Feasibility of point-of-care testing of HIV-exposed infants to initiate ART within 48 hours of birth following in utero HIV infection: the Uwacungo Lwabantwana Study, KwaZulu-Natal, South Africa

**BACKGROUND**

Prevention of mother-to-child transmission of HIV has reduced transmission rates to 1.2% among >300,000 babies born to HIV-infected mothers each year in South Africa. There is increasing evidence that early combination antiretroviral therapy (cART), especially in utero infected children, is effective in reducing the size of the HIV reservoir [1-2].

The aim of this study is to first, to evaluate the feasibility of identifying in utero HIV-infected babies and initiating ART within the first 48 hours of life in the setting of KwaZulu-Natal (KZN), South Africa.

KZN is at the epicentre of the global HIV epidemic, with a population of 10.9m, and where 40% of mothers attending antenatal clinics are HIV-infected.

A secondary aim here is to determine whether early initiation of cART within the first 2 days of life (i.e. diagnosed as a result of point-of-care testing of high risk infants) results in lower viral reservoirs compared to children in whom cART was initiated within the first 1-2 weeks of life, but outside the first 48 hours of life (i.e. diagnosed as a result of delayed blood spot testing undertaken on the first day of life as per standard of care).

The current report describes progress approximately 12 months into the study.

**METHODS**

**Babies at “high risk” of HIV infection are defined as follows:**

1. born to HIV-infected mother and
2. the mother either first tested HIV+ve during labour or there was evidence of ART non-adherence/interupture, as defined by the study protocol questionnaire (Fig 1A).

**Point-of-care HIV PCR testing of the newborn is performed using the Cepheid GeneXpert assay detecting infection within 90 minutes.** If the newborn tests positive, cART is initiated immediately according to South African treatment guidelines.

**Standard of care** is for all babies born to HIV+ve mothers to be tested at birth by dried blood spot testing (DBST), the result being available at ~7 days of age.

Babies with a positive DBST who are not already part of the study are enrolled in the control arm and subsequently three monthly.

**According to the study protocol (Fig 1B), the babies are followed up monthly within the first 6 months of life and subsequently three monthly**.

Efficacy is assessed through plasma viral load, including time to plasma viral load below the level of detection (<20 c/ml), plasma viral reservoir in the peripheral blood proportion of children with viral reservoir (beneath the level of detection at age 12 months and at age 24 months), and anti-HIV immune responses.

**RESULTS**

The study started in July 2015 at Stanger Hospital Kwa-Dukuza, in October 2015 at Edendale Hospital, and is scheduled to be initiated in August 2016 at the Lower Umbilatzi Regional War Memorial Hospital (LWWMR) in Empangeni (Table 1).

We test babies deemed a questionnaire to be ‘high risk’ of infection (Box 1). This number has amounted to 17% of all babies born to HIV+ve mothers. To date, over the first 11 months of the study, 15 babies have been enrolled onto the study, 11 of whom were identified as ‘high risk’ and diagnosed via GeneXpert point-of-care testing.

cART has been initiated as early as 48s of age. Initial viral loads have ranged from 170 c/ml to <20 c/ml after 3 months on cART (Fig 1A).

Based on these preliminary data of 15 infants, as many as 40-50% of utero infected infants receiving either cART initiated within the first 48hrs of life, or cART initiated within the first 2 weeks of life following WPV monotherapy initiated from the day of birth, would typically achieve viral loads of <20 c/ml by 1 month, as did the Misselwa child (4).

Illustrative examples of the diversities of enrollees are shown in Box 1.

**CONCLUSION AND OUTLOOK**

Point-of-care testing of babies identified as ‘high-risk’ of being HIV infected is feasible and leads to early cART initiation within the first 48 hours of life.

Further accumulation of data will allow an evaluation of value of the questionnaire in identifying, from the 15% referred for point-of-care testing, the great majority in utero infected infants, thus enabling cART to be initiated as early as possible.

Second, the study will determine the impact on the HIV reservoir of cART initiation within the first 48hrs of life versus initiation within the period 48hrs to 14 days, as per standard of care.

