### Emerging Drug List

**VACCINES FOR HIV**

<table>
<thead>
<tr>
<th>Generic (Trade Name)</th>
<th>Manufacturer</th>
<th>Indication</th>
<th>Current Regulatory Status</th>
<th>Description</th>
<th>Current Treatment</th>
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<tr>
<td>ALVAC vCP1521 (ALVAC-HIV); AIDSVAX B/E (AIDSVAX®)</td>
<td>ALVAC-HIV (sanofi pasteur); AIDSVAX® (VaxGen, Inc.)</td>
<td>These vaccines are designed to prevent human immunodeficiency virus (HIV) infection (prophylactic vaccine), or if infection has occurred, to control the spread of the virus to other cells (therapeutic vaccine), delaying progression to acquired immunodeficiency syndrome (AIDS).</td>
<td>The combination of ALVAC-HIV vCP1521 and AIDSVAX® B/E vaccines (“prime-boost” vaccine combination) is being evaluated in a phase III trial (RV144) in Thailand.</td>
<td>ALVAC-HIV is one of a group of HIV vaccines that use genetically modified canarypox viruses (CPVs) to carry HIV genes. CPV is non-replicative in human cells. Once administered, the recombinant CPV express the foreign HIV molecules, triggering an HIV-specific immune response. The ALVAC-HIV construct, vCP1521, carries three genes, env, gag, and a portion of pol, from the HIV subtype found predominately in Thailand (CRF01_AE, formerly clade E). HIV gp120 proteins are normally expressed on the outer surface of the virus. They bind to human cells during infection, playing an essential role in virus infectivity and pathogenesis. The AIDSVAX® vaccine contains gp120 surface proteins from two HIV strains. AIDSVAX® B/E is made with genetically engineered gp120 proteins from the viral strain that predominates in Thailand. The goal of AIDSVAX® immunotherapy is to train the immune system to recognize gp120, create antibodies to coat gp120, and so prevent HIV from entering human cells.</td>
<td>The goal of therapy is to keep the level of HIV in the body as low as possible, for as long as possible, delaying the progression to AIDS. Combination antiretroviral therapy is the standard of care for patients who are infected with HIV. There are two classes of antiretroviral medications—reverse transcriptase inhibitors (RTIs) and protease inhibitors (e.g., saquinavir, indinavir, ritonavir). There are nucleoside RTIs (e.g., zidovudine, didanosine, zalcitabine), non-nucleoside RTIs (e.g., nevirapine, efavirenz), and nucleotide RTIs (e.g., tenofovir). In general, treatment includes the use of a combination of at least three antiretroviral medications from different classes, an approach that is commonly referred to as highly active antiretroviral therapy (HAART). The choice of drugs for combination therapy is individualized. It depends on factors such as anticipated viral load.</td>
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Preventive strategies for HIV infection remain abstinence and condom use. Topical microbicides are being developed as a possible preventive approach.6

Cost: There is no cost information on HIV vaccines, because they are not marketed in any country.

Evidence: The combination of ALVAC-HIV and AIDSVAX® B/E has been evaluated in a phase II trial of 133 HIV-negative Thai adults.5 Participants were randomized to receive ALVAC-HIV [106.5 TCID50 (50% tissue culture infectious doses)], administered at zero, one, three, and six months, combined with 200 μg or 600 μg AIDSVAX® (a “boost”) at three and six months. In each group, one participant received placebo for every three who received active vaccine. The vaccines and placebo were administered intramuscularly.5 Results showed that the vaccine combination was safe and well tolerated, and that it induced cellular and humoral immune responses. In the trial, the lymphoproliferative response, a measure of T-cell mediated immune response to gp120 E, was induced in 63% of vaccine recipients compared with 7% of placebo recipients. HIV-specific immune responses were detected in 24% of vaccine recipients. The trial also demonstrated that the higher dose of “boosting” vaccine induced stronger immune responses. Immune responses were not detected in patients who received ALVAC-HIV alone or placebo.5

Based on the safety and immunogenicity data from the phase II study, the US and Royal Thai governments jointly initiated a phase III study (RV144) on September 29, 2003. The primary objective of the trial is to determine if the combination vaccine prevents HIV infection. Its secondary objective is to determine whether the vaccine controls infection among patients who acquire HIV. The trial is set to recruit an estimated 16,000 HIV-negative Thai adults who are 20 to 30 years old. Completion of enrolment was projected to be in the fourth quarter of 2005. Patients will be monitored for three and a half years.1

Adverse Effects: ALVAC-HIV and AIDSVAX® have well documented safety profiles. Evaluated in over 2,000 recipients, including HIV-infected and uninfected adults, children, and newborns, ALVAC-HIV has been found to be safe and well tolerated, with no serious adverse events reported.11 AIDSVAX® was found to be safe and well tolerated in more than 2,500 Thai adults.1 The combination of ALVAC-HIV and AIDSVAX® has been evaluated in approximately 200 Thai adults, and found to be well tolerated, with no serious vaccine-related adverse events or concurrent HIV infections reported.5

Commentary: Significant controversy has surrounded study RV144.
Many researchers argue that the combination of ALVAC-HIV and AIDSVAX® gp120 will not provide protection against HIV, based on earlier trials of the individual components.12,13 They claim that prior studies showed poor immunogenicity and no protective efficacy against HIV when the vaccines were given separately,14-16 and that the phase II results of the combination therapy were inadequate to justify a large trial. For these reasons, a similar phase III trial to be conducted in the US was cancelled by the HIV Vaccine Trials Network (HVTN).17

Proponents of study RV144 argue that the combination of ALVAC-HIV and AIDSVAX® induced better cellular and humoral responses than either component alone, warranting further investigation.12 Based on the complexity of HIV and the pace of progress, it is plausible that the prime-boost combination may not provide immune protection against HIV. It is agreed that regardless of the study outcome, the information gained will advance HIV vaccine development.18 A limitation of any HIV vaccine trial is the potential length of time required to declare that the vaccine is effective (i.e., prevents AIDS).

References:


This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

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