Predictors of nevirapine resistance in Ugandan infants who were HIV-infected despite single dose nevirapine prophylaxis

Jessica D. Church1, Anthony Mwatha2, Laura A. Guay1, Michael C. Thigpen3, Philippa Musoke4, Chineta Eure3, Michelle McConnell3, Mary Glenn Fowler1,3, J. Brooks Jackson1, and Susan H. Eshleman1

1 Johns Hopkins Univ. School of Medicine, Baltimore, MD, USA
2 Statistical Center for HIV/AIDS Research and Prevention (SCHARP), Seattle, WA, USA
3 Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA
4 Makerere Univ. School of Medicine and the Makerere Univ. – Johns Hopkins Univ. (MUJHU) Research Collaboration, Kampala, Uganda

Key words: Nevirapine, resistance, mother-to-child transmission

Background: Single-dose nevirapine (sdNVP) is often used to prevent HIV mother-to-child transmission in resource-poor settings. We analyzed samples from four studies in Uganda to identify predictors of NVP resistance in HIV-infected infants.

Methods: Plasma samples from 6-8 week old HIV-infected, sdNVP-exposed infants were obtained from HIVNET 012, the Repeat Pregnancy Study, the Breastfeeding Study, and the SWEN study (Ugandan arm). Samples were analyzed using the ViroSeq HIV Genotyping System and the LigAmp assay (for sensitive detection of K103N, Y181C, and G190A). If an infant had NVP resistance at 6-8 weeks, samples from 6-12 months of age were also tested.

Results: At 6-8 weeks, NVP resistance was detected by ViroSeq in 36 (45.0%) of 80 infants, and by LigAmp in 33 (45.8%) of 72 infants (LigAmp was only performed for samples with subtype A and D). A higher proportion of infants who were diagnosed with HIV infection at birth (in utero HIV infection) had NVP resistance, compared to infants who were HIV-uninfected at birth (ViroSeq: OR=3.5 [95% CI: 1.3-9.4]; LigAmp: OR=3.9 [95% CI: 1.3-11.4]). Maternal pre-NVP viral load, maternal pre-NVP CD4 cell count, infant viral load at 6-8 weeks, HIV subtype (A vs. D), and infant gender were not associated with detection of NVP resistance at 6-8 weeks. NVP resistance was still detected in 12 (63.2%) of 19 infants tested at 6-8 weeks and in 4 (50%) of 8 other infants tested at 12 months (results from ViroSeq and LigAmp). The resistant variants were present at low levels (detectable only by LigAmp) in 4/12 infants with 6-8 weeks and in 2/4 infants with resistance at 12 months. The proportion of infants who had NVP resistance detected at 6 or 12 months was higher among infants with in utero HIV infection than among infants who were HIV-uninfected at birth (11/15=73.3% vs. 5/12=41.7%), but the difference was not statistically significant (p=0.13).

Conclusions: NVP resistance was detected in 45-46% of HIV-infected infants 6-8 weeks after sdNVP. NVP resistance was associated with in utero HIV infection, but not with HIV subtype, maternal or infant viral load, maternal CD4 cell count, or infant gender. Among infants who had NVP resistance at 6-8 weeks of age, NVP resistance was still detected in 16 (59.3%) of 27 infants at 6-12 months.