

# Treatment Interruption after Pregnancy and Disease Progression: A Report from the Women and Infants Transmission Study

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## ABSTRACT

**Background:** Scheduled antiretroviral (ART) treatment interruption has been associated with accelerated HIV disease progression in some studies. Effects of treatment interruption after ART prophylaxis in pregnancy on maternal health have not been well studied. We evaluated changes in CD4 cell count, CD4%, HIV RNA, and disease progression between women who continued ART after delivery and those who stopped ART at delivery.

**Methods:** Women enrolled in the WITS after 6/1/94 who were ARV naive and had CD4 count > 350 cells/uL were included. CD4 count, CD4% and HIV RNA slope between delivery and 12 months postpartum and progression to class B or C diagnosis were compared between women who continued ART therapy after delivery and women who stopped at delivery. A mixed model analysis was used to compare slopes. Cox models were used to evaluate disease progression.

**Results:** Of 3297 women enrolled to WITS, 1165 were ART naive, 512 of these received ARV, and 206 women had CD4+ cell counts over 350 cells/uL. Women included in this analysis were similar to those excluded except that they had a higher mean CD4 count and lower gestational age at enrollment. Slopes of CD4 count and %, and HIV RNA did not differ between women continuing or stopping therapy after delivery between 2-6 months and 6-12 months postpartum (p=0.35-0.96). No class C events occurred through one year postpartum in either group. New class B events (excluding women with previous class B events) occurred in 8 (9.4%) of 85 women continuing therapy versus 6 (18.6%) of 43 women stopping therapy (RR 2.09, 95% CI 0.79-5.58, p=0.14). Evaluating women receiving ZDV only during pregnancy and those receiving two or more drugs, no differences in slope of CD4 count and % or HIV RNA were seen by therapy type comparing women continuing or stopping therapy. Women on ZDV only who stopped therapy had a RR of 1.24 (0.31-4.95) of class B events over one year compared to those continuing. For combination therapy, the RR was 2.93 (0.64-13.36, p=0.16) for those stopping therapy.

**Conclusions:** The changes in CD4 and HIV RNA levels over one year postpartum were similar between women continuing or stopping therapy after initiation with CD4 counts over 350 cells/uL. No class C events occurred in either group. No significant difference in rates of new class B events was seen, although power was limited. Larger studies with longer follow-up are required to evaluate the risks of stopping ARV prophylaxis after delivery.

## INTRODUCTION

Pregnant women usually without indications for antiretroviral therapy for their own health usually receive highly active antiretroviral therapy (HAART) regimens for prevention of maternal-to-child transmission (MTCT) and stop therapy after delivery.

Recent studies suggesting poorer outcome with CD4-guided treatment interruption rather than continuous HAART have raised the question of whether discontinuation of HAART used for prevention of MTCT after delivery may be detrimental to maternal health. However, these studies used a lower CD4+ cell count for restarting treatment (250 cells/uL) than current clinical guidelines recommend for initiation of therapy (350 cells/uL).

### CD4 Guided Treatment Studies

Study ID	Total N	Criteria to resume Rx	Outcome
Krolwiecek et al <sup>1</sup>	36	CD4 < 350, HIV RNA ↑ 1 log, symptoms	No difference in clinical progression
Stacato <sup>2</sup>	430	CD4 < 350	Lower CD4 with STI, no AIDS; more toxicity in continuous
Trivacan <sup>3</sup>	326	CD4 < 250	RR serious morbidity: 2.27 (1.15-4.76) in STI arm
SMART <sup>4</sup>	5472	CD4 < 250	AHR death/OI: 1.5 (1.0-2.1) in STI arm

1= JAIDS 2006;41:425-9; 2= Lancet 2006;368:459-65; 3= CROI 2006 # 105L; 4= NEJM 2006;355:2283-96.

## OBJECTIVE

Among antiretroviral naive women entering pregnancy with CD4+ lymphocyte counts above 350 cells/uL, to compare outcomes through one year postpartum:

- Change in CD4+ lymphocyte count and %
- Change in HIV RNA levels, and
- Clinical progression to class B, AIDS or death

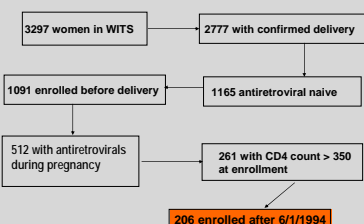
between those stopping therapy at delivery and those continuing.

## METHODS

### Inclusion criteria

- Antiretroviral naive at enrollment
- CD4+ lymphocyte count > 350 cells/uL
- Enrollment after 6/1/1994
- Enrolled early enough to receive antiretroviral therapy before delivery
- Followed through at least one year postpartum.

### Summary of Women Enrolled



### Statistical Methods

- Differences between groups in baseline characteristics compared using t-test and chi-square tests.
- Mixed models used to compare slope of CD4+ lymphocyte count, CD4+ percentage and HIV RNA level between delivery and one year postpartum.
- Cox proportional hazard models used to assess risk of progression to class B condition, AIDS, or death.

