

Efficacy and Safety of Tenofovir DF (TDF), Emtricitabine (FTC) and Efavirenz (EFV) Compared to Fixed Dose Zidovudine/Lamivudine (CBV) and EFV Through 96 Weeks in Antiretroviral Treatment-Naïve Patients

Poster Number
TUPE0064

XVI International AIDS Conference
August 13-18, 2006
Toronto, Canada

JE Gallant¹, AL Pozniak², E DeJesus³, JR Arribas⁴, R Campo⁵, S-S Chen⁶,
D McColl⁶, J Enejosa⁶, and AK Cheng⁶ for the Study 934 Team

¹Johns Hopkins University School of Medicine, Baltimore, MD, USA; ²Chelsea and Westminster Hospital, London, UK; ³Orlando Immunology Center, Altamonte Springs, FL, USA; ⁴University Hospital La Paz, Madrid, Spain; ⁵University of Miami, Miami, FL, USA; ⁶Gilead Sciences, Inc., Foster City, CA, USA



Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Tel: (650)574-3000
Fax: (650)578-9264

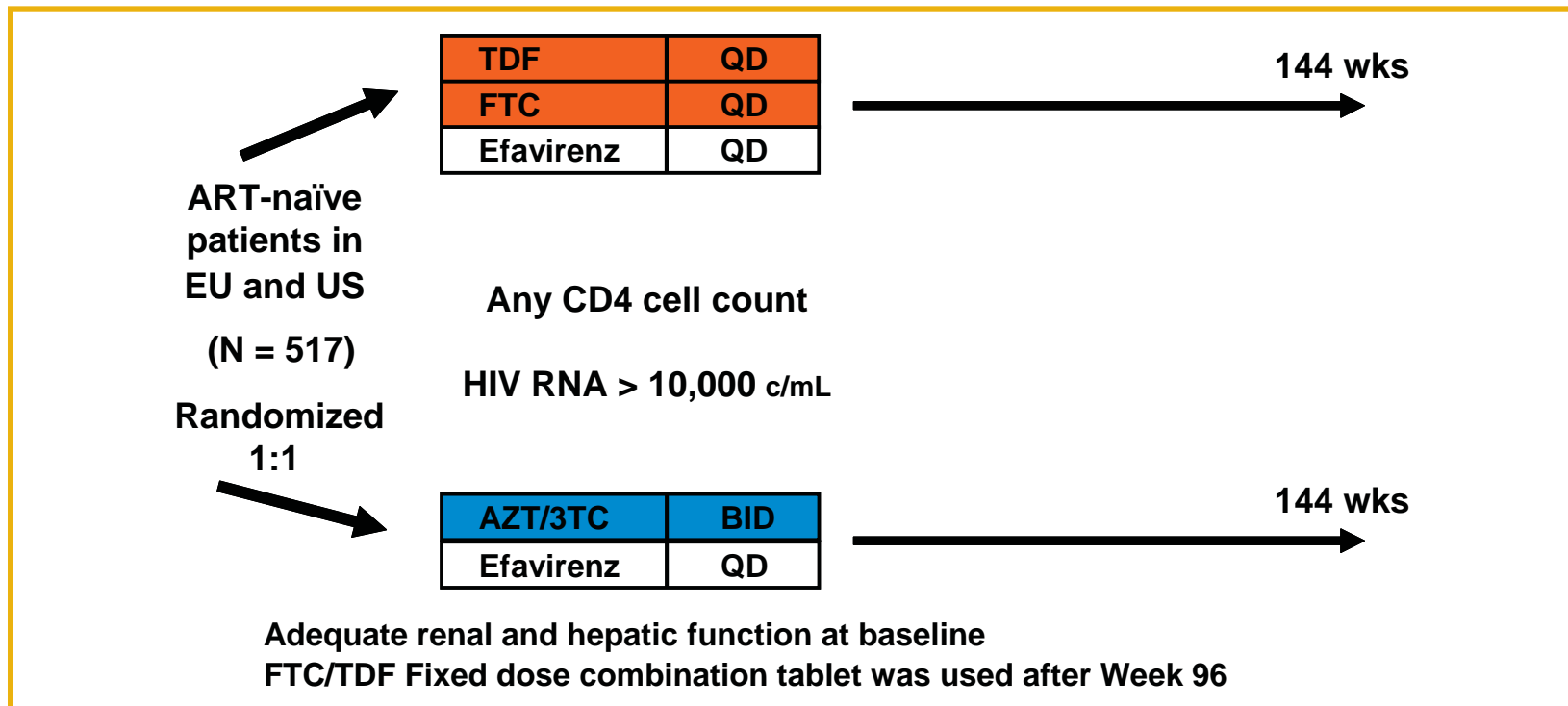
Background

- This is a large phase III trial comparing once daily TDF, FTC and efavirenz (EFV) to twice daily CBV (AZT+3TC) and once daily EFV
- At Week 48, the proportion of patients reaching primary endpoint of HIV RNA < 400 c/mL using the FDA TLOVR algorithm was significantly higher in the TDF+FTC+EFV arm¹
- This presentation provides the results of Week 96 data analysis

