

# Highly Active Antiretroviral Therapy Started in Pregnancy or Postpartum Suppresses HIV-1 RNA but Not HIV-1 DNA in Breast Milk



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## Abstract

**Background:** The rationale for using highly active antiretroviral therapy (HAART) to prevent mother-to-child HIV transmission (MTCT) from breastfeeding depends upon its ability to reduce cell-free HIV-1 RNA, and possibly cell-associated HIV-1 DNA, in breast milk. The ability of HAART to reduce HIV-1 RNA and DNA in breast milk has not been described previously.

**Methods:** We performed a nested cohort study among breastfeeding women enrolled in a randomized clinical trial for the prevention of MTCT in Botswana. We compared whole breast milk HIV-1 RNA and DNA levels among 26 women with AIDS who received HAART (nevirapine, lamivudine, and zidovudine) and a similar group of 26 women who did not receive HAART because they participated in the trial before HAART became available in October 2002. Breast milk collection occurred at either 2 or 5 months postpartum. Treated women began HAART in pregnancy or the postpartum period, at least 2 months prior to breast milk collection.

**Results:** Twenty-four (92%) of 26 women in the HAART group had plasma HIV-1 RNA < 400 copies/ml within 2 months of breast milk sampling, compared with 1 (4%) of 26 who did not receive HAART. Women in the HAART group received treatment for a median of 98 days (range: 67-222 days) at the time of breast milk sampling. 23 (88%) of 26 had whole breast milk HIV-1 RNA < 50 copies/ml, compared with 9 (36%) of 25 women who did not receive HAART ( $P = 0.0001$ ). In a multivariate logistic regression model controlling for baseline CD4 cell count and baseline plasma HIV-1 log RNA, the receipt of HAART remained significantly associated with suppression of breast milk HIV-1 RNA to < 50 copies/ml ( $P = 0.001$ ). Breast milk supernatant results were similar to those for whole milk. In contrast, whole milk HIV-1 DNA was unaffected by HAART. Among women who received HAART, only 13 (50%) of 26 had HIV-1 DNA < 10 copies/million cells, compared with 15 (65%) of 23 of those who did not receive HAART ( $P = 0.28$ ).

**Conclusions:** HAART effectively suppressed cell-free HIV-1 RNA in whole breast milk and breast milk supernatant, and may therefore reduce the risk of MTCT during breastfeeding. However, HAART initiated in pregnancy or the early postpartum period had no apparent effect on cell-associated HIV-1 DNA in breast milk. The relative contribution of cell-free and cell-associated HIV-1 to MTCT during breastfeeding requires further study, and clinical trials to determine MTCT rates among breastfeeding women receiving HAART are needed.

## Background

- Rationale for using HAART to prevent MTCT from breast milk depends largely upon its ability to reduce cell-free HIV-1 RNA, and possibly cell-associated HIV-1 DNA, in breast milk

- Reduction in plasma viral loads through HAART prevents MTCT in the antepartum and intrapartum periods
- Efficacy during breastfeeding supported by natural history studies: less breastfeeding MTCT among women with lower breast milk HIV-1 RNA

- The ability of HAART to reduce HIV-1 RNA and DNA in breast milk has not been described previously

## Methods

- Nested cohort study among breastfeeding women enrolled in a randomized clinical trial for the prevention of MTCT in Botswana

- Compared whole breast milk HIV-1 RNA and DNA levels among 26 women who received HAART (NVP, 3TC, and ZDV) and a similar group of 25 women who did not receive HAART

- HAART given to those with CD4 < 200 or AIDS-defining illness

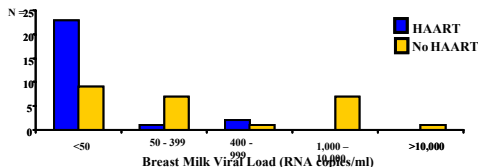
- started in pregnancy or postpartum, at least 2 months prior to breast milk collection
- Non-HAART women participated in trial before HAART became available in October 2002, and had baseline CD4 counts < 250

- Breast milk collection occurred at either 2 or 5 months postpartum

## Baseline characteristics, by HAART status

	HAART (N=26)	No HAART (N=25)	P-value
Median age (years)	28 (range: 20-40)	27 (range: 19-39)	0.62
Median baseline CD4 cell count (cells/mm <sup>3</sup> )	161 (range: 65-245)	146 (range: 40-249)	0.98
Median baseline (or pre-HAART) HIV-1 RNA (copies/ml)	45,200 (interquartile range: 22,050-171,500)	104,000 (interquartile range: 31,300-204,000)	0.32
Milk samples collected at 2 months (vs. 5 months) postpartum	81%	77%	1.0
Median duration of HAART at time of sample collection (days)	98 (range: 67-222)	---	---

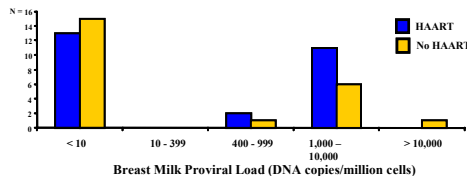
## Results: Comparison of HIV-1 RNA in whole breast milk, by HAART status



	VL < 50 copies/ml	VL ≥ 50 copies/ml	Univariate P-value	Multivariate P-value*
HAART	23 (88%)	3 (12%)	0.0001	0.0006
No HAART	9 (36%)	16 (64%)		

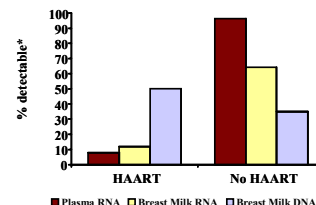
\* controlling for baseline CD4 cell count and baseline HIV-1 log RNA

## Results: Comparison of HIV-1 DNA in whole breast milk, by HAART status



	DNA < 10 copies/million cells	DNA ≥ 10 copies/million cells	Univariate P-value
HAART	13 (50%)	13 (50%)	0.28
No HAART	15 (65%)	8 (35%)	

## Percentage of Breastfeeding Women with Detectable Plasma HIV RNA, Breast milk HIV RNA, and Breast Milk HIV DNA, by Receipt of HAART



\*limit of detection: plasma HIV-1 RNA ≥ 400 copies/ml, breast milk HIV-1 RNA ≥ 50 copies/ml, breast milk HIV-1 DNA ≥ 10 copies/million cells

## Conclusions

• HAART effectively suppressed cell-free HIV-1 RNA in whole breast milk, and may therefore reduce the risk of MTCT during breastfeeding

• However, HAART initiated in pregnancy or the early postpartum period had no apparent effect on cell-associated HIV-1 DNA in breast milk

• The relative contribution of cell-free and cell-associated HIV-1 to MTCT during breastfeeding requires further study

• Clinical trials to determine MTCT rates among breastfeeding women receiving HAART are needed