## RESULTS

### Comparison of Women included in Analysis and the Remainder of Women in WITS

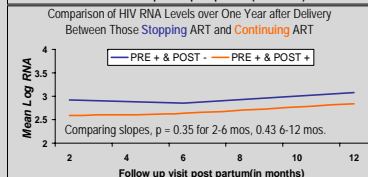
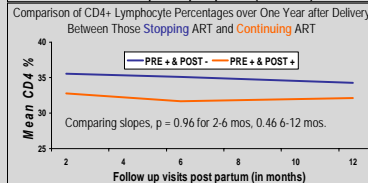
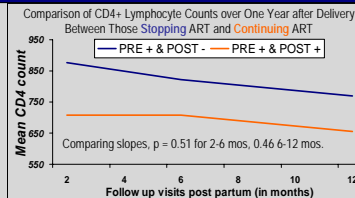
	Current, n= 206	Remainder, n= 3091	p
Age, mean	27.2 (16.5-42.7)	28.1 (14.4-44.8)	0.80
Race/ethnicity			0.96
White	22 (10.7%)	340 (11.0%)	
African Amer.	98 (47.6%)	1503 (48.6%)	
Latina	75 (36.4%)	1055 (34.1%)	
Other	11 (5.3%)	193 (6.2%)	
Gestational age, mean	16.1 (5-38)	21.6 (1-43)	<0.001
Enrollment CD4+ count			1
<350 cells/uL	0	1090 (35.5%)	
350-500 cells/uL	84 (40.8%)	544 (17.6%)	0.47*
> 500 cells/uL	122 (59.2%)	881 (28.5%)	
Not available	0	576 (18.6%)	
Log HIV RNA, mean	2.90 (0.5-4.4)	2.85 (0-6.49)	0.71
CDC events			
Class B or worse	59 (28.6%)	861 (27.9%)	0.81
Class C	6 (2.9%)	171 (5.5%)	0.11

\*Comparison of CD4 350-500 and > 500 cells/uL groups only since the study design excludes the other rows in the "Current" group.

### Comparison between Women Stopping ART at Delivery and Those Continuing Therapy

Characteristic	Stopped N= 59	Continued N= 147	P
Age, mean (range)	25.9 (17.9-36.8)	27.7 (16.5-42.7)	0.04
Race/ethnicity			0.43
White	8 (13.6%)	14 (9.5%)	
African American	29 (49.2%)	69 (46.9%)	
Latina	21 (35.6%)	54 (36.7%)	
Other	1 (1.7%)	10 (6.8%)	
Gestational age, mean (range)	16.1 (6-35)	16.1 (5-38)	0.97
Enrollment CD4			0.03
350-500 cells/uL	17 (28.8%)	67 (45.6%)	
> 500 cells/uL	42 (71.2%)	80 (54.4%)	
Log HIV RNA, mean (range)	2.63 (0.5-3.6)	3.00 (0.5-4.4)	0.23
CDC classified event			
Class B or worse	15 (25.4%)	44 (29.9%)	0.52
Class C	2 (3.4%)	4 (2.7%)	0.80

## RESULTS



### Disease Progression Among Women Continuing or Stopping Therapy at Delivery

Progression to Class B Event:  
 Stopped therapy: 12/47 (25.5%) RR 2.09 (0.79-5.58)  
 Continued therapy: 10/87 (11.5%) Reference  
 No women in either group progressed to AIDS/died during follow-up

### Comparison According to Type of ART during Pregnancy

To further evaluate effects of stopping therapy after delivery, ART use during pregnancy was categorized as:

- Zidovudine monotherapy, n= 103
- Combination therapy: two or more drugs, n= 100
- Monotherapy other than ZDV excluded, n= 3.

No difference in slopes of CD4+ cell count, CD4+ percent, or log<sub>10</sub> HIV RNA between those continuing or stopping therapy, according to therapy used during pregnancy.

### Risk of Disease Progression According to ART during Pregnancy

Risk of progression to new class B disease among women stopping ART at delivery compared to those continuing therapy:

- ZDV monotherapy: RR 1.24 (0.31-4.95) p=0.76
- Combination ARV: RR 2.93 (0.64-13.36) p=0.16

No women in either group progressed to AIDS/death.

## SUMMARY

- Among ART-naïve women entering pregnancy with a CD4+ lymphocyte count > 350 cells/uL and initiating therapy, changes in CD4+ cell count and percent and HIV RNA levels were similar over the first year postpartum among women stopping or continuing therapy after delivery.
- No women in either group progressed to AIDS or death during follow up.
- No significant differences were seen in rates of progression to CDC class B events, but non-significant increased relative risk, especially among women stopping combination ART regimens, is noted.

## CONCLUSIONS

- These data are reassuring that stopping antiretroviral prophylaxis after delivery did not lead to a more rapid decline in CD4+ lymphocytes, rebound in HIV RNA levels, or progression to AIDS or death over the first year postpartum compared to continuing antiretroviral drugs.
- The relatively small sample size, derived from a study of over 3,000 women, limits the power to detect differences in progression and underscores the difficulty in evaluating the best strategy for managing pregnant women who receive ART strictly for prophylaxis of MTCT.
- Additional studies are needed to evaluate this question including combining data from several cohorts and including additional laboratory markers to assess risk of HIV progression and other complications.

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