Poster Number

H-1235

48th Annual ICAAC / IDSA 46th Annual Meeting
October 25-28, 2008
Washington, DC, USA

The 48-Week Efficacy and Safety of Switching to Fixed-Dose Efavirenz/Emtricitabine/Tenofovir DF in HIV-1-Infected Patients Receiving HAART

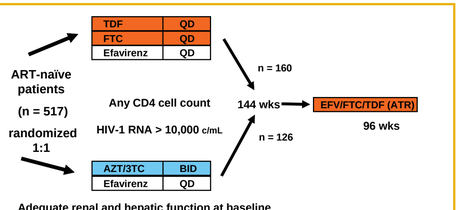
E DeJesus,[1] A Pozniak,[2] J Gallant,[3] J Arribas,[4] Y Zhou,[5] A Cheng,[5] and J Enejosa[5]

[1]Orlando Immunology Center, FL; [2]Chelsea & Westminster Hosp, London, UK; [3]Johns Hopkins Univ, Baltimore, MD;
[4]Univ Hosp La Paz, Madrid, Spain; [5]Gilead Sciences, Inc., Foster City, CA, USA

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

Background / Methods

Figure 1. Study Design



- Study 934 is a 144-week randomized trial comparing the safety and efficacy of emtricitabine/tenofovir DF (TVD) or the individual components versus lamivudine/zidovudine (CBV) both in combination with efavirenz (EFV) in treatment-naïve patients
- After completing 144 weeks, patients in both arms were given the option to switch their antiretroviral regimen to the fixed-dose combination efavirenz/emtricitabine/tenofovir DF (ATR) once daily taken on an empty stomach, preferably at bedtime
- Results after 48 weeks of follow-up post-switch are presented

Results

Table 1. Demographic and Disease Characteristics (At Time of Switch)

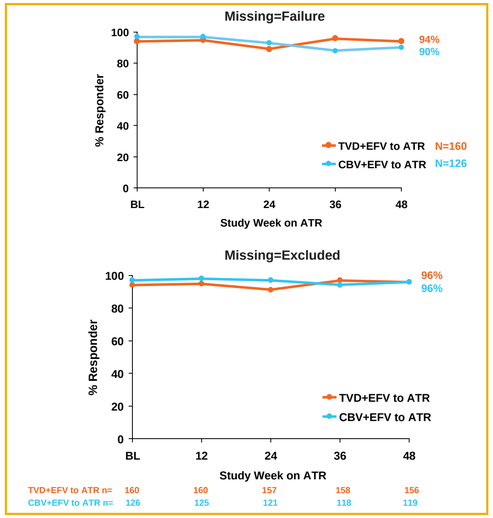
	TVD+EFV to ATR (n = 160)	CBV+EFV to ATR (n = 126)
Age[a]	40	39
Female	11%	13%
White	64%	67%
Black	21%	13%
Hispanic	12%	16%
HIV-1 RNA <400 copies/mL	99%	99%
HIV-1 RNA <50 copies/mL	94%	97%
CD4+ (cells/mm^3)[a]	534	500

a. Median values

- 12 patients discontinued study prior to Week 48 (post-switch)
  - 1 patient died from cardiac arrest due to cardiac dysfunction assessed as unrelated to study drug
  - 1 patient experienced virologic failure
    - Had unconfirmed HIV-1 RNA >400 copies/mL prior to switch (Week 144 on CBV+EFV), subsequently achieving <50 copies/mL after switch; virologic rebound demonstrated 36 weeks after switch
    - Resistance testing showed M184V, K103N prior to switch; at failure: K65K/R, K70K/E, M184V, K103N
  - 2 patients discontinued due to adverse events (MAC and anal cancer, both assessed as unrelated to study drug)
  - 8 patients either withdrew consent, were lost to follow-up or discontinued for other reasons

Results (cont'd)

Figure 2. Proportion with HIV-1 RNA <50 copies/mL



Change in CD4 Cell Counts

- 48 weeks after switch, mean CD4 count increased +1 cells/mm^3 and +21 cells/mm^3 in patients switching from TVD+EFV and CBV+EFV, respectively

Table 2. Most Frequent Treatment-Related Adverse Events[a]

