

Key Trials in HSV-2 Suppression and HIV

Research Question: Does HSV-2 suppressive therapy in HIV-negative people reduce risk of infection with HIV?

Trial and intervention tested	Sites	Trial Participant Population	Outcome Measure	Results
HPTN 039 Acyclovir 400mg 2x/day	South Africa, Zambia, Zimbabwe (women) Peru, US (MSM)	1400 HIV-negative, HSV-2 infected heterosexual women; 1900 HIV-negative, HSV-2 infected men who have sex with men (MSM); 3,300 total participants	HIV incidence	2008 No protective effect
NIMR, AMREF, LSHTM Acyclovir 400 mg 2x/day	Tanzania	820 HSV-2 infected, HIV-negative heterosexual women	HIV incidence	2007 No protective effect May have been due to low adherence (only 50% of participants high adherence) Infrequent follow up (every 3 months)

Research Question: Does HSV-2 suppressive therapy in HIV-positive people reduce risk of transmission to sexual partners?

Partners in Prevention Acyclovir 400 mg 2x/day	Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, Zambia	3,407 serodiscordant couples where HIV-positive partner coinfecting with HSV-2	HIV incidence in partners	2009 No evidence of reduced rates of HIV transmission, but there were reduced rates of genital ulcers and HIV viral load in index partners (those who were HIV and HSV-2 positive and received HSV-2 suppressive therapy)
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Research Question: Does HSV-2 suppressive therapy to reduce genital HIV shedding?

RHRU/Wellcome Trust Acyclovir 400 mg 2x/day for 3 months	South Africa	299 HIV/HSV-2 coinfecting women (CD4>200)	Frequency and quantity of detectable HIV-1 in genital tract and plasma, CD4 cell count	2007 Reduced frequency of HIV genital shedding, lower quantities of genital HIV RNA, lower HIV plasma viral loads compared with placebo
NIMR, AMREF, LSHTM Acyclovir 400 mg 2x/day	Tanzania	484 women co-infected with HSV2 and HIV female sex workers	Frequency and quantity of detectable HIV-1 in genital tract	2007 No significant benefit in reducing levels of genital HIV or HSV2
University of Washington Valacyclovir 500 mg 2x/day	Peru	20 MSM; crossover study	Frequency and quantity of detectable HIV-1 in rectal tissue and plasma HIV-1	2007 Reduction in plasma viral load (53%) Reduction in rectal HIV level (33%)
CDC Acyclovir 800 mg 2x/day	Thailand	67 women HIV/HSV-2 coinfecting; (CD4>200; not on HAART) crossover study	Frequency and quantity of detectable HIV-1 in genital tract and plasma	2007 2.8 fold drop in HIV viral load in cervico-vaginal secretions when on HSV-2 suppressive treatment
ANRS 1285a Valacyclovir 500 mg 2x/day for 3 months	Burkina Faso	140 HIV/HSV-2 coinfecting women not on HAART (CD4>200)	Frequency and quantity of detectable HIV in genital tract and plasma	2006 Reduced frequency of HIV genital shedding, lower quantities of genital HIV RNA (50%); lower HIV plasma viral loads compared with placebo (70%); reduced HSV-2 genital shedding and ulcers
ANRS 1285b Valacyclovir 500 mg 2x/day for 3 months	Burkina Faso	60 HIV/HSV-2 coinfecting women on HAART	Frequency and quantity of detectable HIV-1 in genital tract and plasma	2006 No overall significant impact on genital HIV shedding but reduced HIV shedding for women with detectable genital shedding of HIV; viral load decreased in women with detectable viral load (small numbers so not significant); reduced frequency and quantity of genital HSV-2

Research Question: Does episodic HSV-2 therapy for outbreaks have an impact on levels of HIV in the genital tract, semen or herpes ulcers?

ANRS 1212 400 mg acyclovir 2x/day for 5 days	Ghana and Central African Republic	HIV-positive women with genital ulcer disease	Frequency and quantity genital HIV, plasma HIV, ulcer healing	2006 No impact on HIV genital shedding at day 7, 1 month) or plasma HIV (day 28) Reduced HSV-2 shedding; improved lesional healing
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