

HIV prevention study does not confirm tenofovir gel effectiveness

Women require convenient and effective HIV prevention methods that work within the context of their lives

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Seattle (24 February 2015) – A major study has shown that a vaginal gel containing the antiretroviral drug, tenofovir, was not effective in preventing HIV among a large, diverse population of young South African women.

Findings of the study, known as FACTS 001, were reported at the annual Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, United States earlier today (Tuesday 24 February).

The large-scale study was conducted by the Follow-on African Consortium for Tenofovir Studies (FACTS) from October 2011 to August 2014, and enrolled 2 059 sexually-active HIV-negative women, aged 18 – 30 years, at nine research sites in urban, peri-urban and rural areas of South Africa.

All participants went through an informed consent process and then were randomly assigned to one of two groups of equal size. Half of the participants were assigned to receive a vaginal gel containing tenofovir – for use before and after sex – while the other half received a placebo gel. They were also counselled to use established methods to reduce HIV infection and were supplied with condoms and treated for other STIs.

The main findings of the study showed that:

- There was no difference in the rate of new HIV infections occurring in the vaginal tenofovir gel group compared with the placebo group (i.e. there was no evidence that tenofovir gel was effective in preventing HIV in this population).
- Overall, out of 2 059 enrolled participants, a total of 123 HIV infections occurred, with 61 new HIV infections in the group assigned to tenofovir gel and 62 in the group assigned to placebo. The HIV incidence was 4% in both groups (i.e., four out of 100 women acquired HIV per year).
- The study measured gel use before and after sex in two ways – counts of returned used applicators from all women in the trial, and tenofovir drug levels in vaginal samples at quarterly visits from 214 participants in the tenofovir gel group. Using both these measures, the study found that participants appeared to use the gel as directed at least half of the time, but only a small proportion were able to use the gel consistently with sex. Of the 214 women included in the sub-study, 65% had drug detected in some samples and 22% of them had tenofovir drug detected in all samples.
- While the study found no overall significant association between consistent gel use and HIV protection when analysing returned used applicators from all women in the trial; HIV acquisition rates were lower in women in the sub-study who reported recent sex and had detectable tenofovir in vaginal fluids.
- Vaginal tenofovir gel was safe when used in this population.

Building from the previous experience of ARV-based prevention trials in young women, the FACTS study implemented an intensive adherence programme, including a client-centred counselling approach, motivational text messages and monthly social clubs for participants to discuss adherence challenges and broader social, economic and relationship issues in their lives that might reduce their ability to use the gel. Despite all these interventions, adherence had been insufficiently consistent.

The outcome of FACTS 001 was keenly awaited because of two earlier trials that tested tenofovir gel, including:

- In 2010, the CAPRISA 004 study, involving nearly 900 women in KwaZulu-Natal, reported that tenofovir gel, used before and after sex, reduced the HIV infection rate by 39% among women using the product. The small study sample meant that these results did not provide sufficient evidence to licence tenofovir gel. FACTS 001 has shown that the results of CAPRISA 004 could not be replicated in a large study population comprising diverse women.
- The VOICE study, which tested tenofovir gel among 2 000+ women in three African countries, reported in 2013 that there was no statistically significant difference between women who had been asked to use tenofovir gel on a daily basis (irrespective of whether they had sex) and those given a placebo gel. In this study, overall use of the gel by participants was low.

Professor Helen Rees, FACTS Protocol Chair and Executive Director of the Wits Reproductive Health and HIV Institute (Wits RHI) in Johannesburg commented, “Interviews with participants throughout the study taught us that HIV prevention tools for women must be convenient and take account the complex social and economic realities of their lives.” She continued, “A product that is applied around the time of sex may be suitable for some women, but it did not meet the needs of the majority in our study, most of whom were young, single and lived with their parents. Methods that are easier for women to incorporate into their lives are likely to be more effective.”

Professor Glenda Gray, FACTS Protocol Co-Chair and President of the SA Medical Research Council said: “Great care was taken to ensure that the design of FACTS 001 was sufficiently robust to deliver an authoritative answer and that the conduct of the trial met the highest quality standards. We now know that in this population FACTS 001 disappointingly did not support the results of the CAPRISA 004 study, but it does help chart the course of future research on HIV prevention technology for women, and that in itself has been a worthy investment of resources.”

Professor Gray highlighted that FACTS was an entirely South African research consortium, and the first to have successfully undertaken a large HIV clinical trial of this nature. She went on to note, “FACTS 001 not only provided critical new evidence for the HIV prevention field, the study also developed the research skills of many emerging African scientists across the country.”

The high HIV incidence measured in FACTS 001 reinforces the need for continued research to develop woman-centred HIV prevention methods. Two Phase III trials, known as The Ring Study and Aspire, that are testing a long-acting vaginal ring containing the drug, dapivirine, are nearing completion in various African countries. Other products, including a long-term injectable ARV and an HIV vaccine, are also now in clinical trials.

The FACTS 001 trial was funded by the South African Departments of Science and Technology and Health, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through USAID and the Bill & Melinda Gates Foundation. It was sponsored by the US non-profit scientific organisation, CONRAD, which – together with the pharmaceutical company Gilead – provided gel products for the study.

ABOUT FACTS

The Follow-on African Consortium for Tenofovir Studies (FACTS) is a South African-led research consortium headed by Protocol Chair Professor Helen Rees, Executive Director of Wits Reproductive Health and HIV Institute (Wits RHI), and Protocol Co-chair Professor Glenda Gray, President of the SA Medical Research Council. The consortium is coordinated at the Wits RHI in Johannesburg with data management coordinated by the Perinatal HIV Research Unit (PHRU) in Soweto, South Africa. Other South African research institutes participating in the consortium include the Aurum Institute, the Desmond Tutu HIV Foundation, Maternal, Adolescent and Child Health (MatCH Research), the South African Medical Research Council, Mecru Clinical Research Unit (MeCRU), the Qhakaza Mbokodo Research Clinic, the Setshaba Research Centre and the University of Cape Town.