Results of the FACTS 001 Tenofovir Gel Study

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AVAC Webinar
9 March 2015
Background: CAPRISA 004 results

- Smaller study in KZN showed tenofovir gel provided 39% protection from HIV, but this level was uncertain
- Needed to find out if gel worked in more women across South Africa
- Needed to find out accurate level of protection against HIV
- FACTS 001 aimed at confirming and expanding the findings of the CAPRISA 004 tenofovir gel trial for licensure purposes
Overview of FACTS 001

• Large clinical trial to test if vaginal tenofovir gel was safe for use and prevents HIV infection
• October 2011 – August 2014
• Led by Follow-on African Consortium for Tenofovir Studies, with CORE group based at Wits Reproductive Health and HIV Institute in Johannesburg
• Funded by South African government, USAID and Bill & Melinda Gates Foundation
Study design and population

**Phase III RCT**
18-30 years, HIV negative, sexually active women
Not pregnant,
Willing to use effective contraception and condoms
Enrolled irrespective of HSV-2, Hepatitis B or breastfeeding status

Randomised to pericoital use (BAT 24)

- Vaginal TFV 1% gel
- Placebo gel

Monthly visits 1-27 months
HIV testing, safety assessment, product re-supply
and quarterly CVL

Comprehensive HIV prevention counselling, provision of condoms and contraception, treatment for symptomatic STIs

Primary endpoint = HIV infection
Adherence support strategies

• Participant-centred counselling
  – Motivational interviewing and adherence prescription
  – Supportive materials e.g. models, demo gels
  – Motivational messages e.g. SMS, posters

• FACTS Clubs

• Film drama addressing adherence barriers

• Mean adherence monitor displayed at clinics
Approvals and monitoring

• Approved by the South African Medicines Control Council and local Ethics Committees

• A Data Safety Monitoring Board met 2 times during the study to review the data, ensure the safety of participants and to decide if the study should continue

• An independent monitor (ACRO) visited the trial sites regularly to make sure the study was run ethically and to the highest standard
FACTS 001 Results
Women who joined the study

- 2,059 healthy, HIV-negative sexually active women living in South Africa
- Women who had HSV-2, Hep B or were breastfeeding were allowed to join study
- Ages 18 to 30 years old (Average age was 23)
- 89% were unmarried
- About 60% lived with parents or siblings
- Voluntarily joined study through an informed consent process
What are the FACTS 001 results?

• Vaginal use of tenofovir gel, before and after sex, was not effective in preventing HIV in a diverse study population of young South African women

• Tenofovir gel was found safe for use
FACTS 001 Study Results

Women’s Risk of **HIV** Infection was the same in both groups

- 62 women in placebo gel group
- 61 women in tenofovir gel group

- Of 2,059 participants, 123 women became HIV infected during the study
- Both groups had an average of 4 out of 100 women who became HIV infected
How was adherence measured?

The study measured product use in two ways:

1. Estimated % of sex acts covered was calculated by returned used gel applicator and reported number of sex acts

2. Tenofovir drug levels in vaginal samples

- Both measures showed that women used the gel with sex about half of the time
- One in five women was able to use gel more than 80% of the time
Gel use and HIV protection

• The overall study did not show that tenofovir gel was effective at preventing HIV

• In a sub-study of 214 women (from the tenofovir group), drug levels in vaginal samples were tested

• For women who had tenofovir gel in their samples and reported having had recent sex, there was some level of protection against HIV
What do these results mean?

• Pericoital vaginal TFV 1% gel was safe, but not effective in preventing acquisition in this population

• Women used the product on average in 50-60% of sex acts (based on semi-objective measures)
  – Consistent with tenofovir detection in CVL
  – In women with TFV detected and sexual activity reported, there was evidence of a protective effect

• The majority of participants were not able to achieve sufficiently high levels of gel coverage required for protection

• Urgent need for a range of HIV prevention options for young women which may be easier to integrate into their lives
Are there other microbicide trials?

• Two large trials testing a vaginal ring containing the ARV, Dapivirine, are almost finished

• Ring stays inside the vagina for a month at a time

• Results expected by early 2016
What happens next for FACTS?

- Results have been shared with participants, CABs and staff
- Ongoing dissemination is taking place with communities, national and global stakeholders
- Participants will be invited to find out which group (placebo or tenofovir gel) they were in
- There will not be an open-label extension study, as the results showed that tenofovir gel did not work
Summary

• In FACTS 001 trial tenofovir gel was not effective in preventing HIV infection among young South African women
• Women urgently need more HIV prevention methods that will meet their needs and preferences at different phases of their lives
• On going research for new prevention options, including ARV-based products and vaccines, are promising – and we must all stay committed
Near elimination of HIV transmission in a demonstration project of PrEP and ART

Jared M. Baeten, Renee Heffron, Lara Kidoguchi, Nelly Mugo, Elly Katabira, Elizabeth Bukusi, Stephen Asiimwe, Jessica E. Haberer, Deborah Donnell, Connie Celum, for the Partners Demonstration Project Team

CROI 2015, Seattle
The Partners Demonstration Project is an open-label, prospective interventional study of ART and PrEP for HIV prevention among heterosexual HIV serodiscordant couples.

