

Similar 96-week Renal Safety Profile of Tenofovir Disoproxil Fumarate (TDF) versus Stavudine (d4T) when used in Combination with Lamivudine (3TC) and Efavirenz (EFV) in Antiretroviral Naïve Patients

JE Gallant¹, AL Pozniak², S Staszewski³, B Lu⁴, J Sayre⁴ and A Cheng⁴ for the Study 903 Team

¹Johns Hopkins Univ School of Medicine, Baltimore, MD, USA; ²Chelsea and Westminster Hosp, London, UK; ³University Hospital, J.W. Goethe-Universität, Frankfurt, Germany; ⁴Gilead Sciences, Foster City, CA, USA.

43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy
September 14-17, 2003
Chicago, Illinois
Poster No. H- 840

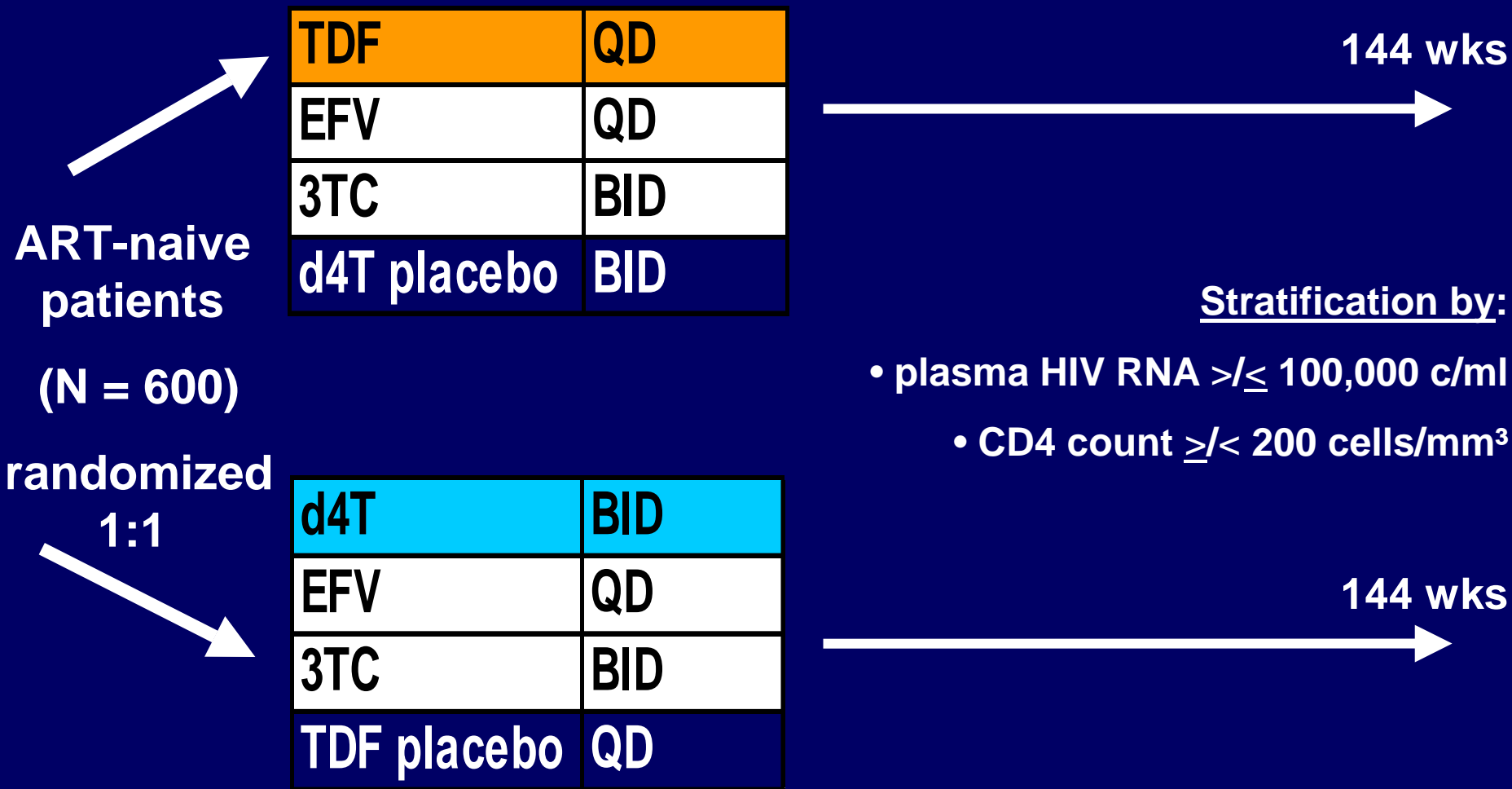
Background

- Study 903 is an ongoing 144 week, randomized, double-blind, international multicenter trial which compares TDF and d4T when used in combination with EFV and 3TC in antiretroviral treatment naïve patients.
- Case reports of renal dysfunction have recently been published¹⁻⁶

Main Inclusion Criteria

- HIV-1 infected patients naïve to antiretroviral treatment
- 18 - 65 years of age
- Plasma HIV RNA $> 5,000$ copies/mL
- No significant laboratory or clinical abnormalities
- No CD4+ cell count criteria
- Serum Creatinine < 1.5 mg/dL
- Serum Phosphorus ≥ 2.2 mg/dL
- Calculated Creatinine Clearance ≥ 60 mL/min

