted infections.

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MHRP Begins Preclinical Testing of mRNA HIV Vaccine

The first immunizations began early this year for MHRP's first preclinical animal study of an mRNA HIV vaccine.

Messenger RNA, or mRNA, vaccines instruct the body to make selected viral proteins, and ultimately train the immune system to recognize and eliminate the virus. Novel immunogens termed "structural mosaics" have been co-designed by Barton Haynes, of Duke University, and Bette Korber, of the Los Alamos National Laboratory, to induce antibodies targeting the V1V2 region of the HIV envelope. These structural mosaics will be expressed through vaccination with the mRNA.

The current study will evaluate the efficacy of structural mosaic mRNA vaccine with or without a protein vaccine boost in the protection of rhesus macaques from repeated challenges with SHIV, a virus that mimics HIV infection in primates.

Researchers will examine cellular, humoral and innate immune responses induced by the candidate vaccines to determine their immunogenicity, the impact of the protein boost and potential mechanisms of protection. The vaccines being tested by MHRP were made by the Duke Human Vaccine Institute in collaboration with the University of Pennsylvania. The Armed Forces Research Institute of Medical Sciences (AFRIMS) is conducting the study.



MOCHI Cohort Study Launches in Kenya



MHRP began enrolling participants in Homa Bay, Kenya, for a new prospective observational study of HIV and other sexually transmitted infections (STIs) called the Multinational Observational Cohort of HIV and Other Infections (MOCHI).

MOCHI will estimate HIV and STI incidence and track the evolution of participants' risk and healthcare-seeking behaviors. The study also facilitates sites' preparedness for future HIV and STI prevention studies by building capacity, evaluating site recruitment and retention and maintaining relationships with affected communities.

The study will engage community members who may participate in future studies, including those designed to test HIV prevention tools as well as interventions to achieve HIV remission. Every 12 weeks, participants respond to behavioral questionnaires and receive clinic-based HIV and STI testing. Participants are also provided HIV home testing kits for use between scheduled visits. Participants diagnosed with HIV may opt to begin antiretroviral therapy and will continue with follow-up visits to monitor early events in HIV pathogenesis and response to antiretroviral therapy. The study is employing novel biometric techniques, like iris scanning, for participant identification.

MOCHI is designed to provide one unified protocol and set of data collection instruments for deployment across multiple sites in diverse regions of world. Homa Bay, a fishing town on the shores of Lake Victoria, has one of the highest HIV prevalence rates in Kenya. MOCHI is MHRP's first study at the site. Once the MOCHI study model is established, MHRP plans to expand to additional countries and regions in the coming years, with a target of enrolling 500 participants in each country where the study is opened.

Walter Reed Program-Nigeria Pilots Community-Led Monitoring to Improve HIV Prevention, Care and Treatment Services

The Walter Reed Program-Nigeria (WRP-N) has completed the pilot phase of a PEPFAR-funded initiative to conduct community-led monitoring of HIV services across 10 states in Nigeria.

Community-led monitoring (CLM) focuses on gathering honest feedback from recipients of HIV services by other community members who are themselves living with HIV. Feedback is collected in a systematic way intended to translate into actionable improvements. WRP-N gathered more than 30 civil society organization representatives and leaders to develop data collection tools, receive training on data collection methodologies and implement the pilot initiative.

"What is unique about community-led monitoring is the trust that exists between the beneficiaries and the people we send out to interact with them," said Dr. Murphy Akpu, Deputy PEPFAR Country Coordinator in Nigeria. "Beneficiaries do not want to offend staff providing the services by critiquing them, so community-led monitoring allows them to speak freely and provide honest feedback."

Community health workers visited more than 200 sites offering PEPFAR-supported HIV prevention, care and treatment services during the pilot program. The civil society organization representatives conducted more than 350 focus groups and administered more than 4,450 questionnaires to collect feedback. Service clients were able to discuss their perceptions of the services, including challenges to access and service preferences.

"This innovation is very unique because it shifts our community members from a point of vulnerability and weakness to one of strength, power and knowledge," said Acapel Mbanusi, a community health worker and key population activist who participated in the monitoring initiative.

"Most of the clients I had the opportunity to interact with expressed their joy and really felt so special to be able to express their experiences accessing HIV services."

MHRP Supports PEPFAR in the Philippines



In 2021, MHRP, along with the Armed Forces Research Institute for Medical Sciences (AFRIMS) and the Department of Defense HIV/AIDS Prevention Program (DHAPP), received PEPFAR funding to develop a military-military partnership in the Philippines.

The first activities under this partnership focus on policy assessment, lab strengthening, clinical training, and diagnostic capabilities to improve HIV prevention, testing, treatment and surveillance. These activities are coordinated through the Joint United States Military Assistance Group (JUSMAG)-Philippines as part of the US DoD's security cooperation partnership with the Armed Forces of the Philippines (AFP).

