

HAART for the Prevention of Perinatal HIV Transmission in Africa. MTCT Plus Program, Abidjan, Côte d'Ivoire

B. TONWE-GOLD¹, D.K EKOUEVI, F.ROUET², I.VIHO¹, M.KONE¹, S.TOURE¹, V. LEROY³, W.EL-SADR⁴, E.J ABRAMS⁴, F.DABIS³ and The MTCT Plus Initiative and the ANRS Ditrane Plus Study Group
1 ACONDA ,MTCT Plus Program, Abidjan, Côte d'Ivoire; 2 CeDRS Laboratory, Abidjan, Côte d'Ivoire;
3 INSERM U593, Bordeaux, France; 4 The MTCT Plus Initiative, Columbia University, New York.

BACKGROUND

Mother-to-child transmission (MTCT) of HIV is estimated to be the cause of 10% of all HIV infections worldwide and of at least 90% of paediatric HIV infections. In resource-poor settings, simple and effective means of prevention of MTCT (PMTCT) of HIV exist. Short antiretroviral (ARV) regimens of Zidovudine (ZDV), ZDV+ Lamivudine (3TC) and/or single-dose Nevirapine (SD-NVP) are validated ARV regimens. While PMTCT programs can effectively prevent most paediatric HIV infections, they usually do not offer HIV care and treatment to the mothers themselves and to the children who become HIV infected. In 2004, HAART (Highly Active Antiretroviral Treatment) for PMTCT was added to the World Health Organization guidelines for perinatal prevention for pregnant women who need ARV treatment for their own health.



OBJECTIVES

We describe use of HAART during pregnancy for women with advanced HIV disease in the MTCT-Plus Initiative in Abidjan.

METHODS

MTCT-Plus is a multi-country (9 countries) care and treatment program built upon existing PMTCT services. It provides pregnant/postpartum women with family-centred HIV care including ARV treatment to the woman, her partner and children. In Abidjan, Côte d'Ivoire, pregnant women identified at PMTCT sites and eligible for HAART receive a regimen of 2 nucleoside reverse transcriptase inhibitors (NRTI) + 1 non nucleoside reverse transcriptase inhibitor (NNRTI), i.e. ZDV+3TC+NVP. Treatment is initiated during pregnancy, as early as 26 weeks of amenorrhea and continued postnatally.

Baseline adherence and psycho-social assessment is done before initiation of HAART, and followed by clinical weekly follow-up visits for 8 weeks using a standardized checklist of clinical symptoms. A more detailed clinical evaluation, including symptom review, physical examination, and review of medication adherence is conducted monthly. Routinely, hepatic and renal functions are measured at baseline and twice-yearly with total blood and CD4 counts. Otherwise, laboratory evaluation is reserved for patients with symptoms or physical findings of illness. Liver function tests in pregnant women on NVP-containing HAART regimen are however monitored closely during the first two months of treatment.

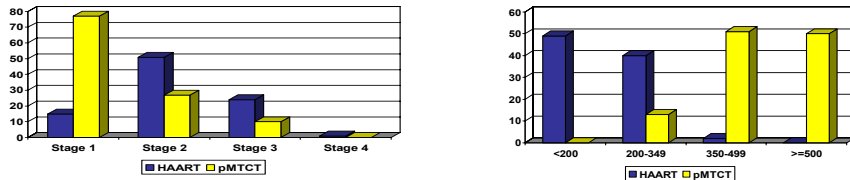
Pregnant women not eligible for HAART receive PMTCT prophylaxis primarily ZDV+3TC from 32 weeks (through three days postpartum) with sd-NVP in labor as recently evaluated (Dabis F, et al. AIDS, in press) or other validated maternal short ARV regimens. All infants receive ZDV (7 days) & sd-NVP on Day 3 irrespective of the maternal drug regimen. Women either use breast milk substitutes or practiced breastfeeding for 6 months. Plasma HIV RNA for paediatric HIV diagnosis is performed on infants at 4 weeks and confirmed at 6 weeks.

Eligibility criteria for HAART during pregnancy in the MTCT-Plus program

- WHO clinical stage 4 irrespective of CD4 count
- WHO stage 2 and 3 and CD4 >350 cells/mm³
- CD4 <200cells/mm³
- Absence of medical contraindications (abnormal liver or renal function, etc)
- Absence of major barriers to adherence

RESULTS

From August 2003 to December 2004, **496** women, 209 pregnant and 287 postpartum enrolled in the MTCT-Plus program in Abidjan. 205 received a pMTCT regimen; 91 began HAART (ZDV+3TC+ NVP in 88 women) at a median of 30 weeks of gestation (range: 17-40 weeks), with a median CD4 count of 185/mm³ (range 16-362 /mm³) and 114 received another PMTCT regimen (described below Table 3)



Characteristic	HAART	pMTCT regimen	p-value
N° of pregnant women enrolled (n=205)	91	114	-
Median age at enrolment (IQR)	28 (25-31)	27 (23-30)	0.08
Median CD4 count at enrolment(IQR)	185 (137-275)	472 (386-610)	<0.001
Median CD4 % at enrolment (IQR)	16.0 (10.7-20.4)	27.1 (23.2-34.1)	<0.001
Median gestational age at ARV initiation	30 (27-33)	33(31-36)	<0.001
Initiation of ARV<28 weeks	24(26.3%)	2 (1.7%)	<0.001

