

Herpes Vaccines: An Interview With Dr. William Halford



By Josh Bloom — October 17, 2016



The beginning of the end of herpes?

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On September 26th, I [wrote about](#) ^[1] Rational Vaccines (RVx), an Illinois-based company, which was formed in 2015 to develop vaccines that would prevent *and* treat herpes simplex virus-2 (HSV-2), which causes genital herpes, and HSV-1, which also causes genital herpes as well as cold sores **(1)**.

At that time, based on unpublished data from a study of the protective effects of their vaccine in mice and guinea pigs **(2)**, it seemed that RVx's live-attenuated herpes vaccine might have a significant advantage over Genocea's GEN-003 subunit vaccine—the first-ever vaccine to treat HSV-2 in humans, which I [discussed in March](#) ^[2].

Still no data or peer review of their claims, but this morning, RVx issued a [press release](#) ^[3] about a Phase I safety study of the company's Theravax (therapeutic) vaccine.

Following is my interview with RVx's Chief Science Officer (CSO), William Halford, Ph.D., who is also an Associate Professor at the Southern Illinois University School of Medicine.

JB: Phase I trials are usually conducted for safety only. Yet, there are data on efficacy of the vaccine, which means that it was tested on people who were already infected. Please explain why. Was a cohort of infected people given a placebo control?

WH: We conducted this trial in the Federation of St. Kitts & Nevis, with a total of 20 enrollees for the primary purpose of evaluating how participants who already suffered with recurrent genital herpes tolerated RVx's live Theravax (HSV-2) vaccine **(3)**. While we were at it, we also collected

some simple metrics of efficacy, which seem to have provided overwhelmingly positive results.

JB: The Phase I trial has been completed, however, you have said that more data are to be expected. Can you give us a rough idea of the timeline for more data?

WH: The vaccinations of trial participants have been completed. But the analysis of their blood antibody responses to the HSV-2 vaccine and participants' reports of their self-reported change in symptoms will be an ongoing process for the next 8 months. Data will be provided and updated on our website, as it becomes available. Our publication goal is to have a paper published in PLOS ONE (open access) by the end of 2017, once we have fully analyzed the entire data set.

JB: There are no indications that your vaccines have been tested prophylactically. Can you comment on the timing and nature of these clinical trials?

WH: Our plan is to accumulate as much safety and efficacy data from Phase I clinical trials in multiple countries, and then make the vaccine available to people who are infected as soon as possible. Human clinical trials for the live Profavax vaccine, RVx's preventative vaccine, will take longer to complete; perhaps 2-3 years. So we have no immediate plans to offer the Profavax vaccine (the prophylactic vaccine) before the vaccine has been vetted in a Phase I clinical trial.

JB: Valtrex (valacyclovir) reduces the frequency and severity of genital herpes outbreaks, but is not very effective in reducing viral shedding, when the virus is being produced, but no symptoms are present (4). Can you comment on the difference between Theravax HSV-2 vaccine and prophylactic Valtrex in this regard?

WH: Yes. Valtrex has limited use in reducing shedding; by most accounts about a 2-fold reduction in shedding. We expect that, given the reductions in symptoms participants are reporting, that the live Theravax HSV-2 vaccine would reduce shedding by 10 to 100-fold, but until we make those measurements, that is little more than speculation.

JB: Will the upcoming data include more participants, more data on the first 20 participants, or both?

WH: The further data we plan to make public over the next 12 months will come from the n=20 people who were enrolled in the 2016 Phase I clinical trial conducted in St Kitts.

JB: The data (number of outbreaks) from the people who received the vaccination were self-reported, a notoriously unreliable method for data collection. In other words, the possibility for the blurring of real and placebo effects becomes a problem. Can you tell us what steps, if any, were taken to ensure that the self-reporting was as accurate as possible?

WH: We did two things. First, we were very diligent in interviewing participants verbally and having participants provide written questionnaires at a different point in time to make sure their story was internally consistent. Second, and more importantly, we took each participant's blood prior to the trial and at the time of each vaccination to measure the change in their HSV-2-specific antibody response. To the best of my knowledge, the vaccine-induced activation of B cells (the type of white blood cell required for the protective immune response) and production of virus-specific antibodies are not susceptible to suggestion or placebo effects.