In March, the Philippines program, in collaboration with the Victoriano Luna Medical Center TB Clinic, supported a World TB Day Virtual Conference. The half-day seminar featured lectures from senior AFP specialists on topics including burden of TB in the military and impact of COVID-19 on TB control; TB/HIV co-infection and TB preventive therapy; and Destigmatizing TB, HIV and other diseases affecting the military. Over 180 AFP health workers attended the event. The AFP also hosted a World AIDS Day virtual event, which included a presentation from MHRP Director Col. Julie Ake on HIV vaccines.

Headquartered in Bangkok, AFRIMS is a joint undertaking between the U.S. and Thai militaries with satellite surveillance and research sites across Southeast Asia. AFRIMS scientists have performed surveillance and developed diagnostic, preventive, and therapeutic countermeasures against infectious diseases for nearly 60 years. This new PEPFAR initiative will leverage and strengthen the established relationships that WRAIR and AFRIMS have built through the Philippines AFRIMS Virology Research Unit (PAVRU).

Monoclonal Antibody Research Seeks New HIV Prevention Tools



MHRP's B cell biology lab, led by Dr. Shelly Krebs, leverages data from the RV217 acute HIV infection cohort and other program clinical research, to identify broadly neutralizing antibodies that may be used to develop new products to add to the existing HIV prevention toolkit.

One study led by the Krebs group showed that elevated B cell immune interactions with the envelope glycoprotein (Env) on the surface of HIV during the

first month of HIV infection predict the development of broadly neutralizing antibodies (bNAbs) years later.

"Either there's something special about the founder virus that exposes vulnerable epitopes for B cells interact with to create those broadly neutralizing antibodies, or there's something special about the people and those B cells themselves that are able to mount those responses," explained Dr. Krebs.

Determining which immunological mechanisms contribute to the development of bNAbs during HIV infection is a major goal to inform vaccine design. Gathering information from people living with HIV who produce bNAbs can provide valuable insight into mechanistic aspects of the immune system that initiate or guide bNAb development.

In the absence of an HIV vaccine, infusions of broadly neutralizing antibodies could themselves be a preventive tool. Future research strategies will involve discovering which monoclonal antibody combinations provide the broadest coverage against circulating strains of HIV. So far, MHRP has identified novel mAbs MHRP01 and MHRP02 and demonstrated them to be broad and potent against a diverse panel of HIV strains.

Comparative Adjuvant Study Fully Enrolls in Kenya

Despite challenges faced during the COVID-19 pandemic, MHRP's Phase 1 comparative adjuvant study, RV460, was fully enrolled in Kericho, Kenya. The experienced community engagement team worked with dedicated participants to ensure the safe implementation of study recruitment and visit procedures. The study is designed to enroll 126 participants and completed enrollment in December 2021.

RV460 evaluates experimental prime/boost HIV-1 vaccine regimens formulated with combinations of different adjuvants, including ALFA, which was developed by scientists in MHRP's Laboratory of Adjuvant and Antigen Research. The study is led by MHRP scientists in partnership with the Kenya Medical Research Institute/Walter Reed Project Clinical Research Center in Kericho, where the study takes place.



AFRICOS Informs HIV Service Delivery in its Ninth Year



MHRP's African Cohort Study (AFRICOS), a multisite, long-term study that evaluates HIV prevention, care and treatment services it supports through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), is entering its ninth year in 2022.

Over the past year, MHRP researchers and collaborators published 13 papers in peer-reviewed journals. A sampling of cohort research reveals the breadth of research conducted under AFRICOS:

- Analysis of longitudinal data revealed that viral load suppression improved dramatically with the transition to the new first line regimen of tenofovir-lamivudine-dolutegravir (TLD), and that even people living with HIV who were well controlled on their old regimen had significantly lower rates of virological failure over time if they switched to TLD than if their treatment remained unchanged.
- AFRICOS also allowed researchers to examine how COVID affected participants' HIV treatment. They observed decreases in clinic visit adherence early in the pandemic, and an increase in viral suppression later.
- Researchers assessed trends in self-reported experienced stigma and the association of experienced stigma with ART adherence and viral suppression among people living with HIV enrolled in AFRICOS. HIV-associated stigma was associated with poor self-reported ART adherence and unsuppressed viral load.
- AFRICOS collaborators also determined that cumulative time with symptoms of depression is associated with increased mortality in people living with HIV.

The AFRICOS study has enrolled more than 3,700 participants as of September 2021, and in the coming year will evaluate how initiatives like multi-month ART dispensing impact adherence and viral suppression.

