FACTS 001: Characteristics of Participants Enrolled in a Phase III Randomised Controlled Trial of Tenofovir Gel for Prevention of HIV-1 and HSV-2

Methods: Between 2006 and2010, we enrolled Thai MSM, age ≥ 18 years, from the Bangkok metropolitan area. Participants completed sexual behavior questions using audio computer-assisted self-interviews, and underwent physical examination, and rectal, urethral, and pharyngeal screening for CT and NG using nucleic acid amplification testing (NAAT). We calculated NNS as the reciprocal of the proportion of asymptomatic MSM with unrecognized infection detected by NAAT.
Results: Of 1,744 participants enrolled, 1593 (91%) had no symptoms or signs of CT/NG at baseline. We detected CT infection in 216 (14%), NG infection in 99 (6%), and CT/NG co-infection in 40 (2.5%). The overall NNS to detect CT and/or NG at any sites was 5 (95% Confidence Interval [CI] 5-6). Among insertive-only MSM (n = 285), the chance of detecting urethral CT infection (NNS 11, 95% CI 8-19) was higher than detecting urethral NG infection (NNS 71, 95% CI 36-2646, $p < 0.05$). Among versatile MSM (n = 1284), the NNS for infection at any site was 7 (95% CI 6-8) for CT, and 14 (95% CI 12-18) for NG. Among receptive only MSM (n = 287), the NNS for infection at rectal was 6 (95% CI 5-9).
Conclusions: Asymptomatic CT and NG infection in this population is high. Given that the NNS in asymptomatic sexually active MSM is low, annual screening using NAAT for all sites can diminish progression of diseases and disrupt transmission. In settings where screening all specimen sites is not available, the rectal swab test should be a priority.

P49.13
Withdrawn

P49.14
HIV-1$^+$/HSV-2$^+$ Co-infection Is Associated with Persistence of CD14$^+$ and DC-SIGN$^+$Antigen Presenting Cells at the Mucosa Independent of HSV Recurrences

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Background: Prior studies demonstrate that HSV-2 seropositivity is associated with higher HIV plasma viral loads & increased genital HIV shedding. We hypothesize that in HIV$^+$/HSV-2$^+$ women, genital HSV outbreaks will be associated with an increase in antigen presenting cells (APCs), which may facilitate recruitment of HIV target cells & contribute to replication & transmission in HIV$^+$/HSV-2$^+$ women.
Methods: A 12-week study was conducted among HIV$^+$/HSV-2$^+$, HIV$^+$/HSV-2$^-$, HIV$^-$/HSV-2$^+$& HIV$^-$/HSV-2$^-$ women to examine the impact of HSV-2 reactivation on mucosal immunity. Vaginal biopsies were collected at baseline & from a lesion & contralateral uninvolved site during a clinical recurrence. Sections from 4 HIV$^+$/HSV-2$^+$& 4 HIV$^-$/HSV-2$^+$ women were evaluated for APCs & results quantified by *in situ* IHC imaging analysis.
Results: At baseline, co-infected women had significantly more CD209$^+$(DC-SIGN) & CD14$^+$(monocytes/macrophages) cells compared to HIV$^+$/HSV-2$^-$&HIV$^-$/HSV-2$^+$ women. After an outbreak, there was an increase in these APCs in HIV$^-$ women at the lesional but not the contralateral site ($p < .02$). However, the response in co-infected women was blunted. For example, CD209$^+$ expression increased from 1002.6 ± 78.6 cells/mm^2 at baseline to only 1132.3 ± 99.4 cells/mm^2 in lesions, but increased in lesions from HIV$^-$ women from 251.3 ± 92 cells/mm^2 at baseline to 795.8 ± 21 cells/mm^2 ($p < .004$). Similarly, there was little or no increase in CD14$^+$ cells in lesions in co-infected women whereas CD14 increased in HIV$^-$ women from 514.5 ± 118.9 to 1291.6 ± 119.7 cells/mm^2 ($p < .04$).
Conclusions: Co-infection is associated with an increase in CD209$^+$& CD14$^+$ APCs in biopsies independent of HSV disease. During clinical HSV recurrences, there is an increase in APCs at the lesional but not the contralateral site, which is more pronounced in HIV$^-$ women. The largest APCs observed were CD14$^+$ monocytes & CD209$^+$ macrophages. These findings provide a potential mechanism for the increased risk of HIV transmission in the setting of HSV-2 co-infection.

Tenofovir Gel: Acceptability and Adherence

P50.01
FACTS 001: Characteristics of Participants Enrolled in a Phase III Randomised Controlled Trial of Tenofovir Gel for Prevention of HIV-1 and HSV-2