The project is being conducted at 4 clinical care sites: Kisumu & Thika in Kenya and Kabwohe & Kampala in Uganda.

The overall goal is to evaluate, using implementation science methods, a scalable delivery system for PrEP and ART for HIV prevention in couples.

- With counseling, adherence promotion, and follow-up designed to reflect approaches suitable for public health clinic settings.
PrEP as a bridge to ART

• For couples initiating ART at enrollment, PrEP is offered through 6 months, then stopped:

• For couples in which the infected partner delays or declines ART, PrEP is continued until 6 months after ART initiation:

• This strategy is supported by mathematical modeling as potentially highly effective and cost-effective (Hallett et al. PLoS Med 2011; Ying et al. CROI 2015, abstract #1106)
Quantifying HIV protection

• HIV incidence was calculated for follow-up time through January 5, 2015

• The comparison was a counterfactual simulation model, bootstrapping data from a prior prospective study of HIV serodiscordant couples (Partners PrEP Study, placebo arm = no PrEP and ART @ CD4 <350 cells/µL), sampling for a subset with a matching distribution of risk scores and duration of follow-up
  – A placebo or delayed provision of ART & PrEP approach was deemed not to be ethical for this study, and using a counterfactual model was consistent with the implementation science approach
### Results: Participant Characteristics

- Between Nov 2012 and Aug 2014, 1013 couples were enrolled. Characteristics are consistent with elevated HIV risk:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% or median (IQR)</th>
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<tbody>
<tr>
<td>Gender, HIV- partner</td>
<td>33% female / 67% male</td>
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<tr>
<td>Age</td>
<td>Median 30 years (IQR 26-36), with 20% &lt;25 years</td>
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<tr>
<td>No children with study partner</td>
<td>56%</td>
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<td>Unprotected sex in the prior month</td>
<td>65%</td>
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<tr>
<td>CD4 count, HIV+ partner</td>
<td>Median 436 (IQR 272-638), with 41% &gt;500 cells/µL</td>
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<tr>
<td>Plasma HIV RNA, HIV+ partner</td>
<td>Median 37,095 (IQR 7058-104,462), with 41% &gt;50,000 copies/mL</td>
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Results: Follow-up

• To date, a total of 858 person-years have been accrued
  – The study is ongoing, with ~42% of planned person-time accrued so far
  – Retention is currently >85% at each quarterly visit
  – Pregnancy incidence is ~20%/year

• Uptake of PrEP and ART are high:
  – *PrEP*: >95% have initiated. Adherence is high (Heffron et al., CROI 2015, abstract #969)
  – *ART*: ~80% have initiated, >90% are achieving viral suppression

• For 48% of follow-up accrued to date, couples used PrEP alone (prior to initiating ART), 27% is PrEP & ART overlapping, and 16% is ART alone.
  – ART increases & PrEP decreases over longer follow-up, reflecting the use of PrEP as a bridge to ART in the partnership.
  – 9% of follow-up time has neither ART nor PrEP in use in the partnership.
HIV incidence

- The observed incidence is a 96% reduction compared to expected, a result that was highly statistically significant.

N=39.7 infections
incidence = 5.2
(95% CI 3.7-6.9)

IRR observed vs. expected = 0.04
(95% CI 0.01-0.19)
or a
96% reduction
(95% CI 81-99%)
P<0.0001

N=2 infections
incidence = 0.2
(95% CI 0.0-0.9)
Summary

• In this open-label demonstration project of integrated delivery of ART and PrEP for prevention in HIV serodiscordant couples, we have observed a 96% reduction to date in incident HIV, compared to expected rates.

• Our study differs substantially from randomized trials of PrEP and ART in its open-label, implementation science approach and its focused recruitment of higher-risk couples.

• Our results demonstrate that PrEP as a bridge to ART is not only feasible but highly effective in preventing HIV transmission in this population.
  – Notably, the majority of person-time accrued to date is PrEP-exposed, emphasizing an important PrEP effect for our results.
Partners Demonstration Project

Investigative Team
- University of Washington: Jared Baeten (protocol chair), Connie Celum (protocol chair), Renee Heffron (project director), Deborah Donnell (statistician), Ruanne Barnabas, Justin Brantley, Benjamin Browning-Roberts, Lynn Harr, Harald Haugen, Lara Kidoguchi, Toni Maddox, Susan Morrison, Jennifer Morton, Kelly Moutsos, Andrew Mujugira, Caitlin Scoville, Bettina Shell-Duncan, Kathy Thomas, Kerry Thomson
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- DF/Net Research (data management); Gilead Sciences (PrEP donation)

Project participants

Funders
- NIH (R01MH095507, R01MH100940, R01MH101027, R21AI104449, R21TW009908, K99/R00HD076679)
- Bill & Melinda Gates Foundation (OPP1056051, OPP47674)
- USAID (AID-OAA-A-12-00023)

The Partners Demonstration Project is made possible by the United States National Institutes of Health, the Bill and Melinda Gates Foundation, and the generous support of the American people through the United States Agency for International Development. The contents are the responsibility of the University of Washington and study partners and do not necessarily reflect the views of any of the study sponsors or the United States Government.