

# **Safety, tolerability and efficacy of Nevirapine based HAART amongst antiretroviral naïve HIV-1 infected patients in India**

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# Aims and Objectives

- **To assess the incidence of and risk factors for adverse events to Nevirapine (NVP)**
- **To assess clinical and immunological response to NVP based HAART**
- **To assess difference in response between two backbone NRTI regimens**

- **Design: prospective follow up study**
- **Setting: Tertiary referral HIV Clinics**
  - **Ruby Hall Clinic, Pune**
  - **Infectious Diseases Clinic, Ahmedabad**

# Methods

- **347 antiretroviral naïve subjects**
- **Follow up**
  - **Clinically monthly**
  - **CD4/CD8 quarterly (by flow cytometry)**
  - **Toxicity parameters: LFTs at one month and as indicated**

## **Adverse events recorded:**

**GI (Nausea, vomiting, diarrhea) Skin rash and  
hepatitis (AST/ALT > 5 ULN)**

**(judged to be definitely, probably or possibly related to NVP)**

# Methods: Drugs

- **2 NRTIs**
  - **AZT/3TC: n=173**
  - **D4T/3TC: n=174**
- **Nevirapine: lead in dose**
- **Non randomization**
- **Adherence assessed by self reporting**

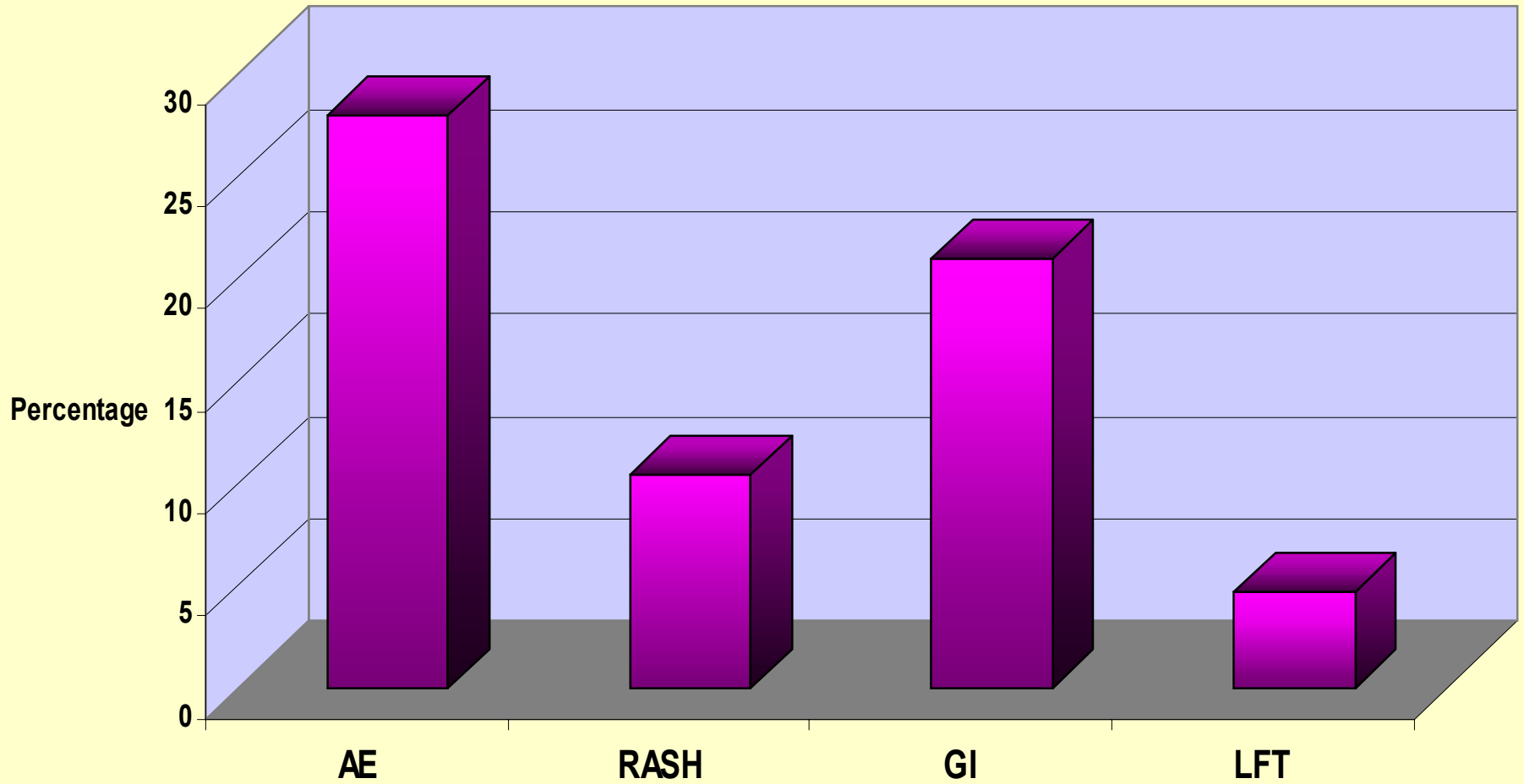
# Methods: Analysis

- **Frequencies of AE documented**
- **Risk factors for AE compared by Mantel-Haenszel chi-square test**
- **Paired t test to assess improvement in CD4 counts**
- **Difference in efficacy between 2 NRTIs assessed by Cox proportional hazard with AZT/3TC/NVP as reference and more than 20% increase in CD4 count defined as responder**
- **All analysis: ITT**

# Table1: Age and sex distribution

<b>Age</b>	<b>Male (n=296) N(%)</b>	<b>Female (n=51) N(%)</b>
<b>&lt;30</b>	<b>46 (15.5)</b>	<b>8 (17.7)</b>
<b>30 - &lt;40</b>	<b>154 (52.0)</b>	<b>20 (35.3)</b>
<b>40 - &lt;50</b>	<b>61 (20.6)</b>	<b>13 (25.0)</b>
<b>50+</b>	<b>35 (11.8)</b>	<b>10 (22.1)</b>