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Background: FACTS 001 is a phase III licensure trial to assess the safety and effectiveness of tenofovir 1% gel applied intravaginally before and after sex in preventing HIV-1 and HSV-2 in women in South Africa. We report on the baseline characteristics of the trial population.
Methods: Participants were screened for eligibility for the trial at nine sites across South Africa from October 2011 until March 2014. Women aged 18–30 years, who were HIV-1 negative, sexually active, using a reliable modern contraceptive, with no travel plans, no recent history of enrolment in another HIV prevention trial, and without evidence of renal or pelvic disease, raised liver enzymes, or pathological bone fractures, who consented to all study procedures, were considered eligible for the trial. Participants were enrolled irrespective of HSV-2 status at enrolment.
Results: 3846 participants were screened and 2059 were enrolled in the trial. The main reasons for exclusion were HIV-1 positive, not willing or able to consent to all procedures, and evidence of proteinuria or glycosuria. At the time of enrolment,

the mean age of participants was 23 years, and the majority of participants were unmarried (88%), lived with parents (62%), had completed school (43%), were unemployed and earned < R1000 in the past three months (73%). Most participants reported having only one regular partner (89%) and a median of 9 (IQR 5-16) sex acts in the past 28 days. The overall prevalence of HSV-2 at enrolment was 42%.
Conclusions: The baseline characteristics of FACTS 001 enrolled trial population reflect those most at risk for HIV infection in South Africa, and in need of new HIV prevention technologies.

P50.02
Meta-analysis of the Effectiveness of Tenofovir Gel in Preventing HIV Infections

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Background: Three clinical trials have been conducted to test whether 1% Tenofovir gel prevents heterosexual transmission of HIV. The CAPRISA 004 study found a reduction of 39% and the VOICE study found a reduction of 14.7% in HIV incidence comparing the Tenofovir gel arm to the placebo arm. The FACTS study is still under way and results are expected early next year. The objective is to estimate the combined efficacy of tenofovir gel using all three studies.
Methods: A meta-analysis was done of the CAPRISA and VOICE results. Additional meta-analyses also included hypothetical results of the FACTS study. The Cochran-Mantel-Haenszel common relative risk was calculated for each meta-analysis. The CAPRISA and FACTS studies had coitally dependent dosing (the so-called BAT24 strategy), while the VOICE study had daily dosing.
Results: A meta-analysis of the gel arms in VOICE and CAPRISA 004, estimates that Tenofovir gel provides 24% protection (95%CI: 2-41%,p-value = 0.03). If the results of the FACTS study was similar to the VOICE study, the meta-analysis estimates 21% protection (95%CI: 2-36%,p-value = 0.03) and if it was similar to CAPRISA 004 the meta-analysis estimates 28% protection (95%CI:11-42%,p-value = 0.003). If the FACTS study showed a null-result (the same number of infections in the Tenofovir gel and placebo arms) then the meta-analysis estimates that Tenofovir gel provides 18% protection (-1-34%, p-value = 0.068). In all instances the test for heterogeneity did not detect heterogeneity between the studies.
Conclusions: If the results of the FACTS study lie between the results of the CAPRISA and the VOICE studies, i.e. provides between 14.7% and 39% protection from HIV infection, one expects the combined efficacy estimate of the three studies to lie between 21% and 28%, with a p-value smaller than 0.03. This would indicate that Tenofovir gel is efficacious in preventing HV infection, when all available efficacy trials are combined.

P50.03
Tenofovir Gel as a Component of the HIV Prevention Mix: Perspectives from Participants, Partners and Community Men in KwaZulu-Natal, South Africa

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Background: Many questions exist with regard to how 1% tenofovir gel could be integrated with existing HIV prevention methods, if it is approved. We explored perceptions of women and men about the gel relative to other prevention methods in the context of CAPRISA 008, an ongoing open-label follow-on trial of tenofovir gel that enrolled uninfected CAPRISA 004 trial participants.
Methods: In-depth interviews (n = 63) and focus groups (n = 8) were held with CAPRISA 008 participants; male partners of 13 women who fully disclosed trial participation and gel use were also interviewed. Four focus groups were held with community men who were not partners of women in the CAPRISA 008 trial. Perspectives on HIV prevention options including tenofovir gel were assessed using an applied thematic analysis approach.
Results: Male condoms and male circumcision were perceived to be the most effective means of HIV prevention by both female and male respondents; however, the difficulty of consistent condom use often negated perceived efficacy while male circumcision faced cultural aversion and was viewed as mainly protecting men. Few respondents reported use of female condoms; most were averse to the thought of using them. Tenofovir gel was generally viewed as an effective means of HIV prevention by both women and men, though there was concern that it is still not licensed by the government and that it is ''not 100% effective.'' Use of tenofovir gel was particularly considered beneficial for women if their partners refuse to wear condoms and was described as easy to use relative to other HIV prevention methods. Few participants reported cases of condom migration. Some men noted that their partner's use of tenofovir gel provided risk reduction benefits to them as well.
Conclusions: Both men and women in KwaZulu-Natal, South Africa perceive tenofovir gel as offering the potential to address limitations in the current HIV prevention method mix.

P50.04
Tenofovir Gel Acceptability and Adherence among Pregnant Women in the United States

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Background: The MTN-008 trial, the first multi-dose study of a microbicide gel (2:1 randomized to tenofovir 1% or HEC placebo gel) during pregnancy, included daily pregnant participant gel insertion at home for 5 days. Because pregnancy may pose unique challenges to consistent gel use and acceptability these factors were assessed.
Methods: Participants completed a web-based computer-assisted self-interview (CASI) at Days 0 and 6 about gel attitudes and behaviors. At Day 6 trained research staff conducted a short interviewer-administered questionnaire with both structured and