

Emerging Drug List

VACCINE FOR HERPES SIMPLEX



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Generic (Trade Name): gD2t-AS04

Manufacturer: GlaxoSmithKline Inc.

Indication: The gD2t-AS04 vaccine is being evaluated for the prevention of herpes simplex type 2 (HSV2) infection. This viral subtype is most commonly associated with genital herpes.

Current Regulatory Status: The gD2t-AS04 vaccine is being evaluated in a phase III trial called the Herpevac trial for women. The trial is being sponsored by the US National Institute of Allergy and Infectious Diseases.¹

Description: Glycoprotein-D is an immunogenic HSV2 protein that has been identified as a key target for T-cell activation. The vaccine contains a truncated form of this protein (gD2t), which acts as an immunological target. It also contains the immunological adjuvant AS04.²

Current Treatment: Antiviral therapies are the gold standard of treatment for genital herpes. Antiviral agents are used to treat acute episodes of genital herpes infection, and to reduce the frequency and duration of outbreaks in patients with recurrent infections. Antiviral drugs that are used to treat genital herpes include acyclovir, famciclovir, and valacyclovir. These drugs interfere with DNA synthesis, so that reproduction of the virus is prevented. Acyclovir was the first antiviral agent used to treat genital herpes. Although it has an excellent safety record, its dosing regimen (five times daily) may result in compliance issues. Famciclovir and valacyclovir, which are better absorbed by the body, can be taken less often than acyclovir.³

Cost: No costing information is available for the gD2t-AS04 vaccine.

Evidence: The efficacy of the gD2t-AS04 vaccine was evaluated in two large phase III trials.⁴ The trials were conducted in adult men and women whose regular sexual partners had a history of genital herpes. Participants were randomized to receive the vaccine or placebo at zero, one, and six months. Study 1 was an efficacy trial that enrolled 847 adults who were seronegative for HSV1 and HSV2. Study 2 was designed to evaluate the safety of the vaccine in 2,491 adults of any serologic HSV status. The primary outcome measure was the occurrence of genital herpes in all participants in Study 1. After the results of Study 1 were analyzed, but before the results of Study 2 became available, the prevention of genital herpes in women was added as an efficacy end point to Study 2.⁴

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The vaccine did not significantly reduce the occurrence of genital herpes when compared with placebo in Study 1 (38% efficacious; 95% CI: -18 to 68).⁴ However, a subgroup analysis revealed a significant reduction in the occurrence of genital herpes in women who were HSV1 or HSV2 seronegative (73% efficacious; 95% CI: 19 to 91; $p=0.01$). In Study 2, the vaccine demonstrated efficacy among HSV1 and HSV2 seronegative women (74% efficacious; 95% CI: 9 to 93; $p=0.02$).⁴ No significant benefit was observed in men or women who were HSV2 seronegative but who had antibodies for HSV1.⁴ Thus, protection seems to be limited to HSV1 and HSV2 seronegative women.

The Herpevac phase III trial for women is designed to evaluate the efficacy of the gD2t-AS04 vaccine in women who are seronegative for HSV1 and HSV2.¹ Begun in January 2003, the trial is expected to enrol 7,550 women between 18 and 30 years old (participants are being recruited). The expected completion date for the trial is April 2008.⁵

Adverse Effects:

The safety of the gD2t-AS04 vaccine was evaluated in a large, multicentre, double-blind, randomized, placebo-controlled trial.⁶ In this study, 7,460 healthy adults without evidence of genital herpes and without regard to HSV serostatus were randomized to receive the vaccine or placebo in a 2:1 ratio. The vaccine was administered at zero, one, and six months. The incidence of solicited local (e.g., redness, swelling) and systemic (e.g., fatigue, headache) reactions occurring within four days of vaccination were significantly higher in the vaccine group compared with the placebo group (82% versus 58% for local, and 35% versus 30% for systemic; $p<0.001$). Most of these events were mild to moderately severe. The incidence of unsolicited symptoms between month 0 and month 7 (without including ongoing solicited symptoms) were similar in both groups (21.9% for the placebo group versus 22.1% for the vaccine group). There was no significant increase in the number of serious adverse events in the vaccine group (2.1%) compared with the placebo group (2.2%) between month 0 and month 7.

Commentary:

The genital herpes epidemic is a global public health problem.⁷ In the US, approximately 22% of people who are 12 years of age or older are infected with HSV2.⁸ Pregnant women who are infected with HSV2 may pass the virus to the baby during birth. This can be a devastating illness for newborns.⁹ Genital herpes is also a risk factor for the spread of HIV in adults.³ Many who are infected with HSV2 have no symptoms, and this contributes to the spread of the disease. The development and widespread use of a safe and effective vaccine are practical strategies for controlling the epidemic.¹⁰ Mathematical modelling of the results of Study 1 and 2 indicates that the widespread use of the vaccine could affect the spread of genital herpes in men and women.¹¹

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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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