1. Gallant JE, DeJesus E, Arribas JR, et al. Tenofovir DF, emtricitabine and efavirenz vs. zidovudine, lamivudine and efavirenz for HIV. N Engl J Med 2006; 354:251-60.

Methods

Figure 1. Study Design



Statistical Analysis

- Non-inferiority trial with 48 week primary endpoint
- Efficacy endpoint: Time to Loss of Virologic Response (TLOVR)
 - Similar to ITT Missing = Failure, Switch = Failure (switching EFV to NVP due to CNS toxicity was not considered failure)
 - Requires confirmation for success
 - FDA-required endpoint for presentation in U.S. Prescribing Information of newly approved antiretrovirals
- Week 96 Efficacy Patients:
 - Patients with baseline NNRTI-R mutations and patients who completed the Week 48 study with HIV RNA below limit of quantification but did not consent to participate in the study extension from Weeks 48 – 96 were excluded from the analysis

Results

Table 1. Baseline Characteristics (ITT)

	TDF+FTC+EFV (n = 255)	CBV+EFV (n = 254)
Age ^a (yrs)	36	37
% Female	14%	13%
% White	56%	61%
% Black	25%	20%
% Hispanic	15%	16%
Weight ^a (kg)	75	74
HIV RNA (log ₁₀ copies/mL) ^a	5.0	5.0
% HIV RNA > 100,000	52%	50%
CD4+ (cells/mm ³) ^a	233	241
% < 200	42%	41%
% < 50	15%	11%

a. Median values

Table 2. Summary Outcomes (Week 96 TLOVR < 400 c/mL)

	TDF+FTC+EFV (n = 232)	CBV+EFV (n = 231)
Responder	75%	62% ^a
Non-responders	25%	38%
Lost to follow up	9%	9%
Adverse Event	5%	12% ^b
Withdrawal Consent / Non Compliance	5%	7%
Virologic Rebound	< 1%	5% ^b
Other	2%	2%
Pregnancy	2%	1%
Death	< 1%	< 1%
Insufficient Virologic Response	< 1%	< 1%

a. p = 0.004
b. p = 0.007

Figure 2. Proportion with HIV-RNA < 400 c/mL (TLOVR) (n = 463)

