

## Evaluation of Emtricitabine within a Triple NRTI HAART Regimen

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### Introduction

- Emtricitabine (FTC) is a once-daily nucleoside reverse transcriptase inhibitor (NRTI) for the treatment of HIV-1 infection
- A triple NRTI regimen is a potential approach to the treatment of HIV-1 infection with the advantage of preserving drug classes for additional treatment options later on in therapy
- Concern over long-term toxicity and adherence to antiretroviral therapy has led to the study of simpler antiretroviral regimens including triple nucleoside combinations and once-a-day medications

### Methods

- This analysis was undertaken retrospectively to compare the antiretroviral activity at Week 48 of FTC + d4T + ABC to 3TC + AZT + ABC in treatment-naïve HIV-infected patients using:

- proportion of patients (%) with HIV-1 RNA ≤ 400 copies/mL
- proportion of patients (%) with HIV-1 RNA ≤ 50 copies/mL
- median change in CD4 cell count from baseline
- incidence of M184V/I mutation in HIV-RT
- incidence of virological failure

- Data from six clinical trials (795 patients) involving the triple nucleoside combination 3TC + AZT + ABC were included in this analysis

- Only adult subjects who were ART-naïve were included in the analysis

- All studies must have been at least 48 weeks in duration

- The percentage of patients with undetectable viral load using an intent-to-treat analysis (missing=failure), proportion of patients experiencing virological failure (plasma HIV-1 RNA > 400 copies/mL) and the proportion of patients who developed resistance mutation (i.e. M184V/I) was obtained for all studies. Resistance and virological data for CNA 2002, CNA 3014, and CNAF 3007 were not included because data was not available for this meta analysis

- A weighted 95% confidence interval was used to assess the treatment difference for the following parameters:

- proportion of patients with HIV-1 RNA ≤ 400 copies/mL at Week 48
- proportion of patients with HIV-1 RNA ≤ 50 copies/mL at Week 48
- virological failure at Week 48
- incidence of resistance mutations at Week 48 and/or at end of study

- The studies and main entry criteria included in this analysis are presented in Table 1

### Methods (cont'd)

**Table 1. Study Characteristics**

Trial/Regimen	Main entry criteria	References
MKC-401: FTC + d4T + ABC	HIV-RNA ≥ 1,000 copies/mL, CD4+ >200 cells/mm <sup>3</sup>	Data on File
CNA2002: 3TC + AZT + ABC	HIV RNA ≥ 30,000 copies/mL, CD4+ ≥ 100 cells/mm <sup>3</sup>	Staszewski et al. AIDS 1998, 12: F197-F202
CNAAB 3005: 3TC + AZT + ABC	HIV-RNA ≥ 10,000 copies/mL, CD4+ > 100 cells/mm <sup>3</sup>	Staszewski et al. JAMA, 2001, 285: 1155-1163
CNAF3007: 3TC + AZT + ABC	HIV-RNA ≥ 1,000 ≤ 500,000 copies/mL	Matheron S. et al. Antivir Ther. 2003 8(2):163-71
CNA3014: 3TC + AZT + ABC	HIV-RNA ≥ 5,000 copies/mL	Vibhagool, A. et al. 1 <sup>st</sup> IAS Conference, July 2001: Abstract 63
CNA3003: 3TC + AZT + ABC	CD4+ > 100 cells/mm <sup>3</sup>	Ait-Khaled et al. Antivir. Ther. 2002, 7:43-51
EPV40001: 300 mg 3TC QD (n=54) or 150 mg 3TC BID (n=52) + AZT + ABC	no HIV RNA or CD4+ entrance criteria found	Bowonwatanuwong C, et al. 1st IAS Conference, July 2001, Abstract 4.

**Table 2. Baseline Characteristics and Demographics**

Characteristic	MKC401	CNA2002	CNAAB3005	CNAF3007	CNA3014	CNA3003	EPV40001
N	188	60	282	95	169	83	106
% Male	43%	85%	87%	69%	ndf	ndf	32%
Median Age (year)	33	36	36	34	ndf	ndf	30
Race							
% White	12%	98%	72%	ndf	ndf	ndf	0%
% Black	76%	0%	17%	ndf	ndf	ndf	0%
% Asian	ndf	ndf	ndf	ndf	ndf	ndf	100%
Median HIV RNA (log <sub>10</sub> copies/mL)	4.2	5.0	4.9	4.2	4.8	4.5	4.8
Median CD4+ cell count (cells/mm <sup>3</sup> )	388	360	359	387	331	450	380

\*ndf=no data found

- Baseline Characteristics were comparable across the studies with the exception of race and gender