Study Design: Randomization



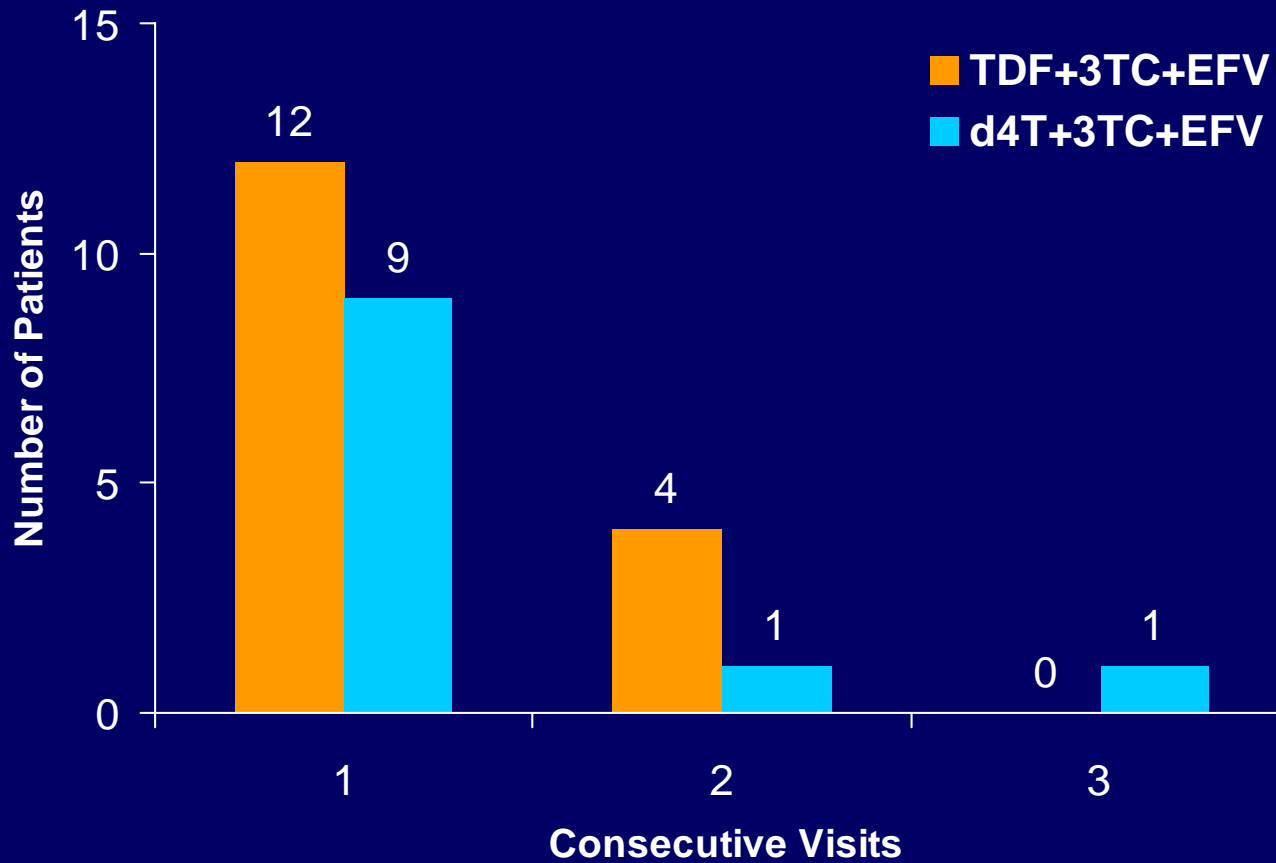
Baseline Characteristics

	TDF + 3TC + EFV (n = 299)	d4T + 3TC + EFV (n = 301)
Mean Age (yrs)	36	36
Range	19 to 61	18 to 64
Weight (kg)	72	72
Female	26%	25%
Race		
White	64%	64%
Black	21%	18%
Hispanic	7%	8%
Asian	1%	2%
Other	7%	9%