# AE in NVP regimes (n=347)



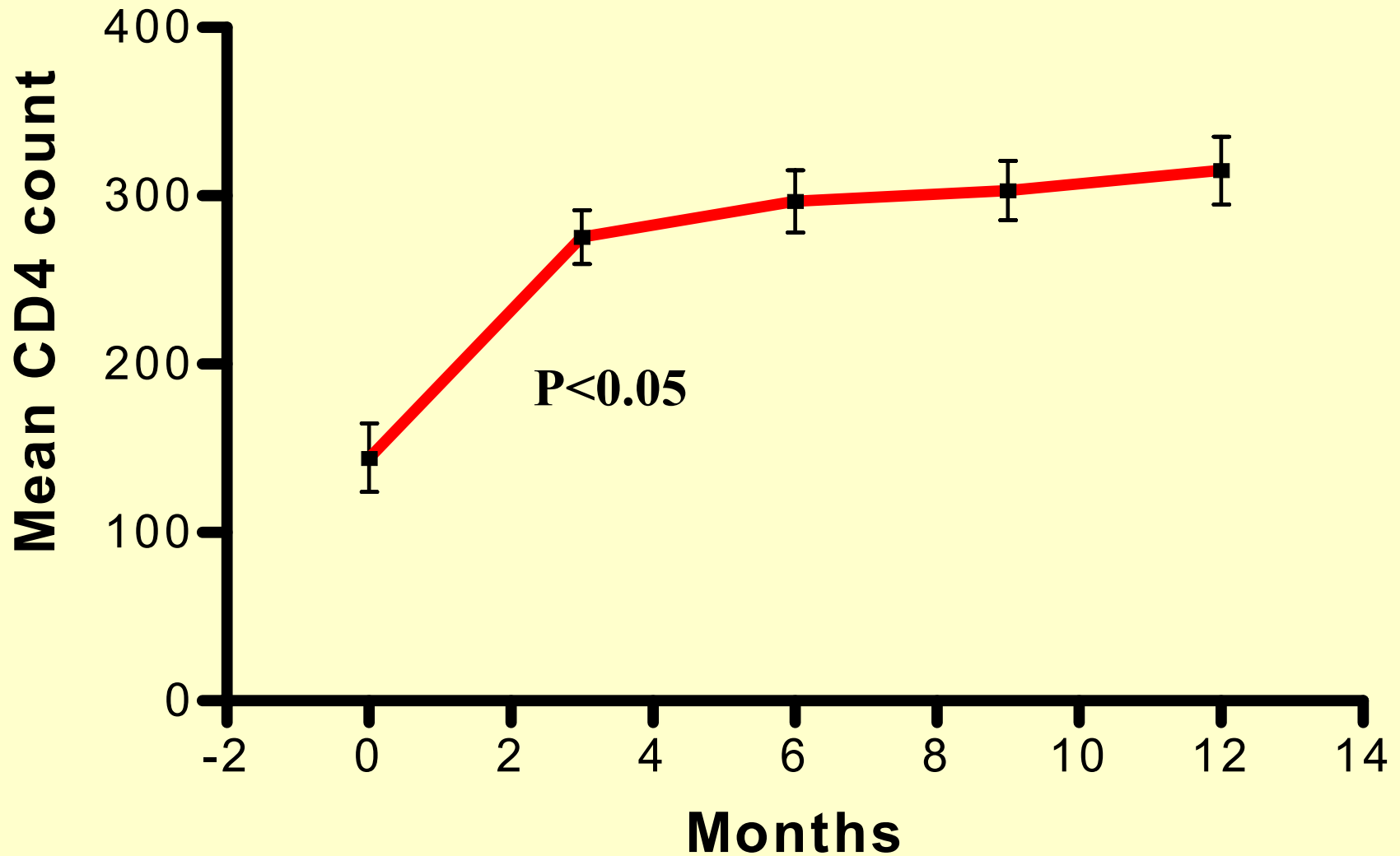
## Table 2: Risk factors for AE

Factor	AE + N (%)	AE – N (%)	RR	95% CI	P value
Female	25 (30.10)	43 (15.0)	1.27	1.09- 1.49	0.002
TMP- SMX	66 (79.5)	208 (72.5)	1.08	0.96- 1.23	0.19
CD4 baseline	Mean±SE 135.8 ±11.4	Mean±SE 143.4±7.8	T value 0.548		0.58
CD8 baseline	842 ±55.6	862±32.0	0.280		0.77
Age	38.2±1.09	37.2±0.55	-0.682		0.51

# Clinical events

- **23 patients developed secondary clinical events on treatment**
- **6 of these died**
- **All of them developed within 3 months of initiation of treatment**
- **Events (excluding deaths due to other unrelated causes/lactic acidosis):**
  - **Adominal Tuberculous adenopathy/fever (12)- 3 died**
  - **Herpes zoster (5)**
  - **Cryptococcal meningitis (2)- 1 died**
  - **Tuberculous Pleural effusion (2)**
  - **Tubercular meningitis (1)- died**
  - **NHL (1)- died**