WRP-T Mobile Male Circumcision Vans Deployed at Week-long Event

Studies have shown medical male circumcision reduces men's risk of heterosexual acquisition of HIV by 59%. Since 2016, the Walter Reed Program-Tanzania (WRP-T), with PEPFAR support, has deployed mobile vans to offer voluntary male mobile circumcision (VMMC) services in hard-to-reach communities. Over a 6-month period in 2021, WRP-T was able to perform 6,664 circumcisions using two mobile vans.

WRP-T's VMMC program has shown that the vans can be highly effective in reaching men 20-34 years old; 71% of their mobile-van clients fall into this age range. The vans can provide VMMC services in hard-to-reach communities, and they can also be deployed during large social gatherings to reach larger number of potential clients.

In December 2021, WRP-T stationed one of its VMMC vans at a Mbeya fairground during a week-long World AIDS Day commemorative event. Over 11 days at the fairground, the WRP-T team was able to perform 239 circumcisions. The average number of clients was 22 a day, which exceeded the 17 client a day average of the previous six-month period.



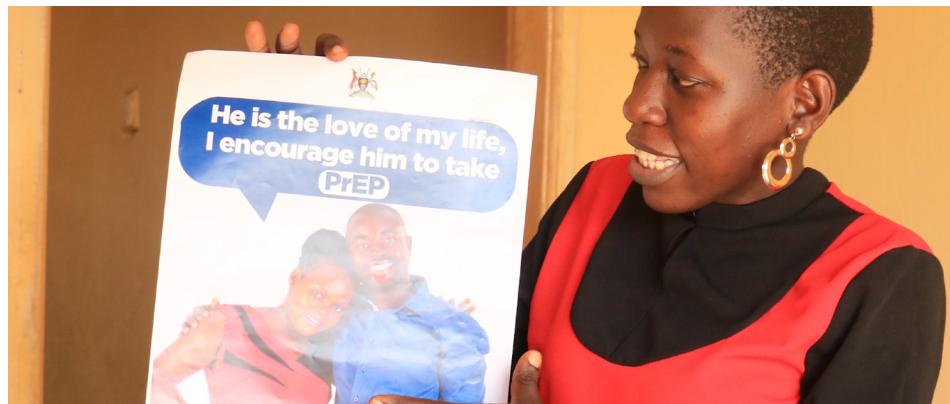
U.S. Ambassador Donald Wright, pictured here with lab supervisors, attendants and technicians, visited WRP-T's mobile clinic at World AIDS Day event fairgrounds.

Behavioral STI Intervention Piloted in Active-Duty Population

MHRP researchers have found that a behavioral intervention designed to decrease sexually transmitted infections (STIs) was feasible to implement in the military setting and was acceptable among a population of active-duty service members and medical beneficiaries who participated in this pilot study at Joint Base Lewis-McChord in Washington state. Findings were published in April in the journal *BMC Public Health*.

STI incidence has reached record numbers in the United States, with similar increases in the military. The Knocking out Infections through Safer sex and Screening (KISS) pilot intervention consisted of a one-time, small group session teaching STI/HIV knowledge and prevention, condom use skills, and interpersonal communication techniques. Following the session, participants' STI and HIV prevention knowledge increased significantly, and almost all reported that they intended to practice safer sex after the intervention.

PrEP Demonstration Project in Uganda Engages Communities



The Makerere University Walter Reed Project (MUWRP), MHRP's partner site in Uganda, is conducting a demonstration project to evaluate feasibility, acceptability and adherence to pre-exposure prophylaxis (PrEP) use among adolescent and young women at risk for HIV.

MUWRP works with clinics and community-based organizations to identify and mobilize key populations for prevention services. MUWRP also works with PEPFAR's DREAMS program beneficiaries, mainly adolescent girls and young women, to educate them about PrEP. Through engaging with the communities and understanding their specific needs, MUWRP has also successfully implemented PrEP in hard-to-reach areas like the fisher folk island communities.

To ensure that PrEP rollout is successful, MUWRP verifies health workers are well-trained, ensures the correct tools are provided, engages peers and recipients with the program and collaborates with the local government leadership.

Uganda has policies and training in place to guide the PrEP rollout process, including extensive reporting tools. These reporting tools are monitored on a weekly basis to ensure that PrEP rollout is reaching all targets as well as ensuring that recipients are receiving PrEP.

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Manufacturing protein vaccines can be complex and costly, which can limit supply. The fractional dosing component of RV546 will provide evidence for whether valuable vaccine can effectively be administered in smaller amounts to maximize supply.

RV546 is being conducted at the Mahidol University Vaccine Trial Centre and the Armed Forces Research Institute of Medical Sciences Royal Thai Army clinical sites in Bangkok, and vaccinations began in early February.

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