

**POSTER 58****MAJOR VARIANT MUTATIONS AS PREDICTORS OF ANTIRETROVIRAL TREATMENT FAILURE IN MOTHERS EXPOSED TO SINGLE-DOSED NEVIRAPINE**

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Single dose NVP (sdNVP) is widely used for prevention of MTCT in HIV infection, but can cause fast development of drug-resistant viral mutations. In this study we investigate whether the presence of sdNVP associated mutations predisposes women to ARV treatment failure. We genotyped 144 women, who were randomized to receive sdNVP in the MTCT Mashi trial in Botswana (pregnant women received zidovudine at 34 weeks of gestation along with sdNVP or a placebo during labor). Twenty-eight percent 40/144 of these women later failed treatment. To evaluate drug resistance mutations, we used RNA bulk sequencing for NNRTI resistance and investigated sdNVP associated mutations at two time points: at pre-HAART and at time of failure to explore potential associations between drug-resistance mutations and treatment outcome. K103N mutations were detected at a pre-HAART time point in a number of women in the cohort, all of which were sdNVP exposed and later failed treatment. Another major NNRTI- mutation, Y181C, was detected in some of the women prior to initiation of HAART. Two NNRTI resistance mutations, G190A and V106M, were found in <20% and <5% of the cohort, respectively. Detectable pre-HAART K103N mutations were observed in the majority of women who initiated HAART within six months of sdNVP exposure compared to women who initiated HAART after six months of sdNVP exposure. Women who had detectable K103N at a pre-treatment time point had a shorter time to treatment failure (P = 0.02). Furthermore, women with high Pre-HAART viral loads (>100,000 copies/ml) had a shorter time to treatment failure than those with low Pre-HAART viral loads (P = 0.002). No significant associations between pre-treatment CD4 count and time to treatment failure was observed.

**Conclusion:** This study shows that effectiveness of NNRTI based HAART may be compromised by prior exposure to sdNVP although some of the failures could not be explained by the detection of NVP resistance mutations prior to HAART as measured by standard genotyping assay.