

BRIEFS OF THE SCIENTIFIC LECTURE HELD ON 30<sup>th</sup> March 2006

Topic:	HPTN 027
Chair:	Dr. Phillipa Musoke
Attendance	
Discussant:	Prof. Francis Miiro, Dr. Phillipa Musoke, Dr. Kenneth Kintu, Makerere University-Johns Hopkins Research Collaboration, Dr. Mary Glenn Fowler (John Hopkins University)
Rapporteur:	Dr. David Meya
Audience:	
Summary:	Prof. Francis Miiro, and Dr. Kenneth Kintu presented a planned phase 1 study that will evaluate the safety and immunogenicity of ALVAC-HIV v CP1521 vaccine in infants. The study will be conducted in Mulago hospital and patients will be recruited from the antenatal clinics in Mulago hospital and subsequently followed-up at the MUJHU research clinics. This study in breastfeeding infants born to HIV+ mothers has the potential to provide significant benefits to the population being studied but to the advancement of HIV vaccine studies.
Main discussion points:	<p>Dr. Glen Fowler opened the discussion with a review on why perinatal HIV vaccines are needed. Although breast feeding improves overall infant survival in resource limited settings, it is associated with a low but ongoing risk of HIV infection. In view of the cultural norms attached to breast feeding, mothers who do not breast feed would be stigmatised. Early weaning has also been associated with growth faltering, malnutrition and increased mortality. She therefore concluded that there is an urgent need to make breast feeding safe for HIV-infected mothers. Various strategies are needed to achieve this including giving antiretrovirals to the mother during breast feeding, antiretrovirals to the infant during breast feeding, exclusive breast feeding, the development of vaccines or a combination of the above.</p> <p>In his background, Prof Miiro noted that the results from this study will complement data from phase I/II and phase III trials of this clade E/B vaccine in adults in Thailand, a trial of the clade B in Uganda and ALVACHIV Vcp1425 in infants in the USA. ALVAC HIV vCP1521 is currently undergoing efficacy testing for prevention of HIV infection among adults in Thailand.</p> <p>He noted that the vaccine is a preparation of live recombinant canary pox virus expressing gene products from HIV-1 env (clade E) gag (clade B) and protease (clade B) coding sequences.</p> <p><b>Study design:</b> This will be a phase I randomised double blind placebo controlled trial of ALVAC-HIV vCP1521 in infants born to HIV-1 infected mothers in Uganda. Mothers with CD4 cells &gt;500 who are attending the antenatal clinic in Mulago hospital will be targeted. Two study arms will constitute a sample size of 50: 40 will be given the vaccine while 10 will be given placebo. Initial dose will be given on or before day 3 after birth, then 4, 8 and 12 weeks after birth.</p>

	<p><b>Primary objectives:</b> To evaluate the safety and tolerance of ALVAC-HIV vCP1521 in infants and to evaluate the immunogenicity (cell mediated and humoral responses) of ALVAC – HIV vCP1521 in infant born to HIV-1 infected mothers with CD4&gt;500cells/<math>\mu</math>L.</p> <p><b>Secondary objectives:</b> To monitor changes in viral load over time in infants receiving the vaccine who are identified as HIV-infected. To monitor changes in CD4 cell counts in all vaccinated infants. To evaluate impact of the vaccine on the infant’s immune response to standard UNEPI immunizations.</p> <p><b>Discussion:</b> He then discussed neonatal immune responses pointing out the potential factors that would influence these neonatal responses including; nature of antigen, timing of immunization, mechanism of protection, presence of maternally derived antibodies, vaccine dose and the type of adjuvant used. In his discussion, Prof Miiro also pointed out that although the predominant HIV clades in Uganda were A&amp;D, clade D was genetically similar to the US clade B virus. Thus the issue of cross clade immunogenicity. The ideal HIV vaccine should be able to generate protective immune responses against all HIV-1 subtypes. It is hoped that this vaccine will be able to induce cross reactivity in non sub type B primary virus and thus overcome the immunologic diversity of envelope proteins.</p> <p><b>Study procedures:</b> Dr. Kenneth Kintu discussed the study procedures that will characterise this vaccine study. After identifying HIV-infected mothers attending the antenatal clinics in Old and New Mulago, mothers will be told about the study and screening will be done after obtaining consent. This would be followed by blood work. If eligible for enrolment, consent will be obtained. Mothers will be encouraged to deliver in Mulago hospital at which time cord blood will be sampled. Four vaccinations will be given to the infant by intramuscular injection in to the right thigh on the dates already outlined. During the study period, the infant will have about 20 clinic visits including the day after each vaccination. Any new problems will be sought for. Blood draws will be done during 9 of these clinic visits for safety and immunogenicity testing. Any reaction to the vaccine, a positive HIV DNA PCR test, fever of 38°C, infection within three days prior to vaccination, an unresolved grade 3 adverse event or an active intercurrent illness may disqualify the infant from further vaccine administration. The study will be monitored for adverse events by among others the site investigators, Ugandan and US Institutional Review Boards as well as the Institutional biosafety committee.</p>
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