Serum Creatinine

Maximum Toxicity Grade 0-96 Weeks in mg/dL	TDF + 3TC + EFV (n=296)	d4T + 3TC + EFV (n=296)
1 (≥ 0.5 from baseline)	10 (3%)	7 (2%)
2 (2.1-3.0)	2 (<1%)	0 (0%)
3 (3.1-6.0)	0 (0%)	2 (<1%)
4 (>6.0)	0 (0%)	0 (0%)

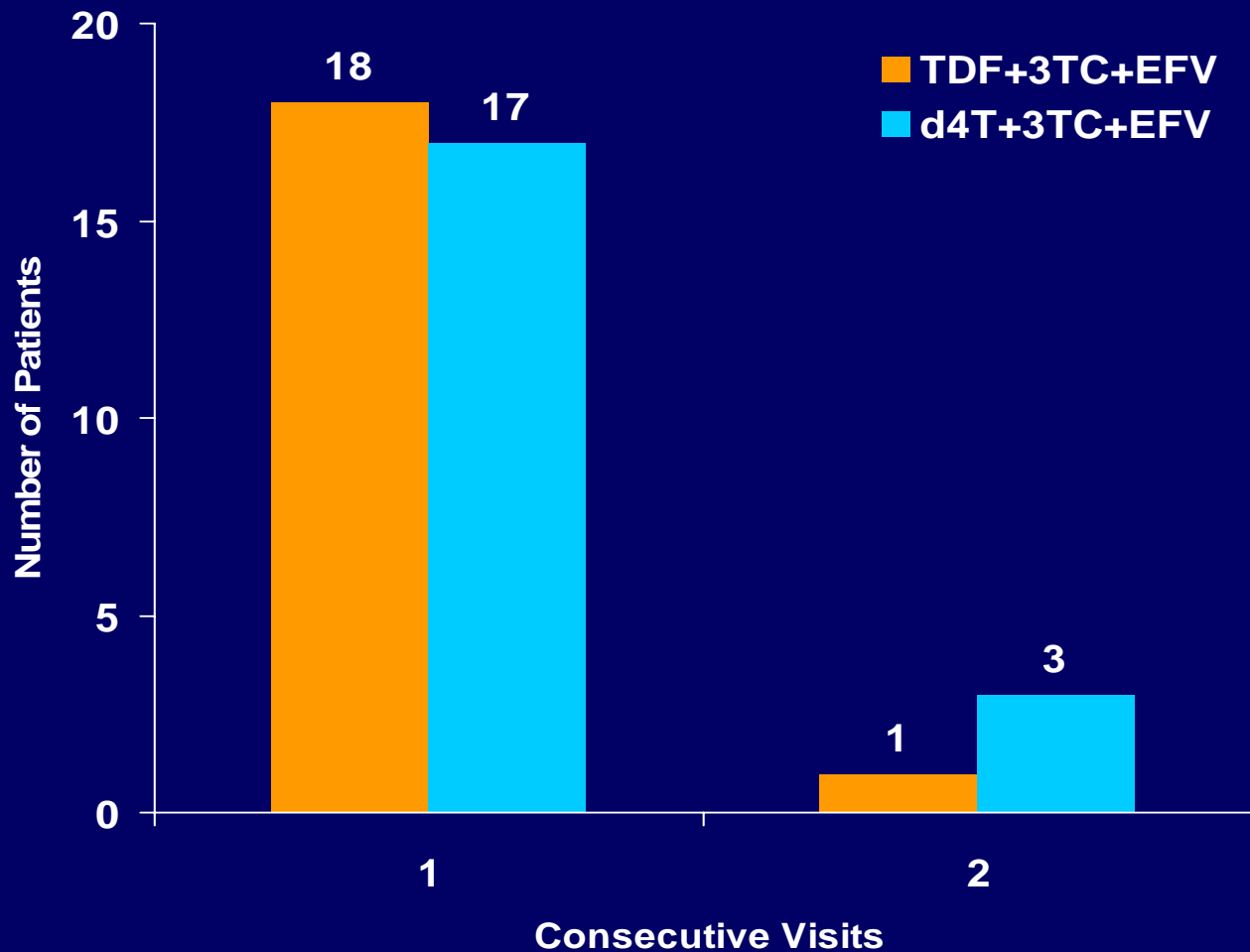
Consecutive Visits with Graded Creatinine



