

News in Context (2008)

HIV Vaccine Trial Canceled

NIAID will not conduct the HIV vaccine study known as PAVE 100. Instead, officials are considering a smaller, more focused trial.

On July 17, 2008, the National Institute of Allergy and Infectious Diseases (NIAID) announced that it will not move forward with PAVE 100, a large phase IIB vaccine trial designed to test a DNA prime, recombinant adenovirus serotype 5 (Ad5) boost HIV vaccine candidate developed by the NIH Vaccine Research Center (VRC).

PAVE 100 was slated to begin last fall but was postponed after an Ad5-based HIV vaccine candidate developed by Merck failed to prevent HIV infection or to reduce viral loads following infection in a phase IIB trial known as the STEP study ([AIDS Clin Care Oct 1 2007](#)). Subsequent analyses showed that the incidence of HIV infection in the STEP study was higher in vaccine recipients than in placebo recipients in the subgroup of individuals who were uncircumcised and who had preexisting Ad5-specific neutralizing antibodies (NAbs). Based on these results and on input from scientists and HIV prevention advocates, NIAID officially canceled plans for the PAVE 100 trial.

Comment: The failure of the Merck Ad5-based HIV vaccine candidate led to substantial public debate on the optimal path forward for the HIV vaccine field. One aspect of this debate focused on the appropriateness of conducting PAVE 100 to evaluate the efficacy of the vaccine candidate developed by the VRC. Proponents highlighted key differences between the VRC vaccine and the Merck vaccine, particularly the use of DNA priming prior to Ad5 boosting and the inclusion of Env in addition to Gag, Pol, and Nef immunogens. Opponents argued that these differences were insufficient to justify a large phase IIB efficacy study, particularly given the high prevalence of preexisting Ad5-specific NAbs that could impair the immunogenicity and the safety of the vaccine.

The decision to cancel PAVE 100 was part of a larger NIAID policy shift to increase emphasis on basic discovery research. As discussed at the Summit on HIV Vaccine Research and Development on March 25, 2008, NIAID will launch new initiatives to address key basic scientific roadblocks in the HIV vaccine field. However, NIAID has also confirmed its commitment to conducting clinical trials of novel or promising HIV vaccine candidates. Several candidates, including adjuvanted DNA vaccines, recombinant poxvirus vectors, and rare-serotype Ad vectors, will continue to be explored in early-phase clinical trials. Regarding the HIV vaccine candidate developed by the VRC, NIAID stated that it will consider a smaller, more focused efficacy study to determine whether this vaccine lowers viral loads following infection. If such an effect is seen, then a larger efficacy trial with this vaccine may be reconsidered.

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NIAID will not move forward with the PAVE 100 HIV vaccine trial [press release]. Bethesda, MD: National Institute of Allergy and Infectious Diseases; Jul 17 , 2008. (<http://tinyurl.com/62cjpz>)