### Results

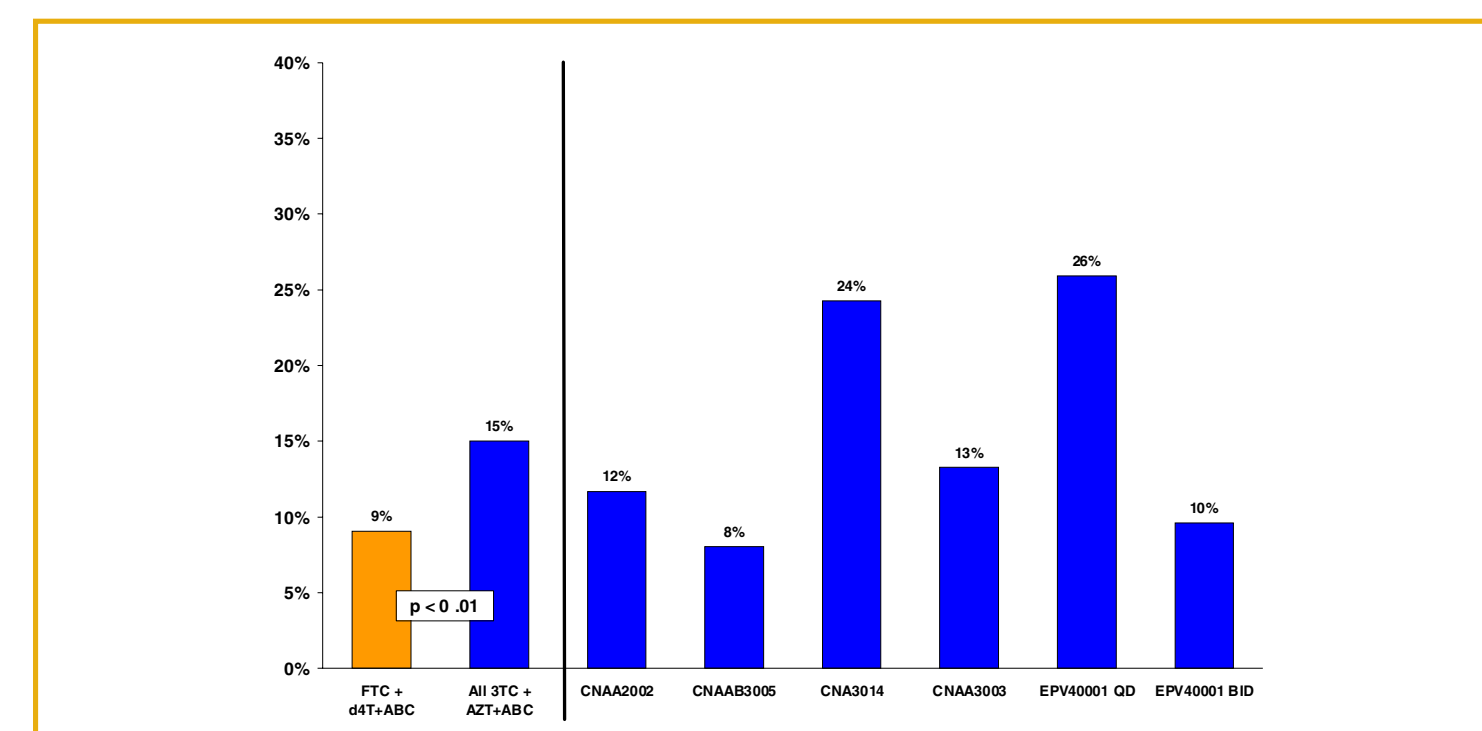
**Table 3. Summary of Efficacy Endpoints at Week 48**

Regimen	FTC+ ABC+d4T	3TC+AZT+ABC							
		All Trials	CNA 2002	CNAAB 3005	CNAF 3007	CNA 3014	CNA 3003	EPV 40001 QD	EPV 40001 BID
% HIV-1 RNA ≤ 400 copies/mL	63	61	65	51	ndf*	64	74	61	75
% HIV-RNA ≤ 50 copies/mL	55	52	43	40	57	59	ndf*	54	67
Median Change in CD4+ cell count from Baseline	+177	na	+118	+107	+110	ndf*	+150	+166	+216

