

# Safety of 6-week triple antiretroviral prophylaxis in high risk HIV-exposed infants



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# BACKGROUND

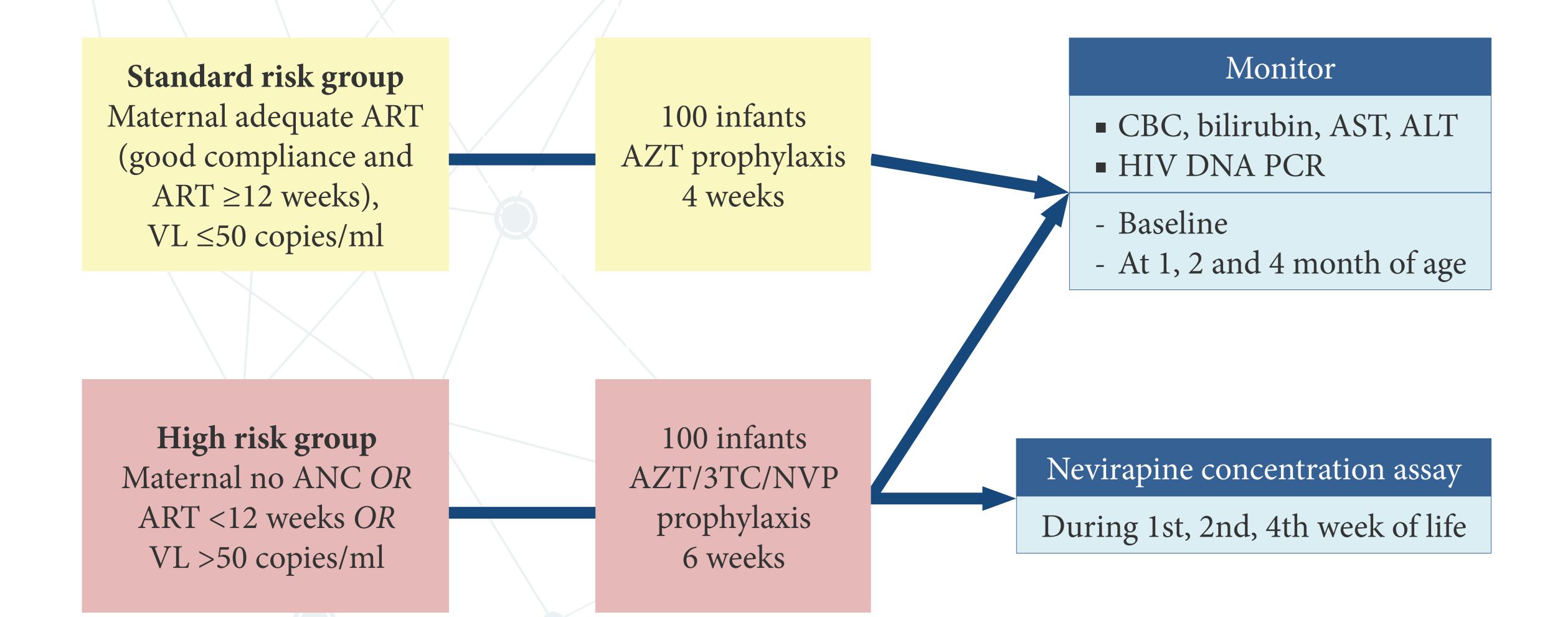
Triple-drug antiretroviral prophylaxis of zidovudine (AZT)/lamivudine (3TC)/nevirapine (NVP) for high risk HIV-exposed neonates is recommended within the Thai national program. However, there are limited data about the safety and drug concentration achieved with this regimen initiated at birth.

# OBJECTIVES

To evaluate the safety of combination neonatal prophylaxis regimen and to describe nevirapine concentration levels during the first 4 weeks of life.