Table 1: Characteristics of pregnant women enrolled in MTCT-Plus program in Abidjan

Among **80** pregnant women on HAART who delivered (median CD4 count of 185 /mm³), 69 live births have been tested so far and **one has been diagnosed as HIV-infected**. **Of note**, this infant's mother (289 CD4 at baseline, WHO stage 2, 4 weeks of prenatal HAART) was known for adherence problems and had refused to take a long term ARV treatment for herself and stopped the HAART regimen the day of delivery. She also presented after 14 days of treatment a grade 2 rash and was non adherent to her treatment during pregnancy. **The rate of early MTC transmission in women on HAART is 1 out of 69 i.e. 1.45%** (upper limit of the 95% confidence interval 7.8%) in an "on treatment" analysis.

Among **114** pregnant women not treated by HAART (median CD4 count of 472/mm³), amongst whom 94 had delivered by the 31st of December, 77 live births have been tested so far and **3 were diagnosed as HIV-infected**. Their mothers had 739, 738 and 522 CD4 counts, respectively, and had taken only single dose of NVP. No case of HIV transmission was identified among the 60 women who received ZDV+3TC+NVPsd. The table 3 presents the cases of HIV infection in neonates according to the prophylactic pMTCT regimen their mothers received.

Maternal CD4 count increase with time on HAART

Characteristic	Value
Number of women on HAART	91
Mean time on HAART (SD)	260 days (136)
Median time on HAART (IQR)	268 days (123-346)
Number of women with 6 months follow up	58 / 91 (64%)
Mean CD4 increase (SD)	279 /mm ³ (186)
Mean CD4% increase (SD)	10.1% (5.9)
Median CD4 increase (IQR)	238 (168-317)
Median CD4 % increase (IQR)	9.1% (6.7-13.4%)

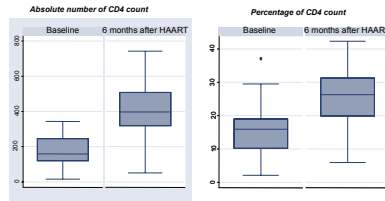


Figure 4: Six month CD4 change for pregnant women on HAART

Table 2: Characteristics of births and rate of MTCT

	HAART	pMTCT regimen	Total
Number of deliveries (as of 31/12/04)	80	94	174
Number of twin births	4	4	8
Number of still births	5/81 (6.2%)	6/98 (6.1%)	11 (6.3%)
Number of live births	76	92	168
Number of neonatal deaths < 28 days	3/78 (3.9%)	1/92 (1.1%)	4
> 28 days	6/76 (7.9%)	1/92(1.1%)	7
Number of live births tested at 4 weeks	69	77	146
Number of HIV-infected infants at 4-6 weeks	1	3	4
Rate of MTCT transmission	1.45% 95%CI (0.00-7.80)	3.89% 95%CI (0.03-9.67)	

	ZDV+3TC+NVPsd	ZDV+NVPsd	SDV	NVPsd
Enrolled	73	24	4	13
Tested	60	4	1	12
Infected	0	0	0	3
IC95% (8.9%)				

Table 3: Different pMTCT regimens in women not eligible for HAART

AGE	WHO	CD4	INITIAL REGIMEN	TRANSITION HAZARD AT EVENT	GRADE 1 OR 2 SYMPTOMS OR EVENT REQUIRING SINGLE DRUG ANY CHANGE	SINGLE DRUG CHANGE
37	2	528	AZT/3TC/NVP	35	RASH GRADE 3	AZT/3TC/NLF
34	1	148	AZT/3TC/NVP	35	RASH GRADE 3	AZT/3TC/NLF
31	2	206	AZT/3TC/NVP	27	RASH GRADE 3	AZT/3TC/NLF
31	3	252	AZT/3TC/NVP	15	RASH GRADE 3	AZT/3TC/NLF
34	2	111	AZT/3TC/NVP	66	HEPATO TOXICITY GRADE 4	AZT/3TC/ABC
35	2	68	AZT/3TC/NVP	84	ANEMIA GRADE 4	D4T/3TC/NVP
23	2	309	AZT/3TC/NVP	45	ACTIVE TB	AZT/3TC/EFV

Table 5: Side effects of pregnant women on HAART

Side effects observed in HAART-treated pregnant women

In the HAART group, **91** women started treatment before December 31st, 2004 amongst whom **80** have delivered so far, 7 women had a single drug switch ; **6 for grade 3 adverse events** before delivery: **rash** (n=4) and **hepatotoxicity** (n=1) attributed to NVP and **anaemia** (5g/dl) attributed to ZDV (n=1) as well as 1 switch for active TB.

CONCLUSION

We found very low early MTC transmission in mothers on HAART similar to rates found in high resource countries. This transmission rate of 1.45% is lower than that found recently in the ANRS study using dual ZDV/3TC therapy from 32 weeks with SD intrapartum NVP (among the 68 HAART eligible women in the study, the six-week estimated rate of peri-partum infection was 8.9% (CI 2.1-15.7%).

Long term follow-up is needed to fully assess the safety and efficacy of HAART in pregnancy in African populations. Other variables such as obstetrical complications (low birth weight, prematurity) as well as the rate of neonatal deaths should be assessed in these populations.

