



HPTN 039 Key Messages

1. The study obtained answers to key scientific questions

- Answered scientific questions it was designed to answer
- Largest trial of herpes suppression ever conducted
- Sites achieved high volunteer recruitment & excellent retention in diverse populations
- Volunteers achieved high adherence to twice daily drug

2. Research indicated that HSV-2, the most common cause of genital herpes, was a risk factor for HIV

- Multiple studies showed 2-3 fold higher risk of HIV acquisition among persons with HSV-2
- ~1/3 of new HIV infections in Africa are estimated to be due to HSV-2 infection
- 20% of adults in the US and ~50% of women in Africa and MSM in Latin America have HSV-2
- HSV-2 infection is very common, but often unrecognized despite frequent reactivations
- HSV-2 is thought to increase HIV susceptibility by creating an easier portal of entry, and by recruiting immune cells to the genital area that are “targets” for HIV entry

3. Suppression of HSV-2, with a standard dose of acyclovir (400 mg twice daily), did not prevent HIV infection among men and women infected with HSV-2

- Additional research is needed to determine if this is because:
 - higher doses, new drugs, or combination drugs are needed to suppress HSV-2,
 - other etiologies of genital ulcers are important, or
 - genital immune activation due to HSV-2 reactivation is responsible

4. Acyclovir reduced the incidence of genital ulcers

- Significant reduction in ulcers & HSV-2 in ‘breakthrough’ ulcers, but less than in prior studies
- Potential explanations, needing additional research in these populations, include:
 - differences in pharmacokinetics of acyclovir,
 - reduced sensitivity of HSV-2 to acyclovir,
 - different etiology of genital ulcers in different parts of the world, or
 - lower adherence than identified through self-report or pill count

5. Safety of study volunteers was (and remains) our top priority

- No serious adverse events related to the study drug were observed
- Acyclovir has been used by 40 million people for 20 years to suppress & treat genital herpes
- Volunteers were provided with condoms, exams, & extensive risk reduction counseling
- Participants who became infected with HIV during the study were referred for appropriate medical care & treatment in their community
- We are grateful to the volunteers, whose willingness to participate & commitment were essential

6. Next steps

- Finish Partners in Prevention study to determine effect of HSV-2 suppression on HIV transmission & disease progression, testing a different hypothesis and mechanism of HSV-2 & HIV interaction
- Research should be undertaken in different populations to understand:
 - Causes of genital ulcers
 - Pharmacokinetics of acyclovir and other HSV drugs in various populations
 - Biology of HSV-2 in HIV negative and HIV positive persons
 - New drugs and vaccines for herpes
- We must continue research to find new HIV prevention tools. Clinical trials are needed to test epidemiologic and biologic observations in order to identify effective interventions