Potential low dose efavirenz study

Current Preferred 3rd agents	Alternatives
Efavirenz	…..
Atazanavir/r	…..
Darunavir/r	…..
Raltegravir	
Elvitegravir/cobi	

Future additions	Alternatives
Dolutegravir	…..

Potential low dose efavirenz study

EFV Dose	efficacy	side effects	other considerations
600	+++	• General • Lipids • CNS • Bone	• Cost • FDC

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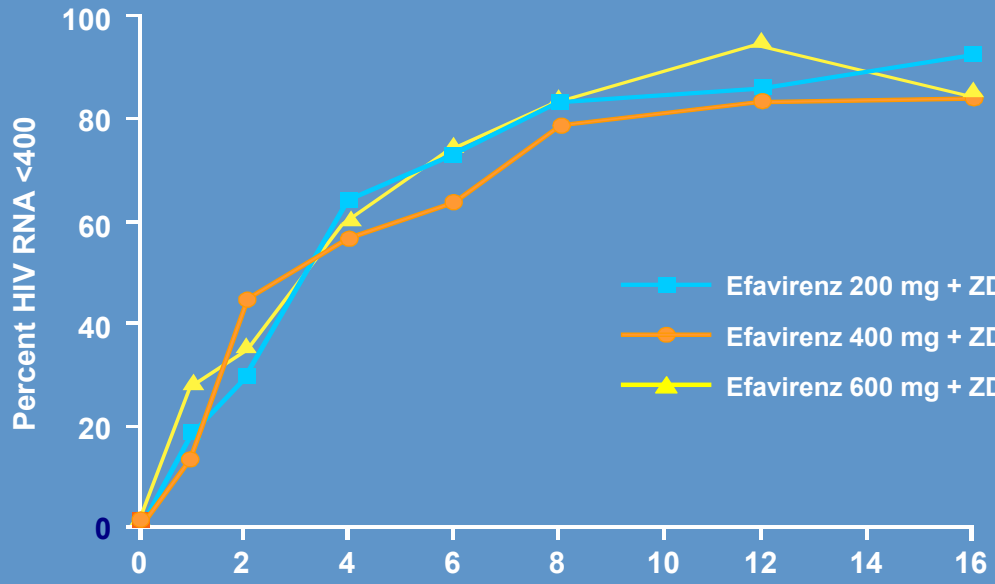
DMP-005 trial

ZDV/3TC + EFV 200, 400, 600 mg OD
HIV RNA < 400 copies/ml after 16 weeks



EFV 200 mg N =	32	34	34	30	29	32	31
EFV 400 mg N =	31	31	33	28	30	28	28
EFV 600 mg N =	32	29	32	28	30	27	28

Haas *et al. 5th CROI* 1998. Abstract 698

Encore1 study design

A randomized, double-blind, placebo-controlled, non-inferiority clinical trial to compare the safety and efficacy of reduced dose EFV with standard dose EFV plus 2N(t)RTI in ART-naïve HIV-infected individuals over 96 weeks

Patient population

ART-naïve HIV-infected adults with no prior AIDS, plasma HIV-1 RNA (pVL) >1,000 copies/mL, 50 <CD4$^+$ T cells/µL <500, creatinine clearance ≥50 mL/min, no pregnancy or nursing mothers

Randomisation

I. TDF/FTC + 400 mg EFV qd

(2 x 200 mg EFV + 1 x 200 mg matched placebo)