**ACKNOWLEDGEMENTS**

Study participants


**REFERENCES**

3. Pembert et al. AIDS 2012
4. Pembert et al. AIDS 2009

**Table 1:** Delivery of study infants into study arms 2015 - Stanger site opened July 09, 2015. Empangeni (LWWMR) scheduled to open August 2016. - LWWMR and district clinics: at LWWMR only, 5,870 deliveries; maternal seroprevalence 2005/06 = 36.9%

<table>
<thead>
<tr>
<th>Study Site</th>
<th>Enrollees to Date (31/12/2015)</th>
<th>Study participants</th>
<th>Study team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stanger</td>
<td>3,944</td>
<td>41.1%</td>
<td>Dineo Bopape, GuguZile Mthiyane, Spazile Zondu, Nomusa Phende, Siphelele Msomi, Nomsa Mabuza, Taryn Leslee, Milton Nkawuse, Sihlebile Hlophe. Nurses/Techns in behalf of the processing lab. Capitated: Gwagwane Simeone</td>
</tr>
<tr>
<td>Edendale</td>
<td>7,572</td>
<td>40.6%</td>
<td>Dineo Bopape, GuguZile Mthiyane, Spazile Zondu, Nomusa Phende, Siphelele Msomi, Nomsa Mabuza, Taryn Leslee, Milton Nkawuse, Sihlebile Hlophe. Nurses/Techns in behalf of the processing lab. Capitated: Gwagwane Simeone</td>
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</table>

**Fig 1A:** Study results of study infants into study arms 2015 - Stanger site opened July 09, 2015. - Empangeni (LWWMR) scheduled to open August 2016. - LWWMR and district clinics: at LWWMR only, 5,870 deliveries; maternal seroprevalence 2005/06 = 36.9%

**Fig 1B:** Overview study design. Top row: Treatment initiation within 48 hours of life after POC testing; bottom row: treatment initiation within 14 days of life as per standard of care.

**Fig 2:** Viral load (A), absolute CD4 count (B) and CD4 percentage (C) at the first day of life in utero infected infants from the PEHSS study (percentile 2000-2005) and cART (progression). (A) & (B) from the current Uwacungo Lwabantwana (UL) study.

**Fig 3:** Time to suppression of viraemia is related to pro-cART viral load. A, Changes in viral load among infants whose utero infected infants enrolled in the Uwacungo Lwabantwana study. B, Time to viral suppression (cART initiated less than level of detection) following ART initiation. Black square: data from PEHSS cohort (published 2002-2005) (B). Blue square: data from the infant study enrolled in the Uwacungo Lwabantwana study. (A) and (B) are part of the study.

**Box 1:** Box 1 case report to illustrate the diversity of the HIV infected infants enrolled, and of their mothers.

- **Case 1:** Initial absolute CD4 count 3516/mm^3, HIV-infected at 17 weeks of age. Viral load achieved at 19 weeks, immediately prior to ART initiation: 210 c/ml. CD4 1750/mm^3 (80%), VL <20 c/ml. Follow-up cART initiated 3 months after birth.

- **Case 2:** Initial VL 4.3m c/ml, CD4 830/mm^3, 3 initial VL 310c/ml. VL <20 c/ml after 3 months on cART.

- **Case 3:** Initial VL 200 c/ml, CD4 150/mm^3 (10%), VL <20 c/ml. Follow-up cART initiated 6 months after birth.

- **Case 4:** Initial absolute CD4 70/mm^3, HIV-infected at 17 weeks of age. Initial viral load was 2.25 x 10^9 c/ml at 1 month old.Triple-drug combination: cART initiated 1 month after birth. CD4 58/mm^3, VL <20 c/ml. No rebounding and no in utero Malformation. CD4 5/mm^3.

- **Case 5:** Mother 20yo, HIV+ve at 26wks. Initial viral load was 15,000 c/ml. Mother: HIV infection confirmed, initiated cART: VL <20 c/ml. Follow-up cART initiated 6 months after birth.

- **Case 6:** Initial absolute CD4 20/mm^3, HIV-infected at 9 months of age. Initial viral load was 2000 c/ml. CD4 20/mm^3, VL <20 c/ml. Follow-up cART initiated 6 months after birth.

- **Case 7:** Initial absolute CD4 20/mm^3, HIV-infected at 9 months of age. Initial viral load was 2000 c/ml. CD4 20/mm^3, VL <20 c/ml. Follow-up cART initiated 6 months after birth.

- **Case 8:** Mother: 20yo, HIV+ve at birth, CD4 20/mm^3, VL <10,000 c/ml. CD4 50/mm^3, VL <20 c/ml. Follow-up VL initiated 6 months after birth.

- **Case 9:** Mother: 20yo, HIV+ve at birth, CD4 5/mm^3, VL <20 c/ml. Follow-up VL initiated 6 months after birth.