

Restricting HIV-1 Replication with High-Dose Valacyclovir

May 20, 2013

G Brennan

Patients infected with herpes simplex virus 2 (HSV-2) have an increased risk of HIV-1 infection. In addition, HSV-2 reactivation in co-infected patients is associated with elevated plasma and genital HIV-1 levels as well as increased risk of HIV-1 transmission to HIV-negative partners. Multiple trials have demonstrated that, on average, co-infected patients taking the anti-HSV medications acyclovir or valacyclovir experience a reduction in HIV-1 plasma viremia. However, it is unclear if this reduction in HIV-1 levels is an indirect effect attributable to decreased HSV-induced inflammation, or if the medication is directly inhibiting HIV-1 reverse transcription. In a recent report published in *JAIDS*, Drs. Tara Perti (University of Washington), Anna Wald (Vaccine and Infectious Disease Division), and their collaborators demonstrate that HIV-1 viremia was lower in patients treated with high-dose valacyclovir compared to standard dose acyclovir, even though valacyclovir had no additional effect on HSV-2 shedding in these patients. These data are consistent with previous studies suggesting that acyclovir and valacyclovir treatment may directly inhibit HIV-1 replication.

To determine whether or not HSV-2 suppression is correlated with HIV-1 suppression, Perti, et al. treated 28 Seattle-area anti-retroviral therapy (ART) naïve patients co-infected with HIV-1 and HSV-2. Patients were randomly assigned to one of two groups, receiving either the standard dose of acyclovir, or high-dose valacyclovir treatment for 12 weeks. After a two week washout period during which they received no drug, patients switched study arms, receiving the opposite treatment for another 12 weeks. HSV shedding was measured daily, while HIV-1 viremia was quantified weekly. A subset of patients also underwent more frequent HIV-1 testing at the initiation of valacyclovir treatment to determine the kinetics of HIV-1 decline.

The team found that there was no difference in the amount of HSV-2 genital shedding (RR 0.95; 95% CI 0.66-1.37; $p=0.78$), shedding episode duration ($p=0.68$), or quantity of HSV-2 DNA detected ($p=0.67$) when comparing the acyclovir- and valacyclovir-treated arms. Although they did not find a difference in HSV-2 suppression, the team found that HIV-1 RNA is lower in patients receiving high-dose valacyclovir (0.27 log₁₀ copies/mL, 95% CI -0.41 to -0.14 log₁₀; $p<0.001$) compared to standard dose acyclovir.

In this study, the authors report a modest decrease in HIV-1 plasma viremia for patients treated with high-dose valacyclovir relative to acyclovir treatment. There was no difference in HSV-2 shedding between the two study arms; therefore, HSV-2 mediated inflammation is unlikely to account for the differences in HIV-1 viremia reported in this study. Taken together, these data suggest that valacyclovir may directly inhibit HIV-1 replication. “Further investigation is needed to determine if...high-dose valacyclovir, which is much less expensive than ART, could have a role in delaying HIV progression and decreasing HIV transmission for persons in developing countries who are not yet eligible for ART according to their national HIV treatment guidelines,” said Dr. Perti.

[Perti T, Saracino M, Baeten JM, Johnston C, Diem K, Ocbamichael N, Huang ML, Selke S, Margaret A, Corey L, Wald A.](#) 2013. High-Dose Valacyclovir Decreases Plasma HIV-1 RNA More Than Standard-Dose Acyclovir in Persons Coinfected with HIV-1 and HSV-2: A Randomized Crossover Trial. 63(2):201-8.

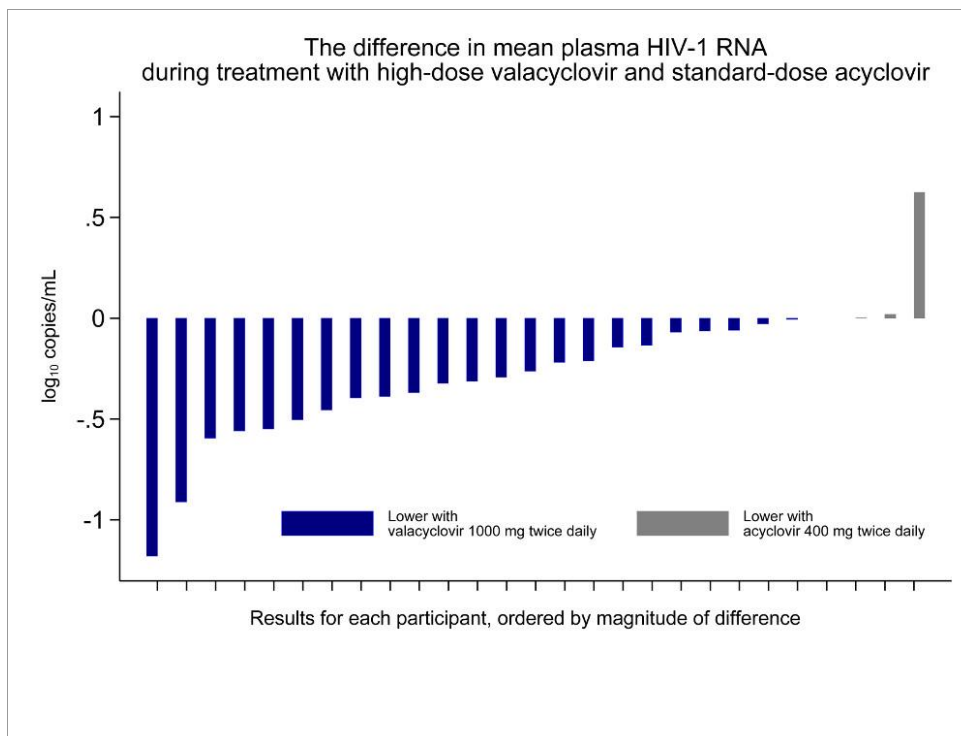


Image courtesy Dr. Tara Perti

Difference in mean plasma HIV-1 RNA for each patient on high-dose valacyclovir versus standard-dose acyclovir. Each patient is represented by a bar. Blue bars are patients whose mean HIV-1 level was lower on high-dose valacyclovir, while gray bars are patients whose HIV-1 RNA level was lower on standard-dose acyclovir.