

Developing an HIV vaccine

March 2011

Crucell and the International AIDS Vaccine Initiative (IAVI) jointly announced an agreement in November 2004, in which Crucell agreed to develop AdVac® vectors for use in IAVI's AIDS vaccine development program.

In August 2005, Crucell and Harvard Medical School were jointly awarded a US\$19.2 million (€15.9 million) grant by the US National Institutes of Health (NIH) to develop new adenovirus vector-based vaccines against HIV/AIDS.

The Investigational New Drug Application (IND) for Phase I of the trial with Harvard Medical School (supported by the NIH) was approved by the FDA in January 2008.

In April 2008, Crucell announced the start of a Phase I clinical study of the novel recombinant HIV vaccine. The vaccine is based on Crucell's AdVac® and PER.C6® technologies, using adenovirus serotype 26 (rAd26) as vector, and is jointly developed by Crucell and the BIDMC, funded by a grant from the US National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. The rAd26 vector is designed to avoid pre-existing neutralizing antibodies to the more commonly used adenovirus serotype 5 (Ad5). Phase I clinical studies are being conducted at the Brigham and Women's Hospital in Boston, USA and are focused on assessing the safety and immunogenicity of the vaccine in several trials including single and multi-dose regimens.

In October 2009, preliminary results of the Phase I study were presented at La Conférence AIDS Vaccine 2009 in Paris, France. The presentation was given by Dr Dan H. Barouch, MD, PhD, Associate Professor of Medicine, Division of Vaccine Research, Department of Medicine, BIDMC, Boston, USA. The preliminary results of this study were updated at the AIDS Vaccine 2010 conference in Atlanta, GA in September 2010, confirming the safety and immunogenicity of the HIV candidate vaccine vector.

In August 2010 Crucell announced its participation in an international Phase I clinical trial in the United States and Africa of a combination of two AdVac®-based AIDS vaccine candidates, Ad26.ENVA.01 and Ad35-ENV, in healthy adults who are not infected with HIV. The clinical trial has started in October 2010 and will be led by the International AIDS Vaccine Initiative (IAVI), representing a collaboration between IAVI, Crucell, the Ragon Institute, and Beth Israel Deaconess Medical Center (BIDMC), a major teaching hospital of Harvard Medical School.

The Ad26.ENVA.01 vaccine candidate used in this study is manufactured by Crucell, while the Ad35-ENV vaccine is developed by IAVI. Both vaccines candidates are based on Crucell's proprietary AdVac® technology. The planned Phase I trial of the vaccine combination, which follows a Phase I trial of the Ad35-ENV vaccine by IAVI and a Phase I trial of Ad26.ENVA.01 by the Harvard-Crucell consortium, supported by the National Institute of Allergy and Infectious Diseases (NIAID), represents a key step towards proof of concept studies to evaluate the efficacy of the vaccine combination in humans.

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About HIV

Human immunodeficiency virus or HIV is a retrovirus that causes *acquired immune deficiency syndrome* (AIDS), a condition in which the immune system begins to fail, leading to life-threatening infections. HIV infection is pandemic.

Global HIV / AIDS burden

According to the 2009 AIDS Epidemic Update, (a joint report by the United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO), the number of people living with HIV worldwide continued to grow in 2008, reaching an estimated 33.4 million. The total number of people living with the virus in 2008 was more than 20% higher than the number in 2000, and the prevalence was roughly threefold higher than in 1990. The continuing rise in the population of people living with HIV reflects the combined effects of continued high rates of new HIV infections and the beneficial impact of antiretroviral therapy. As of December 2008, approximately 4 million people in low- and middle-income countries were receiving antiretroviral therapy—a 10-fold increase over five years (WHO, UN Children's Fund, UNAIDS, 2009).

In 2008, an estimated 2.7 million people were newly infected with HIV and it is estimated that 2 million people died of AIDS-related illnesses (source: WHO).

Geographical distribution

Sub-Saharan Africa is more seriously affected by HIV and AIDS than any other region of the world. Since 2001, when the United Nations Declaration of Commitment on HIV/AIDS was signed, the number of new infections in sub-Saharan Africa has fallen by 15%, equating to around 400,000 fewer infections in 2008. In many parts of Asia, HIV incidence has also declined. In Eastern Europe, after a dramatic increase in new infections amongst injecting drug users, the epidemic has leveled off considerably. However, in some countries there are signs that HIV incidence is rising again.

How HIV is transmitted

HIV is transmitted through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV, such as blood, semen or breast milk. Infection can happen during sexual activity, blood transfusions, sharing needles or through an exchange between mother and baby during pregnancy, childbirth, or breastfeeding.

Symptoms

Opportunistic infections such as pneumocystis carinii are common in people with AIDS. They also have a higher risk of developing various cancers such as Kaposi's sarcoma, cervical cancer, and cancers of the immune system known as lymphomas.

Current treatment and prevention

The only known methods of prevention are based on avoiding exposure to the virus. Once infected, antiretroviral drugs (ARVs) can significantly delay the progression of HIV to AIDS and allow people to live relatively normal, healthy lives.