- **Overall AIDS associated mortality: 5.7% at 12 mo's**

# Improvement in mean CD4 counts



# Table 4: Overall CD4 improvement (>20%)

<b>Months (n=evaluable)</b>	<b>Number Responders (ITT)</b>	<b>Percentage</b>
<b>3 (n=347)</b>	<b>187</b>	<b>53.8</b>
<b>6 (n=347)</b>	<b>233</b>	<b>67.1</b>
<b>9 (n= 240)</b>	<b>152</b>	<b>63.3</b>
<b>12 (n=105)</b>	<b>68</b>	<b>64.6</b>

## Table 5: Baseline characteristics of 2NRTIS regime

	<b>Regimen1 (AZT+3TC+NVP) N=173 n (%)</b>	<b>Regimen2 (D4T+3TC+NVP) N=174 n (%)</b>	<b>P value</b>
<b>Age categories</b>			
<b>&lt;30</b>	<b>34(18.5)</b>	<b>20(11.5)</b>	
<b>30 - &lt;40</b>	<b>88(50.9)</b>	<b>86(49.4)</b>	
<b>40 - &lt;50</b>	<b>41(22.5)</b>	<b>33(18.9)</b>	
<b>50 +</b>	<b>10(8.1)</b>	<b>35(20.1)</b>	
<b>CD4 baseline</b>	<b>159.4 ± 9.4</b>	<b>129 ± 9.5</b>	<b>0.02</b>
<b>Gender</b>			<b>0.49</b>
<b>Male</b>	<b>148(83.2)</b>	<b>148(80.5)</b>	
<b>Female</b>	<b>23(16.8)</b>	<b>28(19.6)</b>	

