HVTN100 phase 1/2 vaccine trial results promising: phase 2b/3 trial to commence

At the AIDS 2016 meeting in Durban, Linda-Gail Bekker (Deputy Director, Desmond Tutu HIV Centre) presented findings from the HVTN100 trial conducted in South Africa. In this trial, 185 participants received a five-injection vaccine series and 37 received a placebo. The series combined the same two vaccines tested in the earlier RV144 trial in Thailand, with several tweaks: the vaccines were modified to target HIV clade C, common in sub-Saharan Africa, and were administered with a new adjuvant and a booster injection to prolong the period of protection.

In the earlier RV144 trial, the vaccine combination was 60% effective 1 year after vaccination, but only 31% effective 3.5 years after vaccination. Larry Corey (HVTN Principal Investigator; President and Director Emeritus, Fred Hutchinson Cancer Research Center) explains that after the RV144 trial, researchers who wanted to learn more about the correlates of protection were able to identify several physiological responses associated with vaccine efficacy, including polyfunctional CD4 T-cell responses to the viral envelope and high titers of specific types of antibodies. The level of these physiological responses was sufficiently high in the recent HVTN100 trial to move forward with an efficacy trial, named HVTN702.

Bekker says, ‘We are very busy at present preparing for HVTN702, which will launch in the Republic of South Africa in November 2016 and will be the trial to prove whether this vaccine regimen is efficacious to prevent HIV infection in a Clade C virus region. It will enroll 5,400 South Africans between the ages of 18 and 35 years and we will follow them for 24–36 months. We will have our definitive results in 5 years.’

HVTN702 will certainly face hurdles. Robert Gallo (Director of the Institute of Human Virology, University of Maryland School of Medicine) observes ‘No one has yet solved the problem of the longevity of critical antibodies,’ a challenge evident in the RV144 findings, but emphasizes, ‘[HVTN702] is an important trial. It should go forward and I’m all for it.’ Expectations for vaccine effectiveness may be increasing over time as well. Peter Hale (Executive Director, Foundation for Vaccine Research) says, ‘Ten years ago I said if we had an HIV vaccine that was 60% effective we would have a stampede. Ten years later, I’m not so sure. It’s become clear there are other confounding factors. We really should aim for 80% effectiveness.’

Looking toward the future, Corey says, ‘You don’t go into doing these experiments without a reasonable degree of optimism, cautious optimism. Success is defined by moving forward and getting us to a globally effective HIV vaccine. Whether we do that through one trial or we do that through a trial that then has to be extended in some way to get where we want to go, well OK.’

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Conflicts of interest

There are no conflicts of interest.

Kristin N. Harper
Seattle, Washington, USA.
Correspondence to Kristin N. Harper
Seattle, WA, USA. Tel: +1 314 550 5191; E-mail: kristin.nicole.harper@gmail.com
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