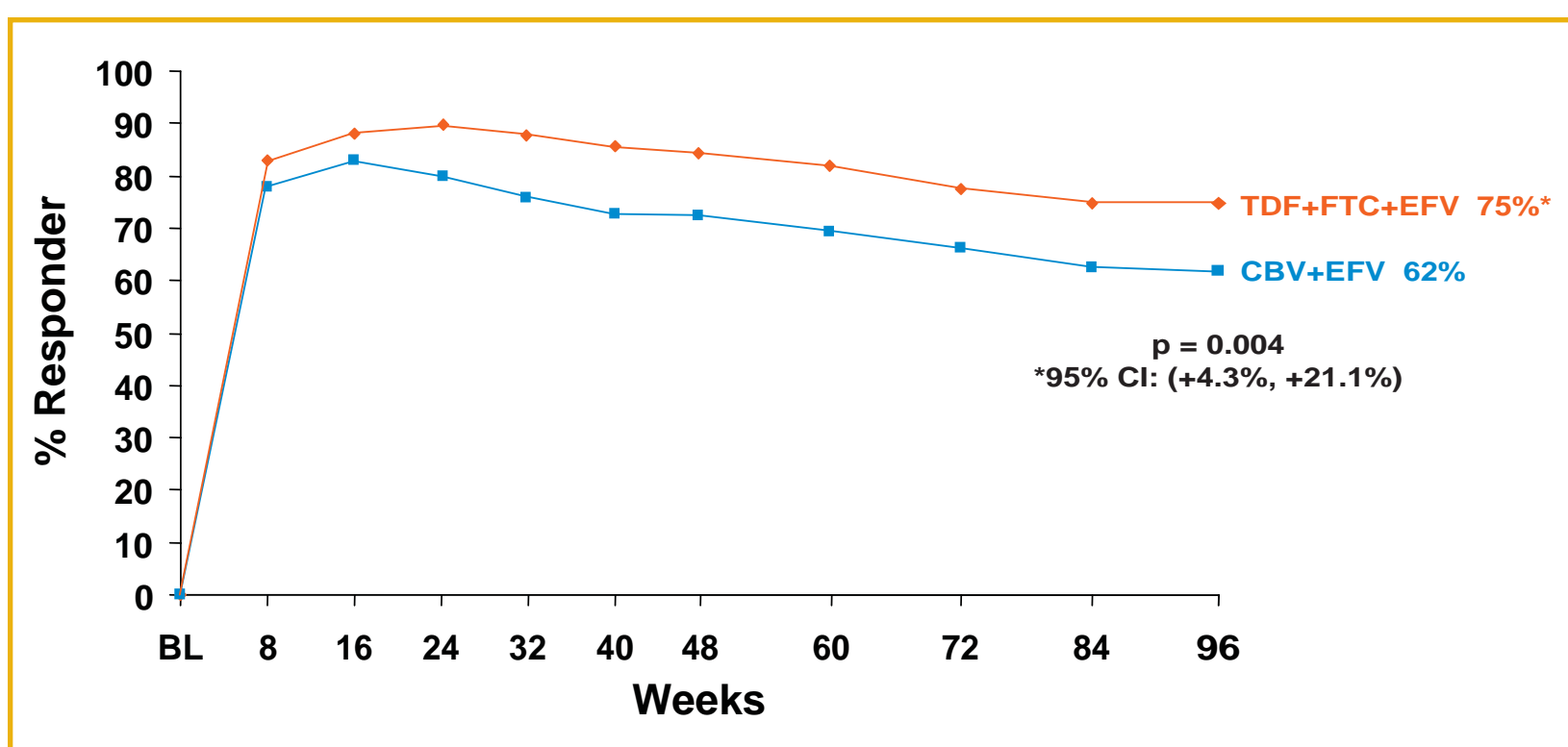


Figure 3. Proportion with HIV-RNA < 50 c/mL (TLOVR) (n = 465)

