

## **TRACK C: EPIDEMIOLOGY AND PREVENTION SCIENCES**

**Presented Tuesday, 20 July at 13:00 in Session Room 6**

**Abstract Number: TUSS0503**

**Do systemic and genital tract tenofovir concentrations predict HIV seroconversion in the CAPRISA 004 tenofovir gel trial?**

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**Background:** CAPRISA 004 is a two-arm, double-blind, randomized, placebo controlled trial assessing the effectiveness and safety of 1% tenofovir (TNF) gel in 889 women. 98 participants became HIV positive. This pharmacology study assesses whether the presence or absence of TNF is associated with HIV seroconversion in CAPRISA 004.

**Methods:** TNF and tenofovir diphosphate (TNF-DP) exposure in blood, genital tract secretions, and vaginal and cervical tissue were measured in 50 HIV seroconvertors and compared to 40 HIV negative women who had high sexual frequency and high gel use. For HIV+ women, samples closest to estimated date of infection were selected. For women who remained HIV- for the entire duration of the trial, samples were obtained from a high-gel use visit (A) and an exit visit (B). TNF and TNF-DP concentrations were measured by validated LC/MS/MS methods. Data are expressed as median [IQR].

**Results:** Age of HIV+ and HIV- subjects were 23(20-25) and 27(23-31)yrs. Samples from HIV+ women were obtained 15 (14-121) days after the estimated time of infection, and 5(3-8) days after gel use. Samples in HIV-women were obtained 3(2-6) or 5(3-8) days after reported gel use, for visit A and B respectively. TNF was detected in genital tract secretions in 36% of HIV+ and 83% of HIV- women. TNF was detected in blood in 9% of HIV+ and 30% of HIV- women. Tissue biopsies in HIV+ subjects were obtained 24(18-48) days after last reported gel use: TNF was detected in 20% of vaginal and 13% of cervical tissues: TNF-DP was detected in 16% of vaginal and 7% of cervical tissues.

**Conclusions:** More HIV- women had detectable TNF concentrations compared to HIV+ women. Final unblinded TNF and TNF-DP data will be presented according to active or placebo randomization status.

## Abstract: TUSS0504

Safety of 1% tenofovir vaginal microbicide gel in South African women: results of the CAPRISA 004 trial

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**Background:** A microbicide is urgently needed, especially for women who cannot negotiate mutual monogamy and condom use. The CAPRISA 004 trial assessed the effectiveness and safety of candidate microbicide, 1% Tenofovir gel.

**Methods:** We conducted this randomized, placebo-controlled trial among 18 to 40 year old urban (Durban) and rural (Vulindlela) women (n=889) followed for up to 30 months. Women were instructed to insert a dose of either 1% tenofovir or placebo gel within 12 hours prior to coitus and a second dose as soon as possible afterwards, but within 12 hours. Safety assessments included monthly pregnancy tests, quarterly pelvic exams, and blood draws at months 3, 12, 24 and study exit.

**Results:** Women's average ages were 23.3 and 25.1 years, respectively at Vulindlela and Durban, and 93.5% and 96.4% of women were single respectively. A total of 4692 adverse events (AEs) were reported, including one death, 38 other serious AEs, and six fractures. No serious AEs were considered related to use of tenofovir gel. The most frequently reported AEs were influenza (436 patients), vaginal discharge (312 patients) and vaginal candidiasis (244 patients). We identified severe hypophosphatemia in 22 women (15 in Vulindlela and 7 in Durban). No moderate and one severe elevated creatinine level was identified. We identified 53 pregnancies, 34 in Vulindlela and 19 in Durban, with 4 and zero pre-term deliveries respectively. 283 women in Vulindlela and 29 women in Durban had vaginal discharge and 136 and 108 women respectively had vaginal candidiasis. There were nine social harm events in Vulindlela and three in Durban. Unblinded safety results are not yet available but will be presented at the meeting.

**Conclusions:** There are no major differences between the communities in occurrence of adverse events or social harms. We will present conclusions based on unblinded data at the meeting.

## Abstract Number: LBPE27

### Impact of tenofovir gel on the HIV epidemic in South Africa: A mathematical model to estimate the effect of the CAPRISA 004 microbicide trial results

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**Background:** An effective microbicide could add an important new strategy to HIV prevention efforts. The results of the CAPRISA 004 tenofovir vaginal-microbicide-gel trial will be announced at the IAS 2010 conference. We consider the impact of different levels of efficacy of a vaginal microbicide on the HIV epidemic in South Africa.

**Methods:** Assuming that the intervention is rolled-out within the next five years, we fit a dynamical model to HIV prevalence data and project adult prevalence, incidence and mortality. We calculate the overall impact of a vaginal microbicide that reduces male-to-female transmission by 40% and 50%, assuming 50% and 80% coverage.

**Results:** Figure 1 shows the impact on the HIV epidemic at different levels of coverage and efficacy. The impact on incidence is rapid. The impact on prevalence and mortality is slower. If the microbicide efficacy is 40% then, in the next ten years it will avert 271,000 infections with 50% coverage and 460,000 with 80% coverage. If the efficacy is 50% then it will avert 347,000 new infections with 50% coverage and 602,000 new infections with 80% coverage.

**Conclusions:** A vaginal microbicide with an efficacy of 40% to 50% could prevent between 271,000 and 602,000 new HIV infections in ten years depending on coverage. If effective, vaginal microbicides will provide a major new tool for the control of HIV, provided high levels of coverage are maintained. The numbers of infections averted will be calculated based upon the actual CAPRISA 004 results that will be presented at the conference.

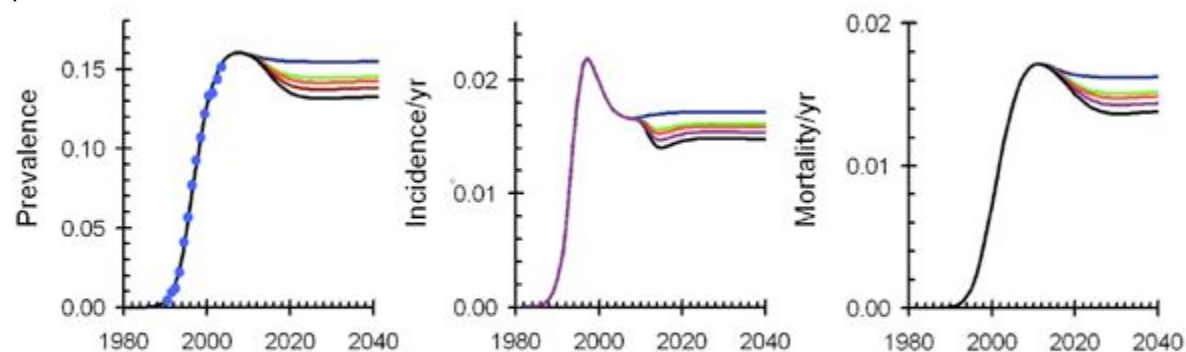


Figure. Left: prevalence; centre: annual incidence; right: annual mortality for HIV in South Africa. Lines, highest to lowest: base line with no expansion of prevention efforts; 50% coverage, 40% efficacy; 50% coverage, 50% efficacy; 80% coverage, 40% efficacy; 80% coverage, 50% efficacy.