The HVTN 505 Study—Background

As HVTN investigators, our common goal is to develop a safe and effective HIV vaccine. The process of achieving that goal is incremental, building on what we learn from preclinical and clinical studies—both the disappointing and the encouraging results. While the vaccine tested in the previous Step Study didn’t prevent HIV infection, the study and its outcomes are natural parts of the clinical research process—and we have learned a lot from the results. Those lessons have been incorporated into HVTN 505, a study that is another small piece that will contribute towards the mosaic of HIV vaccine research.

HVTN 505 could help us learn if a vaccine can help control HIV infection

The purpose of HVTN 505 is to learn if this vaccine can decrease the viral load of people who become infected with HIV. Typically, the lower the viral load, the longer it may take before a person develops symptoms of AIDS. So, an HIV vaccine that lowers viral load may delay the onset of illness, even if it doesn’t prevent HIV infection. The lower viral load may also reduce transmission of the virus to others.

If the 505 vaccine does lower viral loads, scientists will know they are on the right track with vaccines which stimulate cellular (T-cell) immunity. While the vaccine regimen being studied in HVTN 505 itself is not a candidate for FDA licensure, researchers will be able to apply the important information acquired during the study to the development of other vaccines, thereby moving the entire field forward.

HVTN 505 is a very different study from previous HIV vaccine studies

It is important to understand how the 505 Study relates to and is different from other studies you may have heard about. Another recent clinical trial of an HIV vaccine, the Step Study, tested an HIV vaccine that used an adenovirus serotype 5 (Ad5) as a vector (a carrier of the HIV genes). This approach failed to lower the viral loads in men who became infected after vaccination and did not prevent new infections. This vaccine may have increased the chance of HIV infection when some participants, especially men who were uncircumcised and had antibodies to the Ad5 carrier, were exposed to HIV after their vaccination.

While one of the 505 vaccines includes Ad5, there are many differences in the vaccines and how they are administered during the HVTN 505 trial:

• **The vaccine strategy is different.** HVTN 505 uses a prime-boost approach. Participants are “primed” with a DNA vaccine, and then “boosted” with an Ad5 booster shot. The DNA shots, as well as the Ad5 booster, contain more pieces of the HIV DNA than the vaccine in the Step Study, in an effort to heighten the body’s recognition of HIV upon subsequent exposure to the virus.

• **There are fewer Ad5 shots.** Participants in the 505 study will receive one Ad5 shot whereas Step Study participants received three.

• **The Ad5 vector is different.** The Ad5 carrier in HVTN 505 has three genes deleted (two completely and one partially) rather than just one gene deletion as in the Step vaccine. In the laboratory, scientists have noted that this altered adenovirus is “gentler” (it is less able to express adenovirus genes), while maintaining its ability to express and deliver the HIV genes to the immune system. The HVTN 505 study will provide us more information regarding how this particular Ad5 vector works in the human body.

This background document summarizes the scientific reasons for conducting HVTN 505 and explains why this study is the next logical step in the development of an HIV vaccine.

If after reading this you have additional questions or require further scientific detail, please email us at ask@hvtn.org.