II. TDF/FTC + 600 mg EFV qd

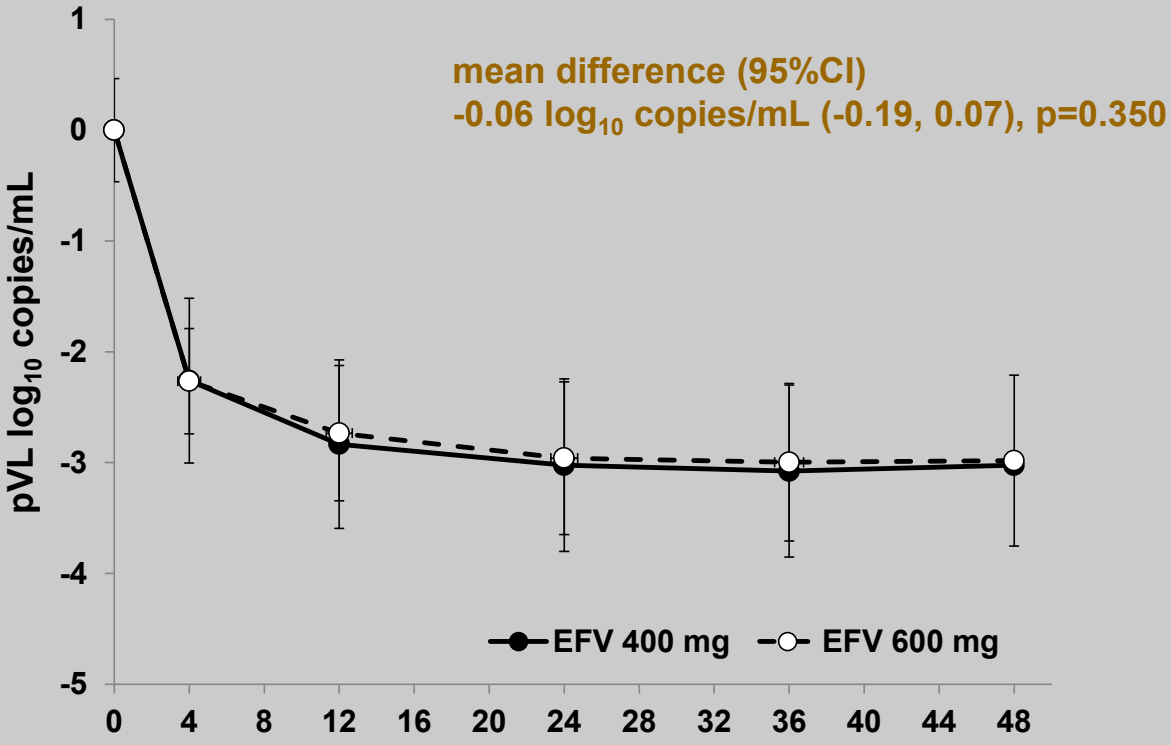
(3 x 200 mg EFV)

