Late breaker oral session

LBO-1.1 ACYCLOVIR ACHIEVES LOWER CONCENTRATION IN AFRICAN HIV−, HSV-2+ WOMEN COMPARED TO NON-AFRICAN POPULATIONS, POSSIBLY EXPLAINING LOWER HERPES SUPPRESSION

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Background Two trials of acyclovir (ACV) 400 mg twice daily as daily suppressive therapy against herpes simplex virus type 2 (HSV-2) proved ineffective for prevention of HIV acquisition. Explanations for this lack of efficacy are unclear. In one of these trials, HPTN 039, ACV was modestly effective in reducing genital ulcers due to HSV-2; however, there was less reduction in the frequency of genital ulcers and higher HSV-2 DNA quantity in breakthrough lesions in women from African sites than in men from US sites. Pharmacokinetic differences of ACV have been proposed as one explanatory variable for these findings.

Methods Sixty-eight HIV-negative, HSV-2 seropositive women participated in a pharmacokinetic study of ACV after completion of HPTN 039 (a phase III, randomised clinical trial of daily acyclovir 400 mg p.o. twice daily). Following a single oral dose of 400 mg of acyclovir, blood was collected over an 8 h period. An LC/MS/MS-based assay determined ACV concentrations. PK parameters were estimated using non-compartmental methods.

Results Sixty-six African women had complete PK data for evaluation. Mean (range) age was 36 (21–54) years and weight was 70 (40–129) kg. The geometric mean (95% CI) for PK parameter estimates were: Cmax 0.31 ug/ml (0.28, 0.34), AUC0-inf 1.59 ug*hr/ml (1.43, 1.76), Tmax 1.56 h (1.40, 1.80), and half-life 2.8 h (2.5, 3.0). This Cmax was lower than 8 comparable single dose ACV PK studies in non-African populations, mean 46% lower (range 28%–59% lower, all p values <0.006). Similarly, AUC was lower than all other studies, mean 38% lower (range 26%–62%, all p values <0.001). In some studies, Tmax was earlier and the half-life was shorter. Subject weight did not explain the differences.

Conclusion Acyclovir exposure in black African women was lower than in comparable ACV studies of non-African populations. These statistically significant differences in drug exposure (Cmax and AUC) may be clinically significant and partly explain the modest effects of ACV on HSV-2 recurrence in these African women.

LBO-1.2 THE POTENTIAL IMPACT OF PRE-EXPOSURE PROPHYLAXIS FOR HIV PREVENTION AMONG MEN WHO HAVE SEX WITH MEN (MSM) IN LIMA, PERU

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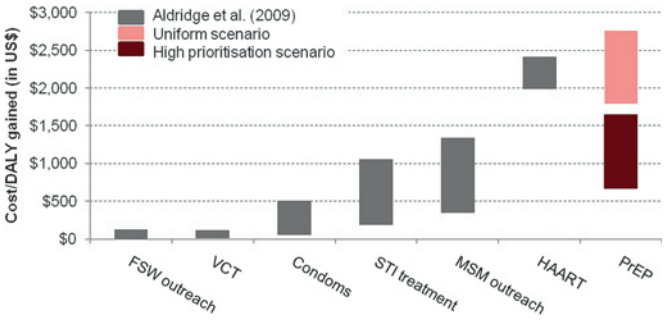
Background HIV Pre-exposure prophylaxis (PrEP), the use of antiretroviral drugs by those HIV uninfected individuals to prevent HIV infection, recently demonstrated effectiveness in preventing acquisition in a high risk population of men who have sex with men (MSM). There is a need to understand if and how PrEP can be used cost-effectively. This study examines the programmatic implications of the iPrEX study: the only randomised controlled trial of PrEP among men who have sex with men (MSM) published last December in the New England Journal of Medicine.

Methods We developed a mathematical model representing the HIV epidemic among Men who Have Sex with Men (MSM) and transgender people in Lima, Peru as a test-case. It considers differential infectiousness by stage, including the impact of antiretroviral treatment and different sexual practices, such as partnerships type and sexual positioning. The model was used to investigate the population-level impact, cost, and cost-effectiveness of PrEP under a range of implementation scenarios, and to develop possible strategies by which PrEP could be implemented.

Results The epidemiological impact of PrEP is largely driven by programme characteristics—coverage, prioritisation strategy and time to scale up—as well as individual's adherence behaviour. If PrEP is prioritised to key groups, it could be a cost-effective way to avert infection and save lives (up to 8% less new infections with 5% coverage). Across all our scenarios the estimated highest cost per DALY gained (US$2755) is below the WHO recommended threshold for cost-effective interventions for the region (<US$4608/DALY gained) see Abstract LBO-1.2 Figure 1. The impact of PrEP is reduced if those on PrEP decrease condom use, especially if the program has low coverage; but only extreme behaviour changes and a low PrEP efficacy would adversely impact the epidemic overall. However, PrEP will not arrest HIV transmission in isolation, due to its incomplete effectiveness, dependence on adherence, and the high total cost of programmes limiting attainable coverage levels.

Conclusions This study quantifies the epidemic and financial implications of different programmatic scenarios. While the implementation of a strategic PrEP intervention has potentially important financial implications (a substantial expenditure would likely be required to generate significant reductions in incidence), PrEP among vulnerable populations could be a cost-effective option comparable to currently available interventions for Men who Have Sex with Men (MSM) populations.



Abstract LBO-1.2 Figure 1

LBO-1.3 SYPHILIS INFECTION AND ASSOCIATED BEHAVIOURS AMONG TRANSGENDER WOMEN, CHICAGO 2010

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Background Transgender women are an underserved and understudied population with unique medical and behavioural risk profiles. High rates of STIs and HIV in this population have been reported, although accurately quantifying STI rates and associated risks is difficult because of limitations in measurement of gender identity, lack of standardised reporting measures, and conflation between Men who Have Sex with Men (MSM) and transgender identities. In 2009 we reported a substantial increase in syphilis among transgender women at our clinic (from two cases in 4 years to ten cases in 1 year); in 2010 we identified 20 new cases, another substantial increase. We