JB: Have you, or are you planning to measure the impact Theravax on asymptomatic shedding? If so, will you be measuring shedding by viral titer, a decrease in transmission during times of asymptomatic shedding, or both?

WH: I absolutely want to run many more trials of RVx's vaccines to address this and many other questions about the efficacy of this live-attenuated HSV-2 vaccine. However, the focus for the moment is more about reducing herpes patients' symptoms than dotting all of the i's and t's necessary to offer a formal scientific explanation as to why the therapeutic HSV-2 vaccine works, and measuring the magnitude of the effect. So, shedding data will be ultimately collected and available, but for now we are focused on determining the frequency of recipients who find the live HSV-2 vaccine more effective than the current standard of medical care; namely, prophylactic valacyclovir. In the current trial, 17 of 17 participants who received the 3-shot vaccination series said they thought the live Theravax vaccine was far superior to antiviral drugs in alleviating their herpes symptoms.

JB: You mention a "functional cure on this horizon." Can you give us an idea of how close the "horizon" may be, and whether this could be due to the Theravax vaccine, or a more effective vaccine that we are not yet aware of.

WH: I think we are on the horizon right now. My team has a tremendous amount of confidence in this vaccine. Should what we expect become reality, herpes could become a disease of the past before long.

JB: Can you provide us with a brief comparison of biochemical, robustness of immune response, and efficacy of Theravax versus the GEN-003 vaccine?

WH: Numerous publications from the Halford Lab between 2011 and 2016 highlight that a live-attenuated HSV-2 vaccine, the active ingredient in the Theravax vaccine, is 50 to 100 times more effective than the GEN-003 subunit vaccine. Three decades of publications document the repeated failure of HSV-2 glycoprotein D-based subunit vaccines, which is the primary active ingredient in the GEN-003 vaccine. Call me crazy, but glycoprotein D subunit vaccines have failed in 6 clinical trials spanning 30 years and involving more than 40,000 participants. So, yes, I predict that GEN-003 will fail like every other gD-subunit vaccine has dating back to when I graduated high school.

JB: Do you have plans to evaluate either vaccine in children?

WH: Not in the foreseeable future. Yes, of course there are important applications of a safe and highly effective live HSV-2 vaccine that will be sufficient to effectively eradicate all diseases

caused by HSV-1 and HSV-2. However, this is a downstream question for the 2020s, and is not the most pressing matter today.

JB: What's next?

WH: Our plans are to write up all the data, publish a paper, and make the vaccine available to people who are already affected by recurrent herpetic disease as soon as possible.

JB: Under the best of circumstances, what is the earliest that the vaccine would be available to herpes sufferers?

WH: Next year.

For my articles on other herpes vaccine candidates, [please see here](#) [4].

Update: Dr. Halford died in July, 2017

Notes:

(1) HSV-1 is the primary cause of cold sores, although it can also readily infect the genital region. HSV-2 is the primary cause of genital herpes. It does not cause significant oral herpes infection. It would be fair to say that HSV-2 has a significant "home-court" advantage, while HSV-1 plays well at home and on the road. About three-quarters of Americans test positive for HSV-1 antibodies.

(2) Animal models of human disease vary greatly in predicting the success of a potential drug in humans. Some models, for example, cancer and Alzheimer's, are terrible. Models for some infectious diseases, including herpes, are usually quite good.

(3) RVx claims a 3.2-fold average reduction in outbreaks in 17/17 people who were given three shots. The other three people were given only two shots, and were removed from the trial before receiving their third shot, they say.

(4) People are contagious during periods of asymptomatic shedding or during active outbreaks.

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[1] <http://acsh.org/news/2016/09/26/herpes-vaccine-update-exciting-news-dont-throw-away-condoms-just-yet-10219>

[2] <http://acsh.org/node/10029>

[3] <http://www.prnewswire.com/news-releases/first-ever-human-trial-of-a-live-attenuated-functioning-therapeutic-herpes-vaccine-300345431.html>

[4] http://acsh.org/search?search_api_views_fulltext=herpes+vaccine