Results 156 (105 women and 51 men) healthy, immunocompetent, HSV-2 positive participants with a history of 1–9 recurrences per year prior to trial entry, or previous suppressive therapy, were randomised by seven US sites between May 2010 and October 2010. 147 completed the trial. Overall, about 9000 swabs for HSV PCR were collected and assayed for HSV DNA by a sensitive and accurate assay that can detect >150 copies/ml. The first results of these assessments will be presented.

Conclusion The trial will provide insight into the antiviral activity of the novel agent AIC316 for genital HSV infections. This trial design presents a robust and efficient method for evaluating antiviral activity of candidate agents for mucocutaneous HSV infections. These initial efficacy and safety results will lead to selecting the dose for further trials with AIC316.

O3-S5.02 FREQUENT BREAKTHROUGH GENITAL HSV-2 SHEDDING ON STANDARD AND HIGH DOSE VALACYCLOVIR

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Background Short, rapidly cleared, subclinical shedding episodes are the predominant form of HSV-2 reactivation in the genital tract. Valacyclovir 500 mg once daily (SD-VAL) reduces the risk of sexual transmission of herpes simplex virus type 2 (HSV-2) by only 48%. We hypothesised that short HSV-2 shedding episodes occur frequently on SD-VAL and that high dose (HD)-VAL could suppress such episodes of genital HSV-2 shedding.

Methods A randomised open-label crossover study using valacyclovir 500 mg daily (SD-VAL) vs valacyclovir 1 gm three times daily (HD-VAL) was conducted in HSV-2 seropositive, HIV seronegative persons with four or more genital herpes recurrences per year or laboratory confirmed primary genital HSV-2 infection in the previous 6 months. Each study arm lasted for 5 weeks, separated by 1 week wash out. Participants obtained genital swabs four times daily, which were assayed for HSV by quantitative PCR. The primary outcome was frequency of genital HSV shedding on each study arm; secondary outcomes included number and duration of HSV-2 shedding episodes and quantity of virus detected.

Results Forty-three participants collected 9981 genital swabs during the study period. 292 (5.8%) of 5008 swabs had HSV detected during SD-VAL, compared to 164 (3.3%) of 4973 on HD-VAL (IRR=0.52, 95% CI=0.43% to 0.63%, p<0.001). Episodes were shorter on HD-VAL (median 7 h, compared to 10 h on SD-VAL, p=0.03) and the median maximum copy number was lower on HD-VAL (3.0 log10 copy/ml vs 2.5 log10 copies/ml, p=0.001). However, the annual episode rate was the same regardless of dose; there were 55 shedding episodes over 3.89 person-years of follow-up during SD-VAL (14.1 episodes/year) and 65 episodes over 3.93 person-years during HD-VAL (16.5 episodes/year, p=0.34).

Conclusion Short bursts of genital HSV-2 reactivation persist during SD-VAL and HD-VAL. Compared to SD-VAL, HD-VAL decreased shedding frequency and episode duration but did not alter episode rate. These data may explain why risk of HSV transmission and HSV-specific genital inflammation persist even in the presence of antiviral therapy. More potent therapies are needed to completely suppress HSV-2 reactivation

ClinicalTrials.gov number NCT00362297.

O3-S5.03 HIGH-DOSE VALACYCLOVIR DECREASES PLASMA HIV-1 LEVELS MORE THAN STANDARD DOSE ACYCLOVIR IN HIV-1, HSV-2 POSITIVE PERSONS: A RANDOMISED, CROSSOVER TRIAL

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Background Standard doses of HSV suppressive therapy reduce plasma HIV-1 levels (0.25-0.5 log10 copies/mL) among HIV-1/HSV-2 co-infected persons, and modestly slow disease progression. Putative mechanisms for this effect include direct inhibition of HIV-1 by acyclovir or indirect reduction by decreasing HSV-associated inflammation. We hypothesised that higher-dose anti-HSV therapy would result in greater reduction in plasma HIV-1 RNA, and that the effect would be mediated by greater suppression of HSV shedding.

Methods 34 participants with HIV-1 and HSV-2 who were not on antiretroviral therapy were enrolled into a randomised, open-label cross-over trial with valacyclovir 1000 mg twice daily or acyclovir 400 mg twice daily for 12 weeks. After a 2 week wash-out, they were crossed over to the alternate treatment arm for 12 weeks. HSV PCR was performed on self-collected genital swabs obtained daily during the first 4 weeks of each treatment period. Plasma HIV-1 RNA was measured weekly throughout the study.

Results Among the 26 participants who completed both arms of the study, the mean age was 44; 21 were men. At entry, mean CD4 count was 525 cells/mm3 (range, 242–1055) and mean plasma HIV-1 RNA 3.9 log10 copies/ml (range 1.2–5.5). The mean plasma HIV RNA was 3.86 log10 copies/ml during acyclovir administration compared with 3.57 log10 copies/ml on valacyclovir; a 0.29 log10 copies/ml reduction (p=0.002). One week after initiation of valacyclovir, plasma HIV RNA decreased by a mean of 0.40 log10 copies/ml. Valacyclovir reduced HIV-1 RNA by ≥0.25 log10 copies/ml in 14 (54%) participants, compared with 3 (12%) on acyclovir. Neither the HSV shedding rate (8.92% vs 8.98% of days, p=0.94), nor the genital lesion rate (4.3% vs 1.1%; p=0.18) differed on acyclovir vs valacyclovir.

Conclusions High-dose valacyclovir reduces plasma HIV-1 RNA levels more effectively than standard dose acyclovir in HIV-1, HSV-2 seropositive persons not receiving antiretroviral therapy. High dose valacyclovir does not provide more potent suppression of HSV reactivation in HIV-1 infected persons than acyclovir, suggesting that the effect of valacyclovir on HIV-1 RNA may not be mediated via HSV suppression.

O3-S5.04 THE POST-TRIAL EFFECT OF PERIODIC PRESUMPTIVE TREATMENT FOR VAGINAL INFECTIONS ON THE INCIDENCE OF BACTERIAL VAGINOSIS AND LACTOBACILLUS COLONISATION

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Background *Bacterial vaginosis* (BV) is a highly prevalent infection that frequently recurs following standard treatment. In a randomised controlled trial (RCT) of oral periodic presumptive treatment (PPT) to reduce vaginal infections among Kenyan women, we observed a decrease in BV and an increase in Lactobacillus colonisation among women randomised to receive 2 g metronidazole +150 mg fluconazole monthly for 12 months. After the trial,