## **METHODS**

- Prospective cohort of infants born from HIV-infected pregnant women in 4 clinical sites in Thailand.
- Neonates with high risk of HIV transmission (mother has HIV RNA >50 copies/mL prior to delivery or received ART <12 weeks) received AZT and 3TC twice daily, plus NVP (4 mg/kg/dose) once daily, for 6 weeks. As a control group, neonates with standard risk of HIV transmission who received 4-week of AZT were also enrolled.
- Blood for complete blood count, aspatate transaminase (AST), alanine transaminase (ALT) were drawn at birth, aged 1, 2 and 4 month.
- Adverse events were graded according to DAIDS toxicity table 2014.
- Sparse plasma NVP concentrations were collected at week 1, 2 and 4 and assayed by a validated liquid chromatography-triple quadrupole mass spectrometry assay. Target NVP plasma trough concentration for prophylaxis was >100 ng/mL.



#### **RESULT**

- From October 2015 to August 2016, 94 infants were enrolled.
- 31 neonates received triple ARV prophylaxis and 63 infants received AZT only.

Table 1. Characteristics of HIV-exposed infants and mothers

	Total	4-week AZT prophylaxis	6-week AZT/3TC/NVP prophylaxis (N = 31)	<i>p</i> -value
	(n=94)	(N=63)		
Mothers				
Gestational age at delivery, weeks (IQR)	38 (37-39)	38 (37-39)	38 (36-39)	0.29
Median of maternal age, years (IQR)	30 (21-34)	32 (26-36)	21 (19.5-29)	< 0.001
Premature (<37 weeks), N (%)	16 (17.2)	6 (9.5)	10 (33.3)	0.004
Maternal antiretroviral therapy regimen, N (%) AZT-based TDF-based PI-based NNRTI-based: NVP, EFV	31 (33) 55 (58.5) 26 (27.7) 60 (63.8)	24 (38.1) 35 (55.6) 18 (28.6) 44 (69.8)	7 (22.6) 20 (64.5) 8 (25.8) 16 (51.6)	0.13 0.41 0.78 0.08
Infants				1
Sex, male (%)	46 (48.9)	34 (54)	12 (38.7)	0.16
Median of birth weight, kg. (IQR)	2.8 (2.5-3.2)	2.9 (2.6-3.2)	2.7 (2.4-2.9)	0.02
Birth weight <2.5 kg, N (%)	22 (23.4)	11 (17.5)	11 (35.5)	0.05
Median of height, cm. (IQR)	49.3 (48-52)	50 (48-52)	49 (46-52)	0.17
Median of circumference, cm. (IQR)	33 (32-34)	33 (32-34)	32 (31-33)	0.02

- There was no difference in adverse event rates between triple and AZT prophylaxis (**Table 2**).
- No infants were diagnosed HIV-infected at age 4 months.