\*ndf=no data found

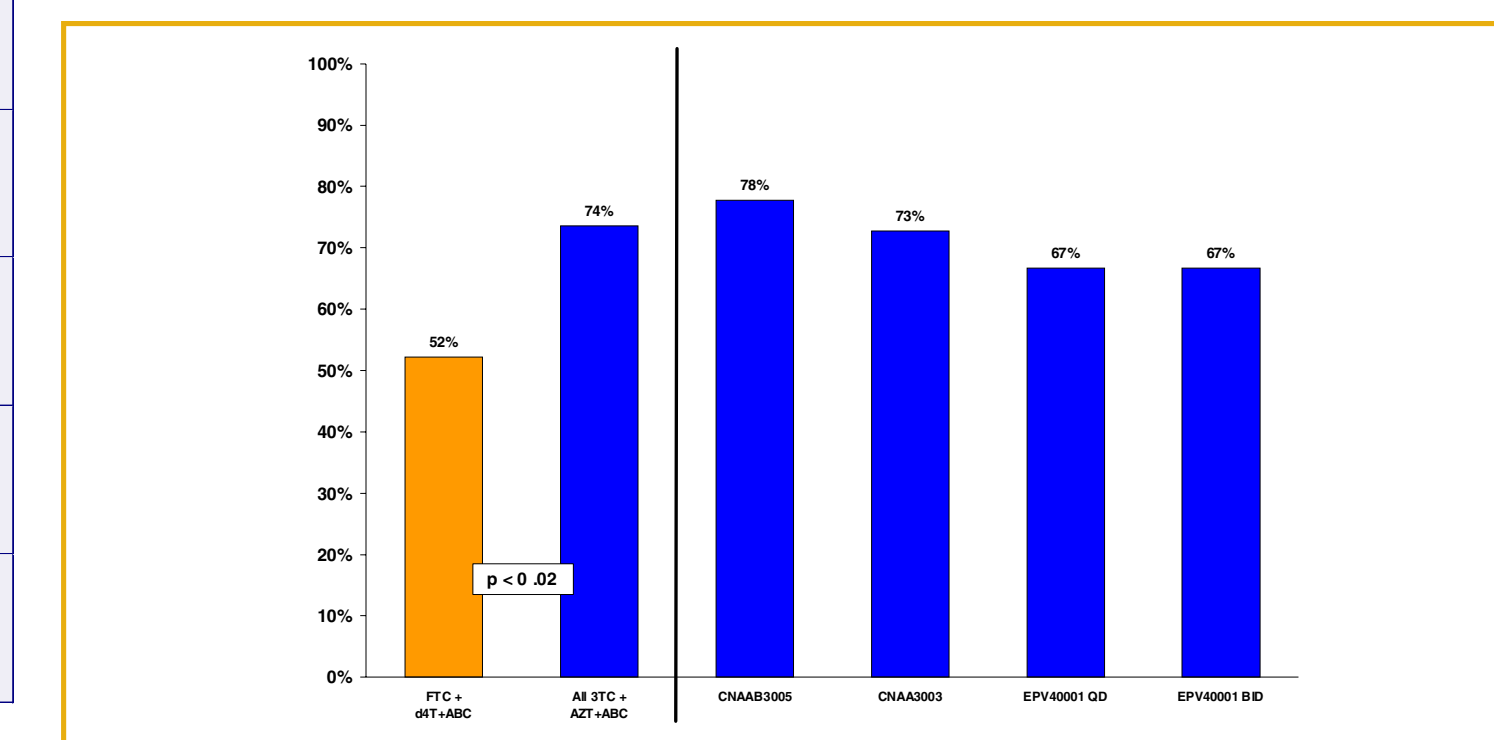
- A total of 188 patients were treated with FTC+ d4T+ABC. At Week 48, 63% had HIV-1 RNA ≤ 400 copies/mL and 55% had HIV-1 RNA ≤ 50 copies/mL
- A total of 795 patients were evaluated from 6 clinical trials of 3TC+AZT+ABC. On average, 61% (range 51-75%) of patients had HIV-1 RNA ≤ 400 copies/mL and 52% (range 40-67%) of the patients had HIV-1 RNA ≤ 50 copies/mL
- The weighted differences between treatment arms for the proportion of patients with HIV-1 RNA ≤ 400 and ≤ 50 copies/mL at Week 48 were not statistically significant

**Figure 1. Overall Proportion of Patients at Week 48 who Experienced Virological Failure (> 400 copies/mL)**



- The virological failure rate was statistically significantly lower for the FTC regimen as compared to the 3TC+AZT+ABC regimens (-4% treatment difference with a 95% CI [-8%, -1%]; p < 0.01)

**Figure 2. Incidence of the M184V/I Mutation in Patients who Experienced Virological Failure**



- The incidence of the M184V/I mutation was statistically significantly lower for the FTC regimen compared to the 3TC + AZT+ ABC regimens (-21% treatment difference with a 95% CI [-37%, -5%]; p < 0.02)

### Conclusions

- In a retrospective analysis of an FTC + d4T + ABC regimen compared to 3TC + AZT + ABC regimens, the FTC regimen resulted in:
  - Similar efficacy
  - Lower rate of virologic failure (9% vs. 15%, respectively)
  - Significantly lower incidence of M184V/I genotypic mutations (52% vs. 74%, respectively) within VFs