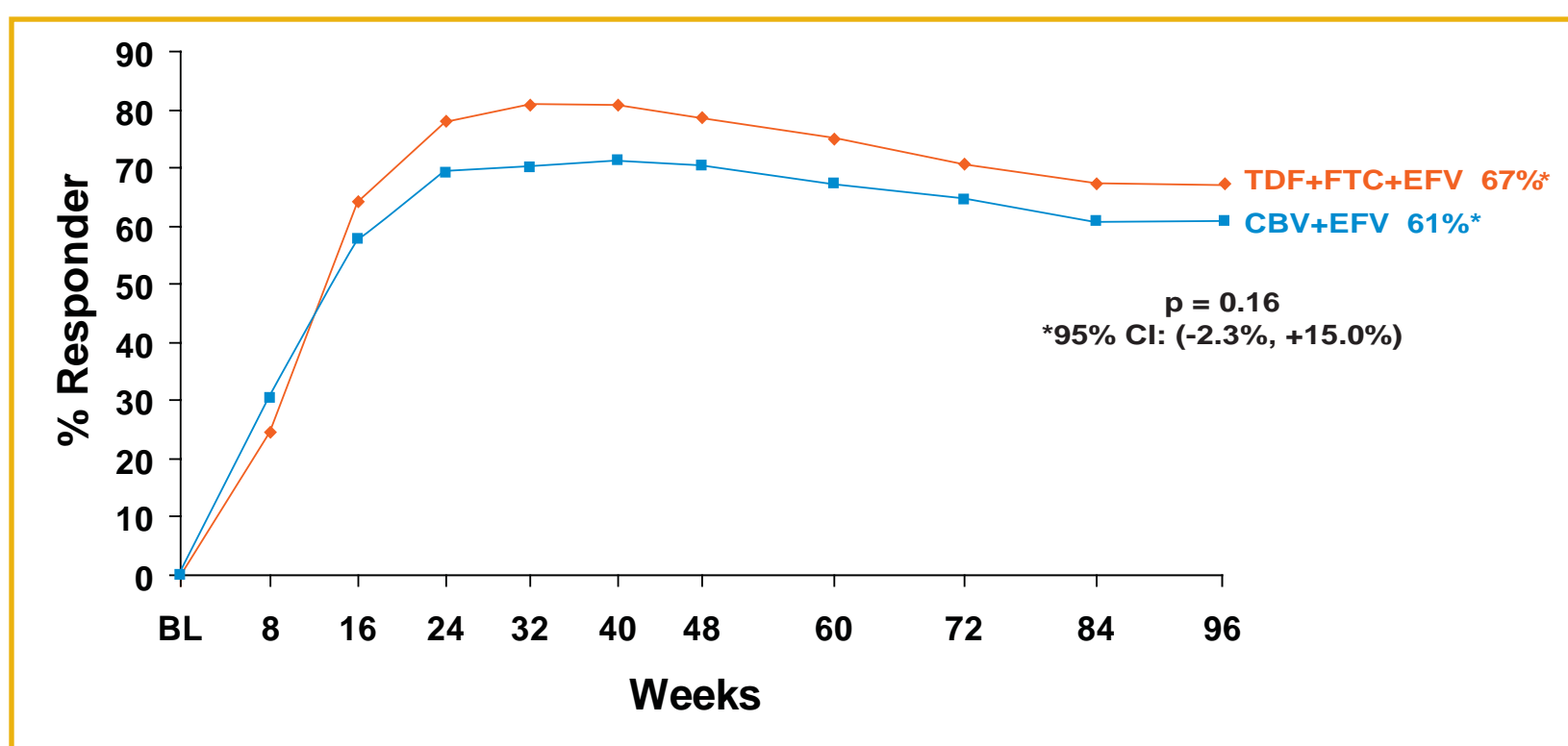
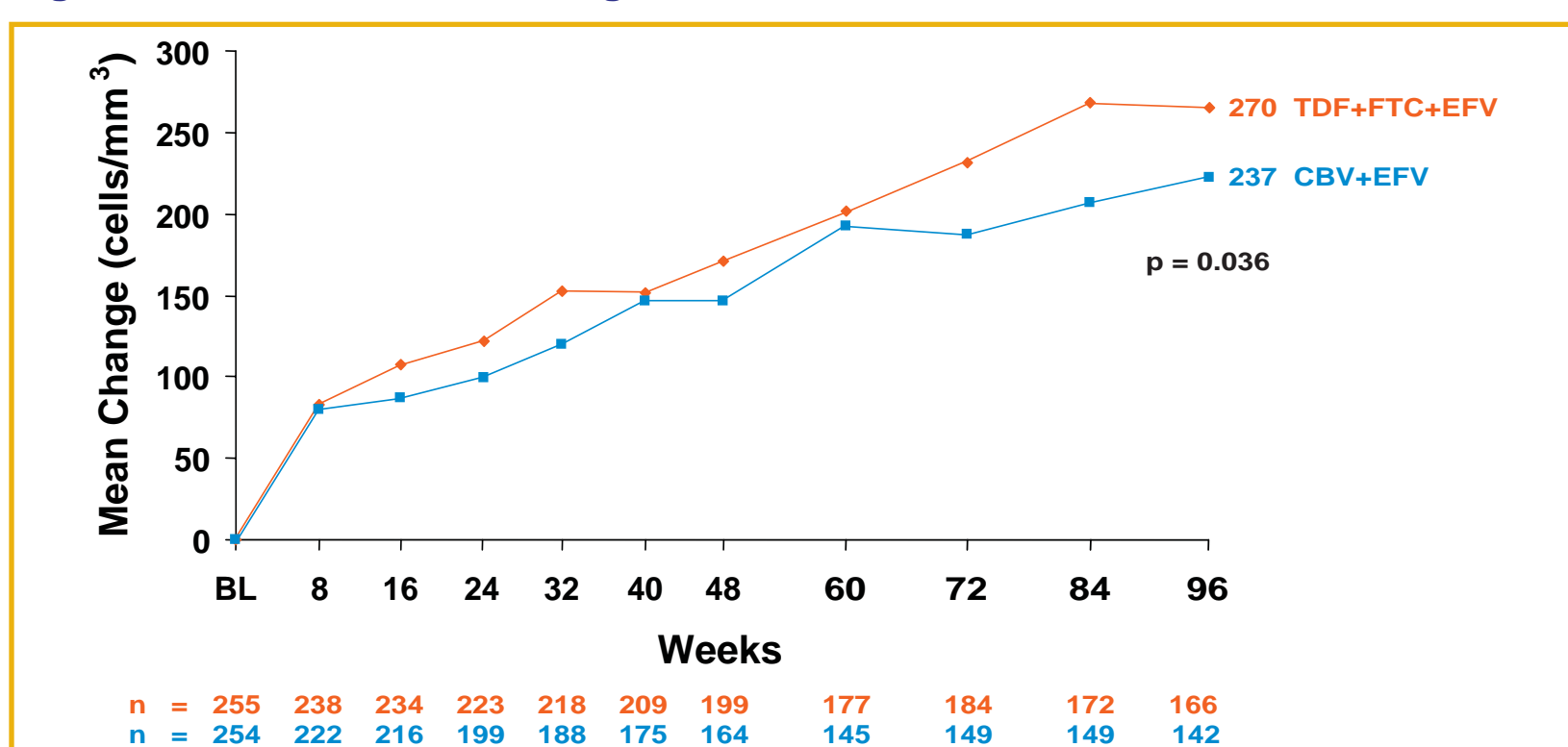


