Clinical testing of experimental vaccines for West Nile virus

Early trials of vaccines for West Nile virus developed for clinical testing in humans have demonstrated positive results.

The virus is transmitted via mosquito bites, and more than 16,000 cases have been reported in the USA since its arrival in New York City in 1999, 684 of which have been fatal. Horse populations are also affected by West Nile virus, and the human vaccine is based on one that has already proved to be successful in trials on animals, including mice and horses.

The vaccine, developed by the National Institute of Allergy and Infectious Diseases' (NIAID) Vaccine Research Center (VRC) and Vical Incorporated, is based on a DNA plasmid containing two genes, one encoding a West Nile virus transmembrane protein and the other encoding a glycosylated envelope protein. This vaccine is to be tested in 15 healthy volunteers. The vaccine developers expect that, when injected intramuscularly, an immune response will be triggered, producing T-helper cells and consequently antibodies, as well as killer T-cells. Barney Graham of the VRC is hopeful about the vaccines prospects, saying, “In our experience in clinical trials, DNA vaccines generally cause few side effects, making them a promising alternative to conventional vaccines.”

Researchers at Acambis have developed a genetically engineered, live attenuated vaccine, using an already approved and licensed yellow fever vaccine. The company’s Chief Scientific Officer, Thomas Monath, explained, “We actually took an existing vaccine against yellow fever, a related virus, and modified it for West Nile”. This vaccine has been shown to be effective in producing high-level neutralizing antibody responses in a Phase I clinical trial, and a Phase II trial is now planned. Anthony Fauci, Director of the NIAID, emphasized that there is some way to go before a completely effective and safe West Nile virus vaccine is available. He did, however, acknowledge the Acambis groups success in modifying an existing vaccine to create an effective hybrid vaccine, saying, “The potential for this is to shave off years in vaccine development.”

Phase II and III trials of prostate cancer vaccine

Cell Genesys Incorporated recently announced that it has received US Food and Drug Administration (FDA) approval for the second Phase III trial of its GVAX® vaccine. The first Phase III trial commenced in July 2004, enrolling 600 patients with radiologic evidence of metastatic disease, with the aim of demonstrating a 33% increase in survival duration with the GVAX vaccine, VITAL-1 (Vaccine ImmunoTherapy with Allogeneic prostate cancer cell Lines), compared with taxotere chemotherapy plus prednonsense.

This second FDA-approved trial (VITAL-2) will enrol approximately 600 patients with prostate cancer symptoms and cancer-related pain. Researchers aim to demonstrate a 33% increase in survival duration with GVAX plus taxotere chemotherapy compared with chemotherapy plus prednonsense.

The company has recently reported additional results from its Phase II trial, which was designed to determine the optimum dosing regimen for the Phase III trial. Based on the results, the highest vaccine dose was selected, and ongoing follow-up in the high-dose group of 22 patients indicates a statistically significant increased antibody response, and based on median follow-up time, final mean survival will be no less than 24.1 months. On the day Cell Genesys reported these results, the President of the company, Joseph Vallner, said, “The data reported today provide further support for the selection of the dosing regimen used in our ongoing Phase III trial of the GVAX vaccine for prostate cancer and we look forward to continuing enrollment in this trial... We hope that our GVAX vaccine may some day offer an improved and less toxic treatment alternative to chemotherapy for patients with advanced prostate cancer”.

Transgene have also reported the results of a Phase II clinical trial into the therapeutic vaccine candidate, MVA-MUC1-IL2. This study enrolled 40 patients who had undergone primary local treatment for prostate cancer by surgery or radiation, but still experienced progression of disease, as evidenced by rising prostate-specific antigen (PSA) levels. Patients were treated with MVA-MUC1-IL2 alone, and a significant increase in PSA doubling time (DT) was observed in 63% of patients. Furthermore, PSA-DT more than doubled in 30% of patients when compared with doubling time prior to vaccination. This increase in PSA-DT is expected to manifest as a slowing of disease progression. Both the GVAX and MVA-MUC1-IL2 vaccines have been well tolerated.

Promising results from the first Phase II clinical trial to combine radiation therapy and a vaccine for prostate cancer, carried out at the National Cancer Institute (NCI), were recently announced. Of the 17 patients receiving the combination therapy, 13 demonstrated at least a threefold increase in immune cell response, whereas no appreciable increase was observed in the eight patients receiving radiation therapy alone. The combination therapy trial followed earlier observations that radiation therapy alters tumor cells, enabling the body’s immune system to destroy them more easily. The primary author of the study, James Gulley, said, “The idea is that you can stimulate the body’s immune system to recognize and attack tumor cells through the use of a vaccine... We have
shown that this therapy is safe and well tolerated – the first step toward finding alternative treatments for patients with localized prostate cancer, especially those at high risk for failing current treatments”.

Vaccine against human papillomavirus set to reduce cervical cancer

Human papillomavirus (HPV) will infect up to 70% of sexually active women during their lifetime, and causes approximately 470,000 cases of cervical cancer per year, making it the primary risk factor for developing the disease.

A vaccine targeting HPV types 16 and 18, which together cause approximately 70% of cervical cancers, as well as types 6 and 11, which are associated with 90% of genital warts, was tested in a recent randomized trial. Researchers at the Ludwig Institute for Cancer Research, Brazil, enrolled 1158 healthy women who were not pregnant, had clear cervical smears and a reported history of no more than four sexual partners. Participants were randomly assigned to receive either the vaccine or placebo intramuscularly on day 1, and months 2 and 6. During the 36-month follow-up, participants were subject to regular gynecologic examinations, including cervical smears and HPV DNA testing. Compared with the placebo group, the incidence of persistent infection or disease associated with HPV types 6, 11, 16 and 18 was 90% lower. Furthermore, vaccinees demonstrated 100% protection against precancerous cervical lesions and genital warts due to these four HPV types.

Luisa Villa of the Ludwig Institute for Cancer Research commented on the vaccine's potential, in particular, its use in developing countries: “In the developed world, full implementation of cervical cancer screening has substantially shifted the burden of HPV infection from cervical cancer mortality to management of precancerous lesions. In these countries, in addition to further reduction in incidence of cervical cancer, universal HPV vaccination might decrease the medical, psychological and economic costs associated with the management of abnormalities detected by screening. Inclusion of HPV 6 and 11 in a vaccine could also diminish the incidence of genital warts. In developing countries that have not implemented screening programmes for cervical cancer, a universal HPV vaccine could substantially reduce the incidence of the disease.”

The results of this trial of Merck’s vaccine follow GlaxoSmithKline’s report last year of their vaccine against HPV types 16 and 18, which was demonstrated to be 100% effective in preventing infection with the virus in a preliminary clinical trial.