

## Fact sheet

### Understanding why vaccinations in the HVTN 702 Uhambo study were stopped

#### Study profile:

- HVTN 702, also referred to as Uhambo, is a Phase 2b/3 study that began in 2016 to test an experimental prime-boost vaccine regimen. It is based on the only vaccine regimen to date to show protection from HIV—the RV144 clinical trial conducted in Thailand, led by the U.S. Military HIV Research Program and the Thai Ministry of Health.
- The experimental vaccine regimen was adapted to the Clade C subtype of HIV that is predominant in southern Africa, where the pandemic is most pervasive.
- HVTN 702 was fully enrolled with 5,407 healthy, HIV-negative men and women between the ages of 18-35 years.
- HVTN 702 was conducted across 14 study sites in South Africa.

#### Outcome of an independent Data and Safety Monitoring Board (DSMB) analysis:

- The study has an independent Data and Safety Monitoring Board (DSMB) that reviews all data regularly to ensure the safety of participants and determine if the study should continue.
- When the timepoint was reached where there was enough data to determine whether the HVTN 702 Uhambo vaccines can prevent HIV infection, an interim DSMB review of the trial was held. This timepoint was when at least 60% of participants had been in the study for more than 18 months. The analysis looked at participants who were diagnosed with HIV after being in the study through 24 months.
- The DSMB assessment concluded that the experimental vaccine regimen we used in the trial did not prevent HIV infection. The vaccine did not increase or decrease the risk of acquiring HIV.
- The DSMB, based on the findings, resolved on 23 January 2020 at the meeting that the experimental vaccine regimen did not show any efficacy and that no further vaccinations with the experimental vaccines be administered.
- The DSMB expressed no concerns related to the safety of study participants.

#### Caring for study participants:

- No further injections of the experimental vaccine regimen will be administered.
- Participants will be progressively unblinded as to whether they received vaccine or placebo.
- Participants who have not completed follow-up will continue to be followed and the study protocol will be amended with specific information around follow-up.
- Participants will continue to receive HIV counseling, HIV testing and monitoring for safety during the follow-up period.

#### The next steps:

- The HVTN is initiating the process of study closure over the next year. As a start, all study participants are being informed in-person of this outcome by the study leadership at each of the trial sites in the country.
- Ethics Committees, local communities and other stakeholders such as the South African Health Products Regulatory Authority (SAHPRA) and National Department of Health were informed of this outcome.
- A protocol amendment is being prepared that will clarify the specifics around participant follow-up.

### Profile of the experimental vaccine regimen tested in HVTN 702:

- The HVTN 702 vaccine regimen consisted of two experimental vaccines: a canarypox vector-based vaccine called ALVAC-HIV and a gp120 protein subunit vaccine administered with MF-59 adjuvant. Adjuvants are used to enhance the body's immune response to the vaccine.
- Both ALVAC-HIV (supplied by Sanofi Pasteur) and the protein vaccine (supplied by GSK) were modified from the versions used in RV144 to be specific to HIV subtype C.
- Additionally, the protein subunit vaccine in HVTN 702 was combined with MF59, a different adjuvant than the one used in RV144, in the hope of generating a more robust and durable immune response. MF-59 has been approved by some regulatory agencies for use with some approved vaccines, but is still experimental in HIV vaccine research.
- Finally, the HVTN 702 vaccine regimen included booster shots at the one-year and 18 month timepoints in an effort to prolong the early protective effect observed in RV144.

### Other global efforts underway in pursuit of a safe and globally effective preventive HIV vaccine:

#### ***The Antibody Mediated Prevention (AMP) studies***

**HVTN 703/HPTN 081 – sub-Saharan Africa**

**HVTN 704/HPTN 085 – Brazil, Peru, Switzerland, US**

Fully enrolled, with **4,625** healthy, HIV-negative populations consisting of: 1) women in Sub-Saharan Africa between the ages of 18-40 years; and 2) men and transgender individuals in the Americas and Switzerland between the ages of 18-50 years who have sex with men. The two studies are underway in **11** countries: Botswana, Brazil, Kenya, Malawi, Mozambique, Peru, South Africa, Switzerland, Tanzania, United States and Zimbabwe. The AMP studies are testing whether a broadly neutralizing antibody (bnAb) called VRC01 can prevent HIV acquisition in people. The results of the two studies are expected in late 2020.

#### ***HVTN 705/HPX2008, also known as Imbokodo***

Fully enrolled, with **2,637** healthy, HIV-negative women in South Africa, Malawi, Mozambique, Zambia, and Zimbabwe between the ages of 18-35 years. Imbokodo is testing an experimental vaccine regimen designed to offer protection against a variety of global HIV strains. The results of the study are expected in late 2022.

#### ***HVTN 706/HPX3002, also known as Mosaico***

The study team aims to enroll **3,800** cisgender men and transgender people between the ages of 18-60 years who have sex with cisgender men and/or transgender people. The study will take place at 57 trial sites in Argentina, Brazil, Italy, Mexico, Peru, Poland, Spain and the U.S. Mosaico will evaluate an experimental vaccine regimen based on mosaic immunogens – vaccine components comprising elements from multiple HIV variants – that aims to induce immune responses against a wide variety of global HIV strains. The study is expected to conclude in late 2023.

### Global partners responding to a global epidemic:

HVTN 702 is part of a larger HIV vaccine research endeavor led by the Pox-Protein Public-Private Partnership, or P5—a diverse group of public and private organizations working to build on the RV144 trial. P5 members include NIAID, the Bill & Melinda Gates Foundation, and the South African Medical Research Council, which funded HVTN 702; the HIV Vaccine Trials Network, headquartered at the Fred Hutchinson Cancer Research Center in Seattle, which conducted HVTN 702; Sanofi Pasteur and GSK, which provided the study vaccines; and the U.S. Military HIV Research Program.