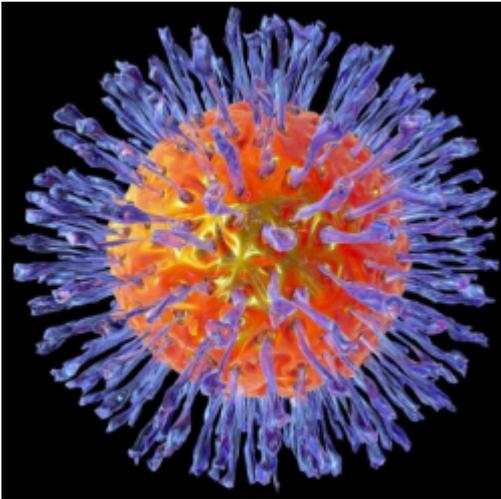


Will An Antiviral Vaginal Gel Help Prevent Herpes? Maybe. Maybe Not.



By Josh Bloom — April 12, 2019



Representation Of A Herpesvirus

Source: <http://astrobiosociety.org> [1]

Sometimes diseases or infections are tough nuts to crack no matter how much money or research effort is thrown at them (e.g., Alzheimer's, Parkinson's). Genital herpes has earned a place on that list.

One experimental vaccine after another has failed, although one of the first ones - Genocea's GEN-003 remains in the running after showing [some efficacy at higher doses](#) [2] after it disappointed in Phase II trials at lower doses. And pritelivir, a promising looking antiviral drug that works by inhibiting viral DNA synthesis ([I wrote about](#) [3] last summer) is now in [clinical trials](#) [4]. Given the enormous number of people suffering from what can be a very bad infection, even a modest success will generate a buzz. There may be a bit of a buzz now. Maybe just a small buzz.

A [recent paper](#) [5] in the *Journal of Infectious Disease* describes the use of a different technique - one that failed in preventing the spread of HIV - a topical (vaginal) gel containing the antiviral drug tenofovir. According to the paper, when used regularly by HSV-2-negative women, tenofovir gel reportedly reduced their rate of HSV-2 infection by 40%. Even though 40% is far from the cure that herpes sufferers have been hoping for, it's better than nothing, right?

Maybe not. That 40% may not be accurate because of some questions about and limitations of the trial and the science behind it. Here are some of them.

1. WHY ARE THEY USING AN AIDS DRUG FOR HERPES?

Pritelivir inhibits the replication of both viruses, albeit by a different mechanism. (This is rather

unusual). In fact, in cultured cells, pritelivir is more potent than acyclovir in inhibiting the replication of HSV-2 (1,2).

2. WHAT ARE THE CLAIMS?

Of the 566 HSV-2-negative women in the VOICE trial, [the authors concluded](#) ^[6] that the use of 1% gel tenofovir gel was "associated with" a 40% reduction of HSV-2 acquisition.

3. WHY THE UNCERTAINTY?

ACSH's Dr. Chuck Dinerstein, Senior Fellow of Medicine, and all around good guy, points out some of the weaknesses and limitations of the study:

- The results are secondary endpoints. In other words, the VOICE trial was designed to study the reduction in HIV transmission (it failed), not HSV-2. This makes the trial less rigorous and the results less certain.
- Adherence to study protocol was low; women did not use the gel regularly. This adds another layer of uncertainty to the data.
- Detection of tenofovir was performed once in the first quarter of a seven-quarter study.
- The determination of whether women used the gel was based on the presence of tenofovir in the blood - a yes-no answer. Tenofovir was either present or not. Without knowledge of the blood levels of the drug, it is impossible to establish a dose-response, which provides strong evidence of a trend.
- There is no information about the women's partners so I wonder whether the incidence of HSV-2 in those partners alone could have accounted for the 40% variation.

3. WHAT DOES THIS ALL MEAN?

Given the inherent limitations of this study, 40% is, at best, an estimate. Dr. Dinerstein wonders whether that number is "mathemagic"- it may mean nothing at all.

4. TAKE HOME MESSAGE

Unfortunately, while tenofovir gel may help a bit, it does not represent a significant advance in the prevention of either HSV-2 transmission. This goal remains elusive. Condoms are about [50% effective](#) ^[7] in preventing transmission. [Suppressive therapy](#) ^[8] with Valtrex is better - 70-80%. It is unlikely that tenofovir gel, at least as a stand-alone therapy, will make much of a difference.

5. ALL IS NOT LOST

Let's not forget that tenofovir (pills, not gel) is entering late-stage trials. Also, tenofovir is significantly more potent than acyclovir in preventing *in vitro* replication of HSV-2 (notes 1 and 2). This does not mean that it will be better in animal or humans. This is where pharmacokinetics (absorption, metabolism, toxicity, etc) come into play. But, on the plus side, tenofovir is already an approved drug, so much is known about its behavior in humans. This represents an enormous advantage over an experimental drug, where all of these parameters - many of which could derail the drug entirely - are unknown.

Best guess: Oral tenofovir is going to work well. Maybe even very well. But don't bet the house on it. The gel? Don't bet a doll house.

NOTES:

(1) For pritelivir inhibition data for HSV-2 see [here](#) [9]

(2) For acyclovir inhibition from HSV-2 see [here](#) [10]

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Source URL: <https://www.acsh.org/news/2019/04/12/will-antiviral-vaginal-gel-help-prevent-herpes-maybe-maybe-not-13944>

Links

[1] <http://astrobiosociety.org/herpes-virus-what-you-need-to-know/>

[2] <https://www.precisionvaccinations.com/genocea-biosciences-gen-003-therapeutic-vaccine-candidate-hsv2-has-not-launched-phase-3-study>

[3] <https://www.acsh.org/news/2018/06/12/herpes-vaccines-dont-work-what-about-drugs-pritelivir-page-aids-playbook-13074>

[4] <https://www.centerwatch.com/clinical-trials/listings/114080/hsv-infection-trial-on-efficacy-safety/>

[5] <https://academic.oup.com/jid/advance-article-abstract/doi/10.1093/infdis/jiz045/5315462?redirectedFrom=fulltext>

[6] <http://academic.oup.com/jid/advance-article-abstract/doi/10.1093/infdis/jiz045/5315462?redirectedFrom=fulltext>

[7] https://www.medscape.org/viewarticle/472427_2

[8] <https://www.cdc.gov/std/tg2015/herpes.htm>

[9] <https://www.selleckchem.com/products/bay-57-1293.html>

[10] https://www.accessdata.fda.gov/drugsatfda_docs/label/2001/018604s018lbl.pdf