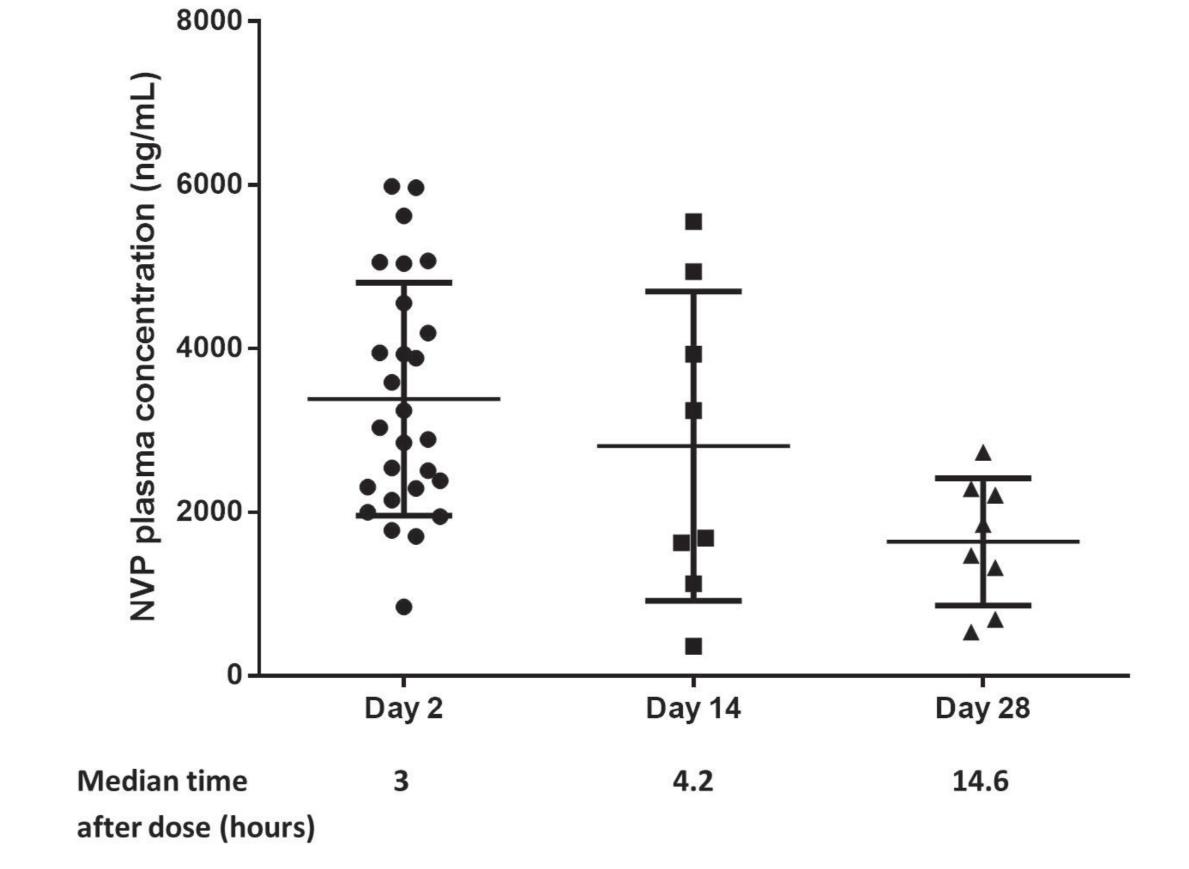


Figure 1. Nevirapine plasma concentrations (ng/mL) stratified by timing of plasma collection

# Table 2. Adverse events in HIV-exposed infants stratified by risk group

Overall, median (IQR) gestational age and birth weight were 38 (37-39) weeks and 2.8 (2.5-3.2) kg, respectively.

	Overall	4-week AZT	6-week	
	(N = 94)	prophylaxis $(N = 63)$	AZT/3TC/NVP  prophylaxis  (N = 31)	<i>p</i> -value
All grade anemia (Hb <11 g/dL at age 1 month, Hb <10.4 g/dL at age 2-4 months)	41.1%	39.9%	43.6%	0.55
Grade 3-4 anemia (Hb <8 g/dL at age 1 month Hb <8.5 g/dL at age 2-4 months)	3.1%	3.1%	3.2%	
All grade neutropenia (ANC <1000/mm³)	3.1%	3%	3.2%	0.94
Grade 3-4 neutropenia (ANC <600/mm³)	0.5%	0.3%	1.1%	
Abnormal AST	1.4%	1.5%	1.1%	0.76
Abnormal ALT	3.8%	4%	3.2%	0.72
Median (IQR) Hb at 1 mo, g/dL	10.4 (9.3-11.7)	10.6 (9.6-12)	9.7 (8.8-11.2)	0.39
Median (IQR) Hb at 4 mo, g/dL	11.7 (11.2-12.3)	11.7 (11.4-12.3)	11.2 (10.6-12.1)	

• NVP concentrations were available from 18 infants: geometric mean (%CV) plasma NVP concentrations were 3075 (67), 2109 (92) and 1438 (72) ng/mL at weeks 1, 2 and 4, respectively. All infants maintained nevirapine concentrations >100 ng/mL during the first 4 weeks (Figure 1).

# CONCLUSIONS

• Characteristics of HIV-exposed infants and mothers are shown in table 1.

Triple ART infant prophylaxis with 6-weeks of AZT/3TC/NVP in high risk HIV-exposed infants appears to be safe with high NVP concentrations being rapidly achieved and maintained during the first 4 weeks of life.

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