

BO11-610 PRELIMINARY RESULTS FROM A PHARMACOKINETIC STUDY OF THE CANDIDATE VAGINAL MICROBICIDE AGENT 1% TENOFOVIR GEL

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Background:

Tenofovir (TFV) is being evaluated as a microbicide. To inhibit viral replication locally, adequate concentration (conc) in the genital tract is crucial. A study is ongoing to assess conc of TFV in 49 women undergoing a single-dose phase followed by a two week phase (once- or twice-daily). The following are results from a subset (n=21) who completed the single-dose phase.

Methodology:

Following an intravaginal dose (4 g) of TFV gel, blood samples were obtained at 0.5, 1, 2, 4, 6, 8, and 24 hr(s) from all participants. Participants were randomized to one of seven time-points [0.5, 1, 2, 4, 6, 8, and 24 hr(s)] for vaginal fluid collection and vaginal biopsies. Total TFV was measured in blood plasma (BP), fluid, and biopsies. An LC/MS assay to measure TFV in tissue was validated at UNC-Chapel Hill.

Results:

Most BP TFV conc were below 5 ng/mL. Four had higher values (up to 19.5 ng/mL) which were not sustained. Vaginal fluid conc were high, generally $1.5-5.0 \times 10^6$ ng/mL through 8 hrs and $4.5-47.1 \times 10^4$ ng/mL at 24 hrs. The mean conc in vaginal tissue at 0.5, 1, 2, 4, 6, 8 and 24 hr(s) were 275×10^3 , 450×10^3 , 186×10^3 , 89×10^3 , 69×10^3 , 24×10^3 and 15×10^3 ng/g of tissue, respectively, (LLOQ=1ng/mL) with a peak at 1-4 hrs. Vaginal fluid elimination appeared linear. Tissue elimination appeared to follow a multi-compartment model.

Conclusion:

Total TFV was detectable in vaginal tissue and fluid up to 24 hrs post single-dose exposure. These results are encouraging and support further study of administering TFV gel in advance of coitus.

BP63-616 MALE TOLERANCE STUDY OF 1% TENOFOVIR GEL FOLLOWING MULTIPLE TOPICAL EXPOSURES

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Background:

Tenofovir (TFV) is currently being evaluated as a potential vaginal microbicide. Participants in microbicide safety studies are counseled to use condoms consistently and correctly; however, they might not be able to negotiate condom use for all sexual activities. This study was conducted to ensure that male partners of the female participants in studies of TFV gel would not be subjected to an undue risk of penile irritation as a result of exposure to the product.

Methodology:

This was a randomized, blinded, single-center study of 1% TFV gel and K-Y Jelly in 36 HIV-negative men. Participants were randomly assigned to treatment groups in a 2:1 ratio within circumcision status as follows: Study Group n, Tenofovir n, K-Y Frequency Duration Circumcised 12 6 daily 7 days Uncircumcised 12 6 daily 7 days TFV gel or K-Y Jelly, 2 ml, was applied to the penis and left on for 6-10 hours for 7 consecutive nights. Each participant had three scheduled visits: screening, enrollment and a final visit after 7 applications. Serum chemistries, complete blood count, and APTT were drawn at the screening and final visit.

Results:

Three of 24 (13%) men in the tenofovir group, 2 uncircumcised and 1 circumcised, reported urogenital symptoms compared to 2 of 11 (18%) men in the K-Y group (one from each circumcision group). The most common symptoms included mild pain (burning, irritation, discomfort) and pruritus. All reported symptoms were felt to be mild. Few mild genital findings were observed. There were no clinically significant changes in the blood values between the screening and final visit. Most men would use their assigned product if it were available.

Conclusion:

Both products were well tolerated with few reports of mild urogenital irritation and few genital findings.