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 = 0.43% to 0.63%, p = 0.001). Episodes were shorter on HD-VAL (median 7 h, compared to 10 h on SD-VAL, p = 0.52, 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 = 0.05) and the median maximum copy number was lower on HD-VAL (3.0 log10 copies/ml vs 2.5 log10 copies/ml, p = 0.001). However, the annual 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 HSV-1 RNA levels more effectively than standard dose acyclovir in HSV-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 HSV-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,
women were invited to continue follow-up in an open cohort study. These post-trial data were analysed to test the hypothesis that the treatment effect would persist in the absence of PPT.

Methods Data were obtained from women who completed all 12 RCT visits and attended ≥1 cohort study visit within 120 days of their final RCT visit. We used Andersen-Gill proportional hazards models to estimate the post-trial effect of the intervention vs placebo on the incidence of BV by Gram stain (Nugent score ≥7) and Lactobacillus species by culture on Rogosa agar.

Results The RCT enrolled 310 subjects (155 per arm), of whom 165 (83 active and 82 placebo) were included in this analysis. Included subjects were slightly older (median [IQR]: 53 years [29–59] vs 30 years [26–35]; p < 0.001) and reported a longer duration of sex work (median [IQR]: 6 years [2–11] vs 3 years [1–6]; p < 0.001) compared to those excluded. At the final RCT visit, which represented the baseline visit for this analysis, demographic and behavioural characteristics were similar by arm. The prevalence of BV at the final RCT visit was 16% in the active arm and 43% in the placebo arm (p < 0.001). The post-trial incidence of BV was 260/100 person-years (p-yrs) in the active arm vs 358/100 p-yrs in the placebo arm (HR = 0.76; 95% CI: 0.51% to 1.21%). The prevalence of Lactobacillus colonisation at the final RCT visit was 17% in the active arm and 15% in the placebo arm (p = 0.51). The post-trial incidence of Lactobacillus colonisation was 180/100 p-yrs in the active arm vs 127/100 p-yrs in the placebo arm (HR = 1.42; 95% CI: 0.85% to 2.71%).

Conclusions Despite a decrease in BV and an increase in Lactobacillus colonisation during the RCT, the effect of PPT was not sustained during the 120 days following cessation of the intervention. New interventions that reduce BV recurrence and promote long-term Lactobacillus colonisation without the need for ongoing PPT or suppressive therapy are needed.

Abstract 03-S5.05 Table 1

<table>
<thead>
<tr>
<th>Stage</th>
<th>N</th>
<th>Median RPR at diagnosis</th>
<th>% With increased RPR within 14 days following treatment (95% CI)</th>
<th>% With titres increased by one dilution following therapy (95% CI)</th>
<th>% With titres increased by ≥2 dilutions following therapy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>115</td>
<td>1:16</td>
<td>30.4 (22.2 to 39.7)</td>
<td>80.0 (63.1 to 91.5)</td>
<td>20.0 (8.4 to 36.9)</td>
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<tr>
<td>Secondary</td>
<td>218</td>
<td>1:64</td>
<td>17.0 (12.2 to 22.6)</td>
<td>97.3 (85.8 to 99.9)</td>
<td>2.70 (0.1 to 14.2)</td>
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<tr>
<td>Early latent</td>
<td>132</td>
<td>1:32</td>
<td>15.9 (10.1 to 23.3)</td>
<td>85.7 (63.7 to 97.0)</td>
<td>14.3 (3.0 to 36.3)</td>
</tr>
<tr>
<td>Total</td>
<td>465</td>
<td>1:64</td>
<td>20.0 (16.5 to 23.9)</td>
<td>88.2 (79.8 to 93.9)</td>
<td>11.8 (6.1 to 20.2)</td>
</tr>
</tbody>
</table>