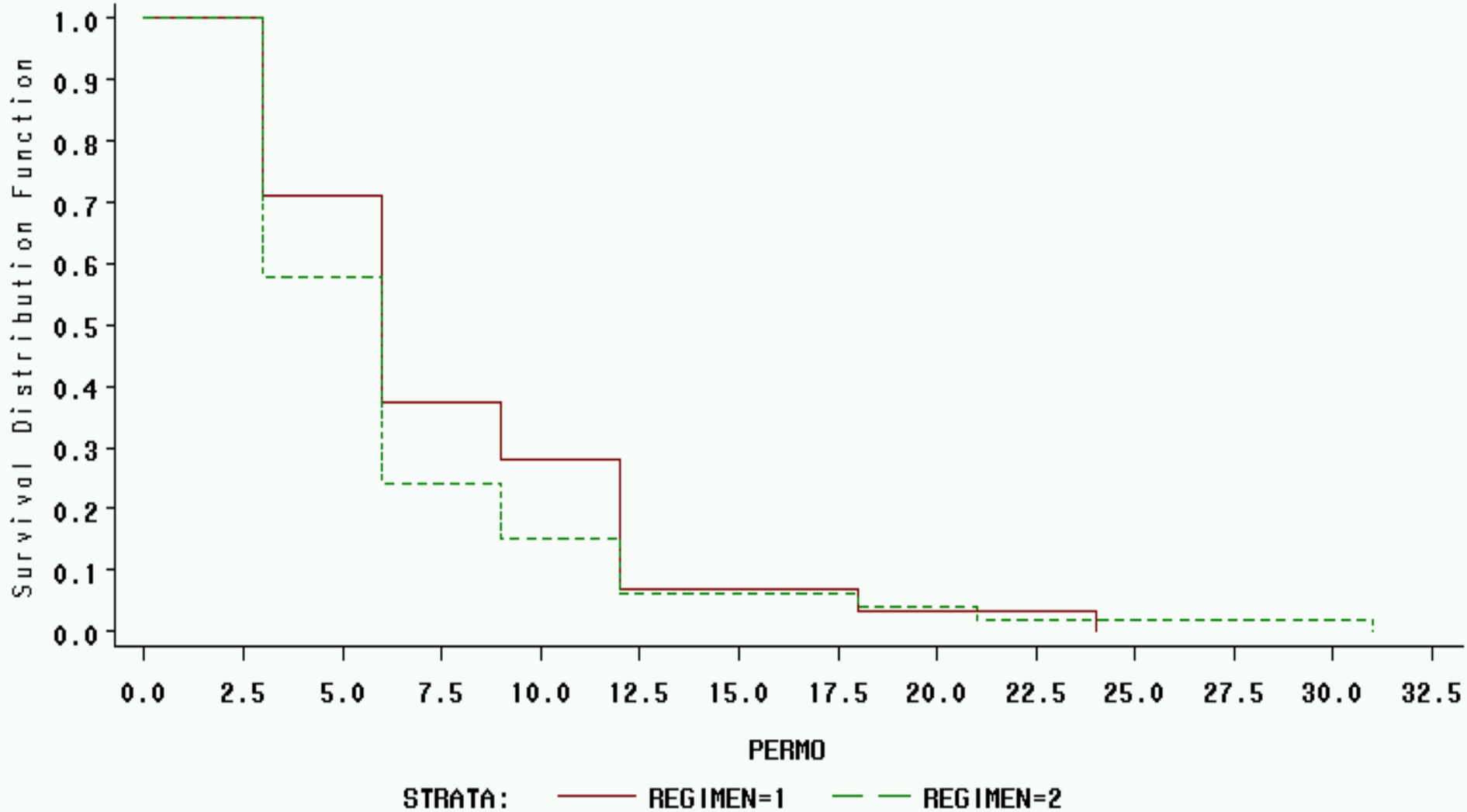
**Table 6: Relative CD4 response of  
AZT/3TC versus D4T/3TC**

CD4 responders	Adjusted RH	95% CI	P value
3 months	1.17	0.87-1.58	0.29
6 months	1.26	0.97-1.65	0.08
9 months	1.28	0.98-1.67	0.07
12 months	1.25	0.96-1.63	0.09

*Reference category: AZT/3TC*

# Kaplan-Meier curves for CD4 improvement in two regimes (equal in time to CD4 response)

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# Conclusions

- **Nevirapine is safe and well tolerated in this largest study from India**
- **Immunological improvement at 1 year is significant on Nevirapine based HAART**
- **Most improvement seen within 6 months of initiation of HAART**
- **Response does not vary with backbone NRTIs (AZT/3TC or D4T/3TC)**
- **Can be positioned as first line HAART, although durability beyond 1 year needs to be further studied**