

BRIEF ON SCIENTIFIC LECTURE HELD ON 12TH AUGUST 2004.

Topic:	Intrapartum Exposure to Nevirapine and Subsequent Maternal Responses to Nevirapine-Based Antiretroviral Therapy
Discussant:	Dr. Paul Bakaki, Investigator, MU-JHU Research Collaboration
Chair:	Dr. Israel Kalyesubula
Rapporteur	
Audience	
Summary	<p>This paper was selected from the journal of <i>N Engl J Med</i> 351;3 published in July 15, 2004. Authors included Jourdain G, Ngo-Giang-Huong N, Le Coeur S, et al Work was done by over 100 investigators and coordinators from 37 hospitals.</p> <p>Paul gave the following background to the study</p> <ol style="list-style-type: none"> 1. Most PMTCT programs in developing countries give NVP, AZT or both for prophylaxis against infant infection 2. Unfortunately NVP/AZT resistance mutations have been observed following the prophylactic doses, in up to 15-45% of mothers following NVP 3. Yet NNRTI-based combination ARV regimens are recommended as first line for HIV treatment in these developing countries 4. The current study was designed to determine if single dose intrapartum NVP could compromise efficacy of NVP containing regimens <p>The study aimed at assessing whether the rate of virologic response to HAART deferred between women exposed to intrapartum NVP vs those not exposed and studying the association between virologic failure and resistant mutations detectable at 10 days.</p> <p>Methods this was a multi-center (37 centers), double-blind, randomized, placebo-controlled trial. The participating women were evaluated at 10 days, 6 wks, 4 months postpartum. They received a complete physical exam, hematology, viral studies done in the maternity before being referred to internists for ARVs. The women with CD4s less than 250/cc at any time postpartum were offered HAART While on HAART, monthly clinical evaluation, CBC, LFTs & viral loads were done at 3 and 6 months and CD4 cells at 6 months.</p> <p>The first line regimen was chosen according to clinical & biological assessment, the cheapest initially being protease based and later NVP based</p> <p>Genotyping and analyzing for mutations associated with resistance to NNRTIs and NRTIs was done on 256 women</p>

	<p>The viral load was assessed using standard (limit of detection <400 copies/cc) or ultra sensitive (limit of detection <50 copies/cc) methods.</p> <p>Results: None of the 10 women who had repeat NVP dose in the same pregnancy had NNRTI resistance mutations. NNRTI resistance mutations were detected in 42% of the women at or above the median viral load compared to 20% of those below the median viral load (p=0.001). At 3 months after initiation of HAART there was no difference in viral suppression between women exposed to intrapartum NVP and those not exposed (34% {80/236 had viral load <50 copies/cc}). At 6 months the viral load was below 50 copies/cc in 49% (92/88) of the women who received intrapartum NVP compared to 68% (28/41) who did not receive intrapartum NVP (p=0.03).</p> <p>The authors concluded as follows: Intrapartum exposure to NVP and high baseline viral load compromised virologic suppression below 50 copies/cc by NVP containing HAART at 6 months. Their routine HIV treatment monitoring markers (clinical and CD4s) did not differ between prior intrapartum NVP exposure and no exposure. Difference in time to initiation of HAART explained by discontinuation of placebo and introduction of cheaper NVP-based pill rather than intrapartum exposure to NVP. Intrapartum exposure to NVP, even in the absence of detectable resistance, may compromise subsequent response to NNRTI based HAART. A significant proportion of women with NVP resistance still responded to NVP containing HAART.</p> <p>Paul proposed that</p> <ul style="list-style-type: none"> • There was a need to conduct similar research studies in Uganda to answer the questions of <ul style="list-style-type: none"> – Intrapartum NVP and response to HAART among moms and infants – Effect of repeated intrapartum NVP – Long term follow up of moms exposed to NVP especially those needing treatment later • The MOH should plan to give AZT from 28 weeks of gestation up to 1 wk postpartum with intrapartum NVP in order to reduce the emergence of resistance to NVP.
<p>Contribution from the audience</p>	<p>The audience concluded that NPV still had a significant role to play in the prevention of Mother to child transmission of HIV since treatment using NVP based regimes appeared to be beneficial to those exposed to it during labour.</p>

