

# **Addition of extended zidovudine to extended nevirapine prophylaxis reduces resistance in infants who were HIV infected *in utero*: the PEPI-Malawi Study**

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## **INTRODUCTION**

Extended nevirapine (NVP) prophylaxis reduces the risk of post-natal HIV transmission, but may induce resistance among infants who are HIV-infected *in utero*. An infant's HIV infection status is often not known when prophylaxis is initiated at birth. We compared NVP resistance in infants who were subsequently found to have been HIV-infected *in utero*, but who were exposed before HIV diagnosis to either extended NVP prophylaxis or extended NVP plus zidovudine (ZDV) prophylaxis in the PEPI-Malawi study. In PEPI-Malawi, there was no difference in efficacy of extended NVP+ZDV vs. extended NVP for prevention of post-natal HIV infection.

## **METHODS**

In PEPI-Malawi, most HIV-infected women received single-dose nevirapine (sdNVP) prior to delivery. Infants were randomized at birth to receive: (1) sdNVP plus one week of ZDV [control], (2) control plus extended NVP prophylaxis, daily to age 14 weeks, or (3) control plus extended NVP+ZDV prophylaxis, daily to age 14 weeks. Prophylaxis was stopped when infant HIV infection was confirmed. Plasma collected at 14 weeks was available from 105 of 161 infants in the extended study arms who were HIV-infected *in utero* (positive HIV DNA test at birth). HIV genotyping was performed using the ViroSeq HIV Genotyping System.

## **RESULTS**

Genotyping results were obtained for 88 (83.8%) of 105 14-week samples. Among the 88 infants with genotyping results, prophylaxis was stopped at a median of 6 weeks of age in both study arms (range 1-14 weeks). At 14 weeks of age, the proportion of infants with NVP resistance was lower in the extended NVP+ZDV arm than the extended NVP arm (28/45=62.2%, vs. 37/43=86.0%,  $p=0.015$ ); none of the infants had ZDV resistance. Addition of extended ZDV to extended NVP reduced the risk of NVP resistance in infants whose prophylaxis was stopped by 6 weeks (19/35=54.3% vs. 30/35=85.7%,  $p=0.008$ ), but not in infants whose prophylaxis was continued beyond 6 weeks (9/10=90.0% vs. 7/8=87.5%,  $p=0.71$ ).

## **CONCLUSIONS**

Addition of extended ZDV to extended NVP prophylaxis significantly reduced the risk of NVP resistance at 14 weeks in infants with *in utero* HIV infection, provided that HIV infection was diagnosed and the prophylaxis was stopped by 6 weeks of age.