Serum Phosphorus

Maximum Toxicity Grade 0-96 Weeks in mg/dL	TDF + 3TC + EFV (n=296)	d4T + 3TC + EFV (n=296)
1 (2.0-<2.2)	9 (3%)	9 (3%)
2 (1.5-1.9)	8 (3%)	7 (2%)
3 (1.0-1.4)	1 (<1%)	1 (<1%)
4 (<1.0)	0 (0%)	0 (0%)

Consecutive Visits with Graded Serum Phosphorus



Proteinuria

Maximum Toxicity Grade 0-96 Weeks in mg/dL	TDF + 3TC + EFV (n = 296)	d4T + 3TC + EFV (n = 296)
1 (30-99)	35 (12%)	46 (16%)
2 (100-300)	18 (6%)	17 (6%)
3 (>300)	0 (0%)	0 (0%)
4 Nephrotic Syndrome	0 (0%)	0 (0%)

Glucosuria

Maximum Toxicity Grade 0-96 Weeks in mg/dL	TDF + 3TC + EFV (n = 296)	d4T + 3TC + EFV (n = 296)
1 (<250)	2 (<1%)	3 (1%)
2 (250-500)	2 (<1%)	1 (<1%)
3 (500-1000)	2 (<1%)	3 (1%)
4 (>1000)	0 (0%)	0 (0%)

Mean Increase from Baseline in Calculated Creatinine Clearance (Calc Cr Cl)

mL/min	TDF + 3TC + EFV (n = 296)	d4T + 3TC + EFV (n = 296)
Baseline	122	125
Week 48	2	8
Week 96	1	4

(Through 96 weeks)

Summary of Results: Parameters through 96 weeks

Parameters through 96 weeks	TDF+3TC+EFV (n = 296)	d4T+3TC+EFV (n = 296)
Graded Serum Creatinine	12 (4%)	9 (3%)
Graded Serum Phosphorus	18 (6%)	17 (6%)
Graded Proteinuria	53 (18%)	63 (21%)
Graded Glucosuria	6 (2%)	7 (2%)
Baseline Calc Cr Cl* (mL/min)	122	125
Mean Change from Baseline in Calc Cr Cl* (mL/min)	+1	+4
Patients with Fanconi's Syndrome	0	0

*Using Cockcroft-Gault Equation

Conclusions

- **The renal safety profile was similar between the patients receiving tenofovir DF or stavudine plus lamivudine and efavirenz through 96 weeks**
- **No patients discontinued study due to tenofovir DF-related renal abnormalities**
- **No patient developed Fanconi's Syndrome through 96 weeks**

References

- ¹Blick G, et al. 10th CROI, Boston, MA, February 10-14, 2003. Poster 718
- ²Reynes J, et al. 10th CROI, Boston, MA, February 10-14, 2003. Poster 717
- ³Creput C, et al. AIDS 2003; 17:935-937
- ⁴Karras A, et al. CID 2003; 36:1070-1073
- ⁵Murphy MD, et al. CID 2003; 36:1082-1085
- ⁶Shere-Wolfe KD, et al. CID 2002; 35:1137