Figure 4. Mean Absolute Change in CD4 count from Baseline



Results (cont'd)

Table 3. Resistance Development through Week 96^a

Genotypes	TDF+FTC+EFV (n = 244)	CBV+EFV (n = 243)
Wild Type	4	7
Any Resistance	10	20
EFV-R	10	18
M184V/I	2	9 ^c
TAMs	0	1
K65R	0	0

a. Excludes patients with baseline NNRTI-R mutations (n = 487)

b. p = 0.017

c. p = 0.036

Table 4. Adverse Events Leading to Study Drug Discontinuation Through Week 96

Safety Population	TDF+FTC+EFV (n = 257)	CBV+EFV (n = 254)
No. w/ any Adverse Event ^a	12 (5%)	28 (11%) ^b
Adverse Event		
Anemia/ ↓ Hgb	0	14 (6%) ^c
Fatigue	0	5 (2%)
Nausea	1 (< 1%)	4 (2%)
Rash	4 (2%)	1 (< 1%)
Drug Eruption	2 (< 1%)	0
Vomiting	0	2 (< 1%)
Neutropenia	0	2 (< 1%)

a. Occurring in more than 1 patient in either arm; patients may have > 1 event

b. p = 0.023

c. p < 0.001

Table 5. Serum Creatinine

Maximum Confirmed Toxicity Grade (mg/dL) ^a	TDF+FTC+EFV (n = 257)	CBV+EFV (n = 254)
1 (> 1.5 – 2.0)	0	1 (< 1%)
2 (2.1 – 3.0)	0	1 (< 1%)
3 (3.1 – 6.0)	0	0
4 (> 6.0)	0	0

a. Confirmed toxicity grade = two consecutive visits

- Through 96 weeks, patients receiving TDF+FTC+EFV had significantly greater median increase from baseline in weight compared to patients receiving CBV+EFV (2.7 kg vs. 0.5 kg, p < 0.001)

Figure 5. Median (Q1,Q3) Glomerular Filtration Rate (Cockcroft-Gault in mL/min)