1:1 (400mg:600mg), stratified by clinical site and screening pVL

Potential low dose efavirenz study

encore 1

Mean change from baseline to week 48 pVL

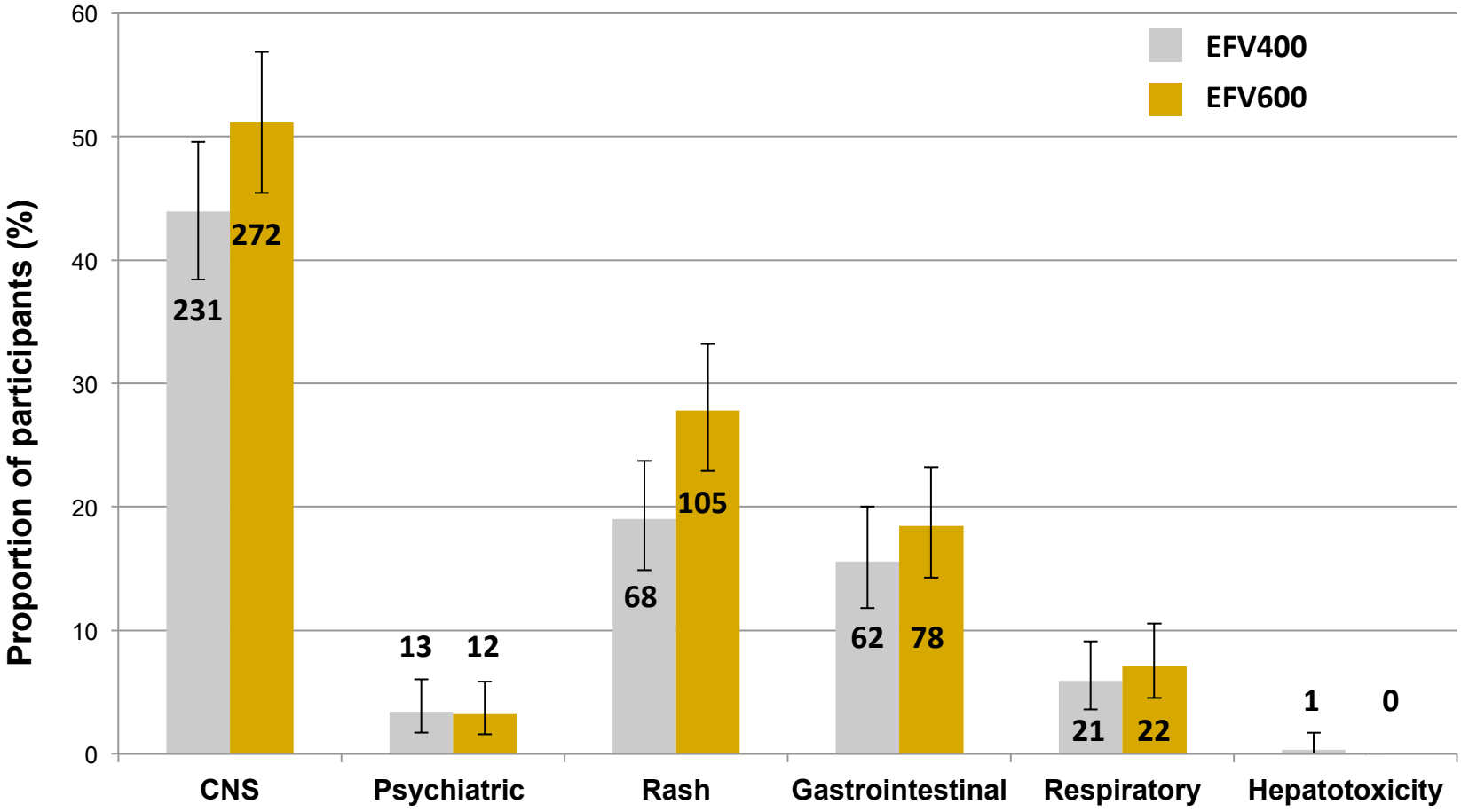


Adverse events - overall

Adverse events	EFV400 n (%)	EFV600 n (%)	Total n (%)
Number of AEs	1,173 (49.8)	1,182 (50.2)	2,355 (100)
Grade 1/2	1,119 (47.5)	1,118 (47.4)	2,237 (95.0)
Grade 3/4	54 (2.3)	65 (2.7)	117 (5.0)

Serious adverse events	EFV400 N=321 n (%)	EFV600 N=309 n (%)	Difference (95%CI)	p
Total numbers of SAEs	31 (46.2)	36 (53.7)		
Number with SAE	23 (7.17)	22 (7.12)	0.05% (-3.98, 4.07)	0.980
Number with SAE related to study drug	3 (0.93)	4 (1.29)	0.36% (-1.98, 1.27)	0.670

Efavirenz adverse events*



*categorised according to the EFV Product Information

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EFV Dose	efficacy	side effects	other considerations
600	+++	• General • Lipids • CNS • Bone	• Cost • FDC
400	+	• General √ • Lipids x • CNS x • Bone ?	• Not FDC (generic) • Reduced cost

Potential low dose efavirenz study

EFV Dose	efficacy	side effects	Other considerations
600	+++	• General • Lipids • CNS • Bone	• Cost • FDC
400	+	• General √ • Lipids x • CNS x • Bone ?	• Acceptability to users • Efficacy: • Healthcare costs
200	-/+	• Could be lower than with 400mg • Could this be similar to newer 3rd agents	

Potential low dose efavirenz study

	Considerations for a study / current plan
Feasibility study	100 subjects
Population	Antiretroviral naïve
Arms	Randomisation 1:1 • Truvada + EFV 200 once daily • Truvada + raltegravir 400 twice daily
Endpoints	Composite endpoint: • Virological efficacy • Toxicity
Future	Pilot data full phase III study