Based on previous research linking herpes as a risk factor for HIV, this study answers key questions but clearly tells us we need to know more about how these viruses interact.

Multiple studies showed a 2-3 fold increased risk of HIV acquisition among persons with HSV-2 infection:

- It is thought HSV-2 creates an easier portal of entry recruiting immune cells that are “targets” for HIV entry
- Learned that suppression of HSV-2, with a standard dose of acyclovir (400mg twice daily), did reduce genital ulcers but did not prevent HIV infection among men & women infected with HSV-2
- The study answered primary and secondary objectives
- Surprises from this study included:
  - 37% reduction in visible genital ulcers (substantially lower than in past studies in the US & Europe)
  - In 2 of the 3 regions, less reduction in amount of HSV-2 in breakthrough ulcers
- Next steps to explore from HPTN 039: 1) acyclovir absorption/pharmacokinetics in different populations, 2) HSV-2 susceptibility to acyclovir from different populations, 3) other etiologies of genital ulcers
- The door is still open to evaluate HSV-2 interventions for HIV infectiousness and transmission

Previous research suggested that acyclovir, the successful treatment for herpes, might be a pathway to HIV prevention.

- Acyclovir has been a safe and effective treatment for HSV-2 for more than 20 years
- Researchers theorized that acyclovir’s ability to suppress HSV-2 and prevent genital outbreaks could block HIV infection in people infected with herpes

This well-designed, conducted, and monitored study reinforced proven prevention strategies and provided safeguards to protect the well-being of study volunteers.

- Volunteers were provided with condoms, regular exams, episodic herpes treatment, and extensive counseling on how to reduce their risk for HIV infection throughout the study
- Largest trial of its kind:
  - 3,172 HSV-2 infected people
  - 9 sites, 5 countries
- Sites achieved high volunteer recruitment and excellent retention
- No serious adverse events related to the study drug
- Full disclosure and full consent
- Participants who became infected with HIV during the study have been referred for appropriate medical care and treatment in their community
- Grateful to volunteers

Millions with genital herpes are at risk, so studies to determine the effect of HSV-2 on HIV are essential along with other initiatives.

- 1/3 of new HIV infections in Africa are estimated to be due to HSV-2 infection
- 20% of adults in the U.S. and ~ 50% of women in Sub-Saharan Africa and men having sex with men (MSM) in Latin America have HSV-2 infection
- Although HSV-2 is common, it is often unrecognized in spite of frequent reactivations
- Partners in Prevention study is determining whether HSV-2 can reduce HIV transmission and delay the rate of progression to AIDS
- Need research on:
  - Biology of HSV: factors related to HSV-2 activation
  - Treatment of HSV: effect of higher doses of current drugs, new drugs, combination therapy on clinical and subclinical HSV
  - HSV vaccines
- Clinical trials are needed to move from epidemiologic and biologic observations in order to identify effective interventions

Adapted from: materials developed by Dr. Connie Celum, Principal Investigator, HPTN 039.