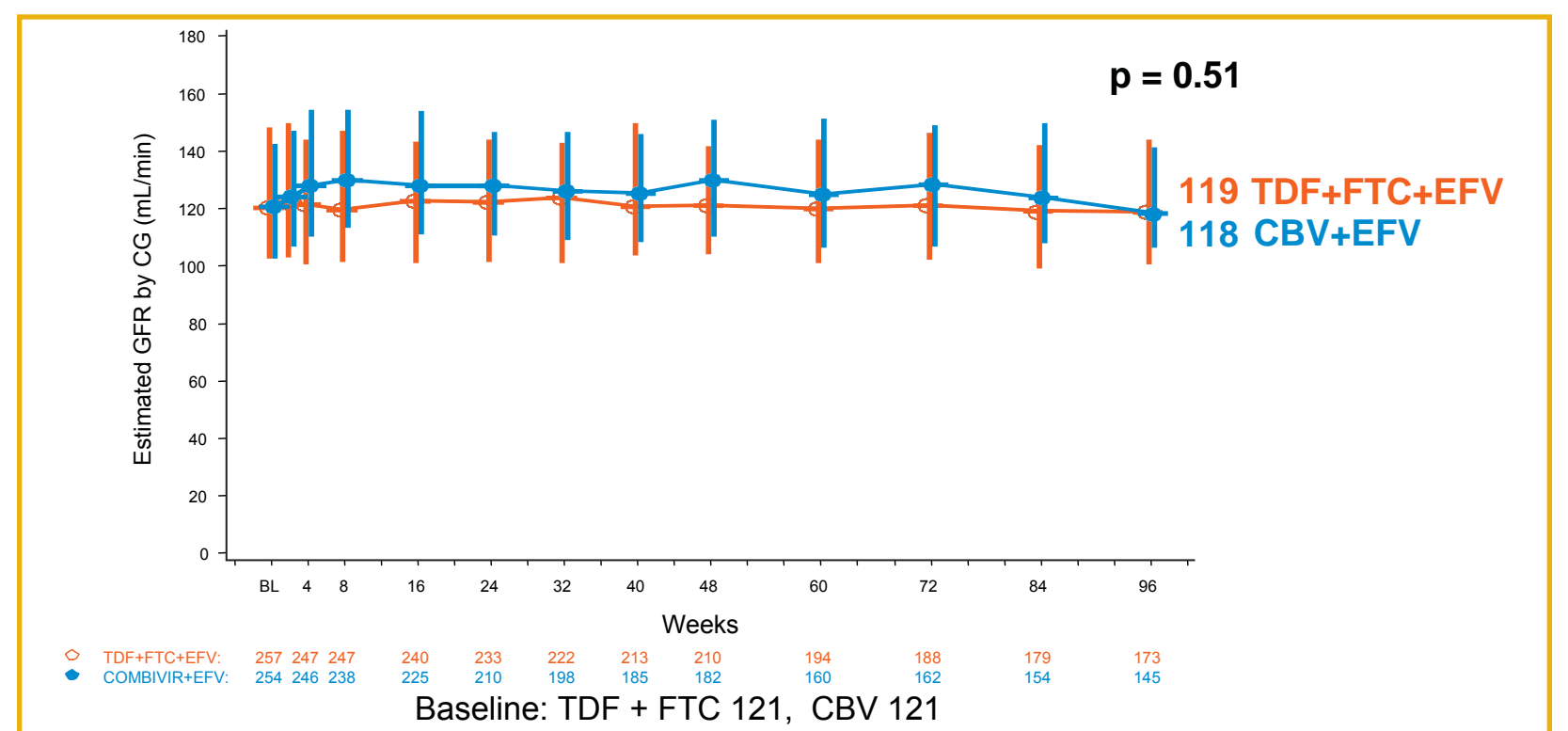


Figure 6. Median (Q1,Q3) Glomerular Filtration Rate (MDRD in mL/min/1.73m²)

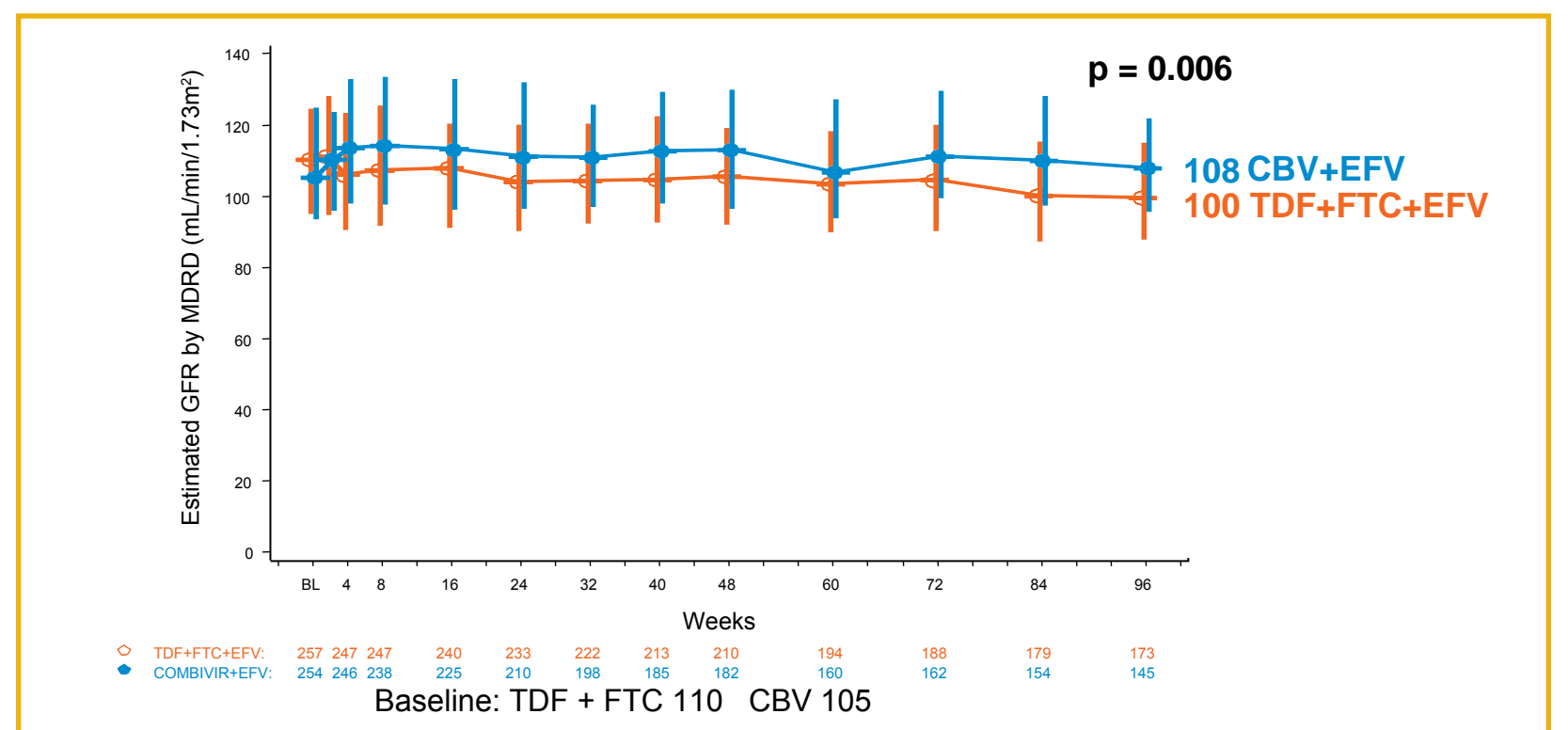


Figure 7. Median (Q1, Q3) Total Limb Fat

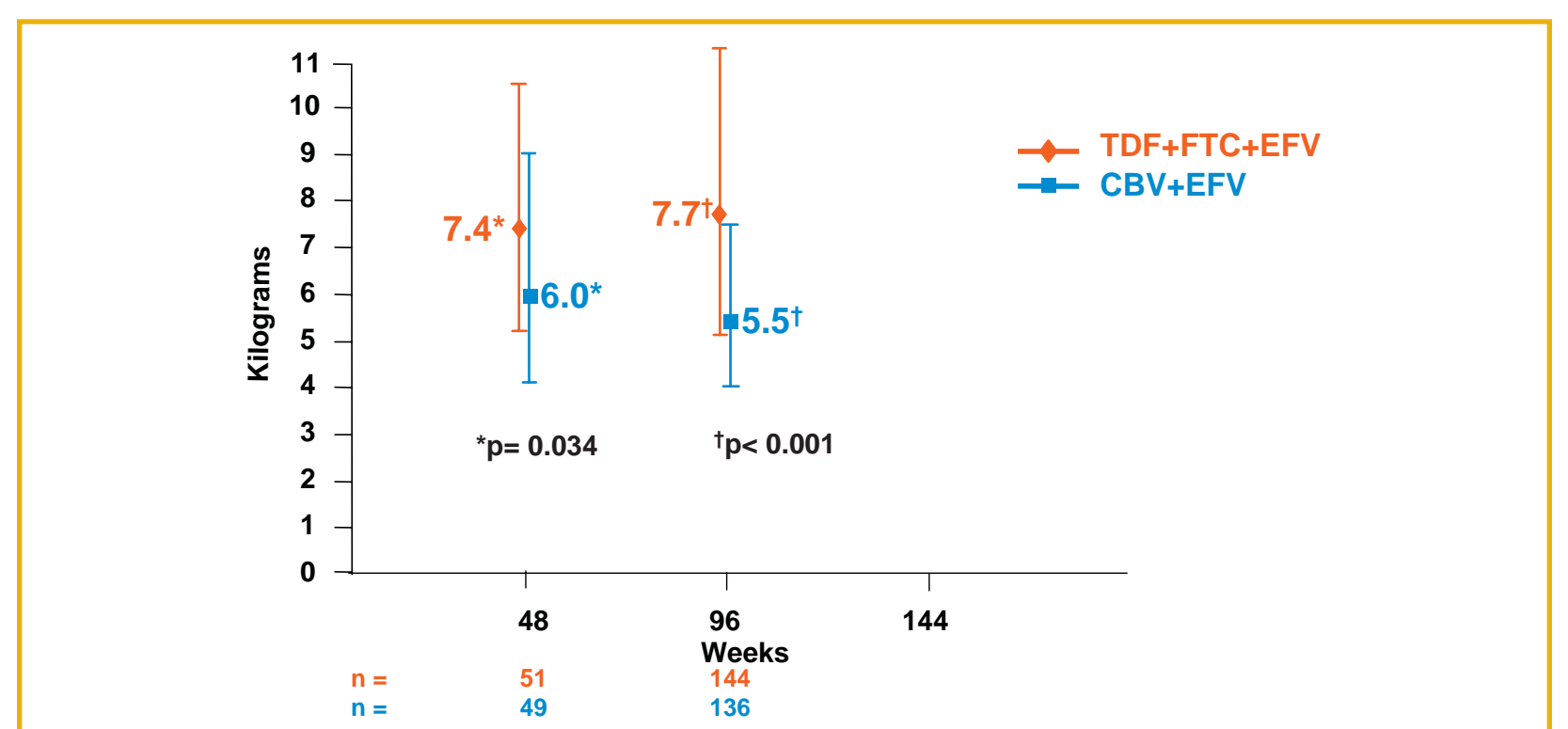
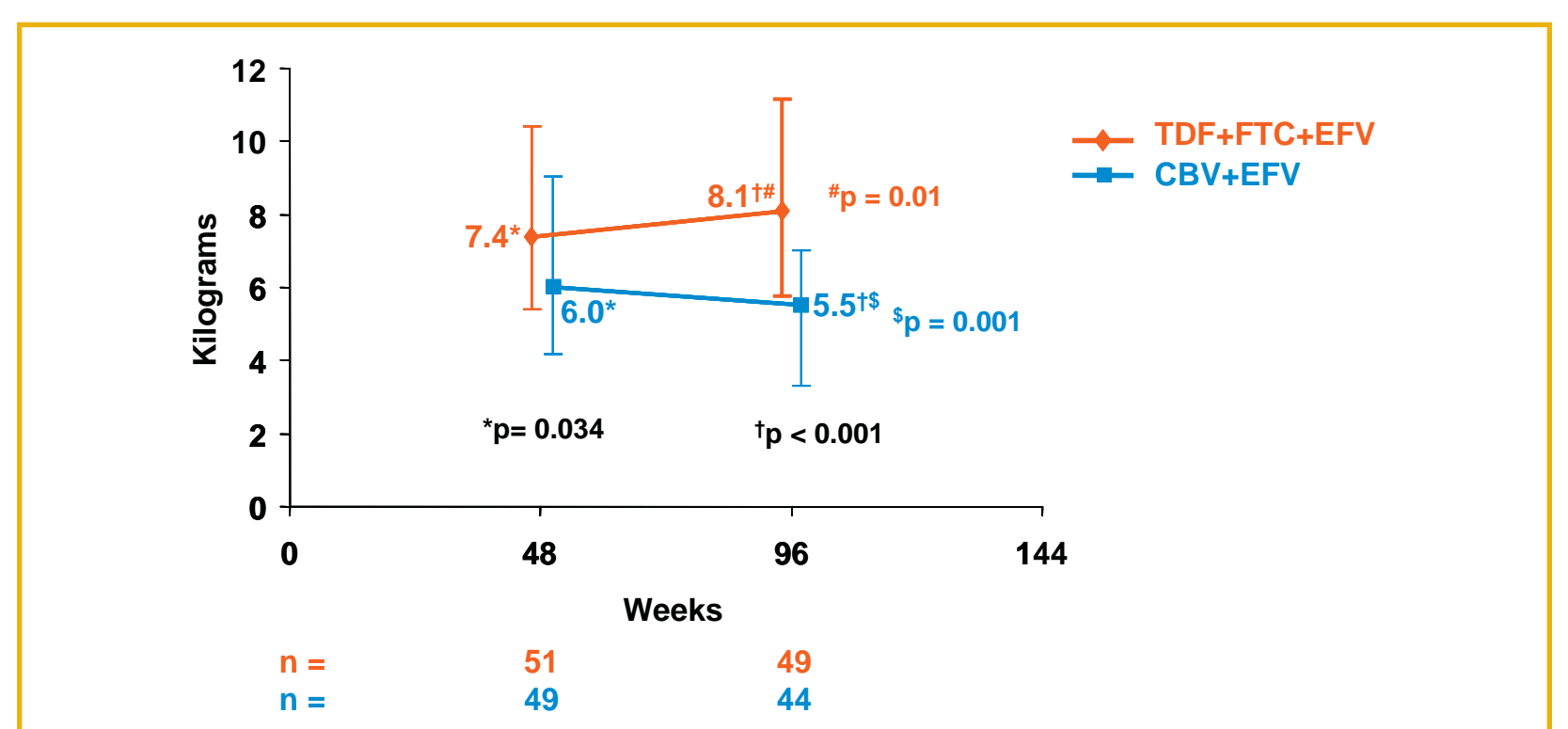


Figure 8. Median (Q1, Q3) Total Limb Fat at Week 96 for Patients with Week 48 Data



Conclusions

- The TDF+FTC+EFV arm was associated with significantly greater virologic suppression to HIV RNA < 400 c/mL and a greater increase in CD4 cell count
- Renal function remained stable through 96 weeks. No patient discontinued due to renal adverse events
- Significantly less M184V/I was seen in the TDF+FTC+EFV arm
- No emergence of K65R mutation was demonstrated
- Significantly higher limb fat was seen in TDF+FTC+EFV arm compared to CBV+EFV arm
 - In a subset of patients with Week 48 and 96 data, a significant median decrease in limb fat was seen in the CBV+EFV arm and a significant increase in the TDF+FTC+EFV arm