	TVD+EFV to ATR (n = 160)	CBV+EFV to ATR (n = 126)
Any Adverse Event	9 (6%)	18 (14%)
Diarrhea	2 (1%)	3 (2%)
Dizziness	1 (<1%)	3 (2%)
Nausea	1 (<1%)	2 (2%)
Headache	1 (<1%)	2 (2%)
Sleep disorder	1 (<1%)	2 (2%)
Nightmare	0	2 (2%)
Insomnia	0	2 (2%)

a. Occurring in >1 subject in either arm; Subjects may have more than 1 AE

- All AEs were ≤ Grade 2 in severity
- None of these adverse events resulted in study discontinuation

Figure 3. Median (IQR) Change Fasting Total Cholesterol through Week 48 (Post-Switch)

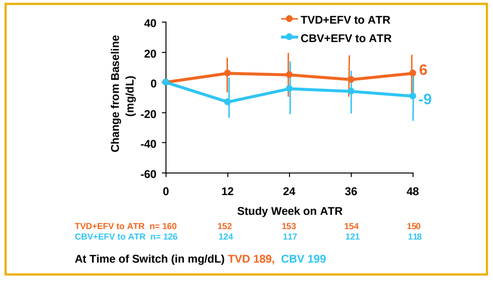


Figure 4. Median (IQR) Change Fasting LDL through Week 48 (Post-Switch)

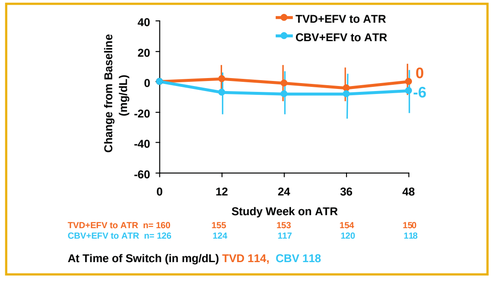


Figure 5. Median (IQR) Change Fasting HDL through Week 48 (Post-Switch)

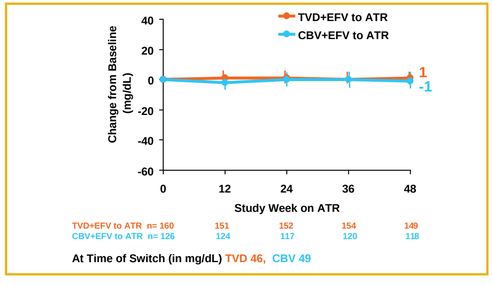


Figure 6. Median (IQR) Change Fasting Triglycerides through Week 48 (Post-Switch)

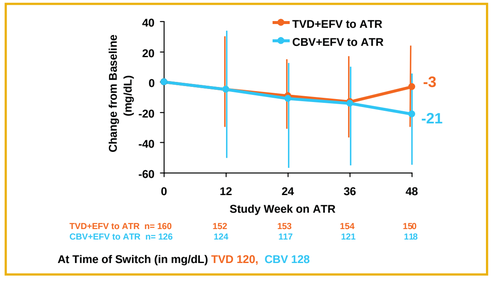
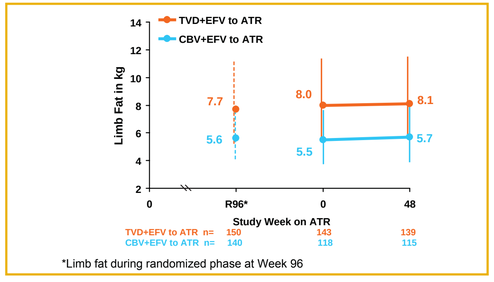


Figure 7. Median (IQR) Total Limb Fat in kg through Week 48 (Post-Switch)



*Limb fat during randomized phase at Week 96

Table 3. Serum Creatinine through Week 48 (Post-Switch)

Maximum Confirmed Toxicity Grade (mg/dL)[a]	TVD+EFV to ATR (n = 160)	CBV+EFV to ATR (n = 126)
1 (>1.5 - 2.0)	0	1 (<1%)
2 (2.1 - 3.0)	0	0
3 (3.1 - 6.0)	0	0
4 (>6.0)	0	0

a. Confirmed toxicity grade = two consecutive visits

Table 4. Serum Phosphorus through Week 48 (Post-Switch)

Maximum Confirmed Toxicity Grade (mg/dL)[a]	TVD+EFV to ATR (n = 160)	CBV+EFV to ATR (n = 126)
1 (2.0 - <2.2)	0	1 (<1%)
2 (1.5-1.9)	0	1 (<1%)
3 (1.0-1.4)	0	0
4 (<1.0)	0	0

a. Confirmed toxicity grade = two consecutive visits

Figure 8. Median (IQR) Estimated GFR by Cockcroft-Gault (mL/min) through Week 48 (Post-Switch)

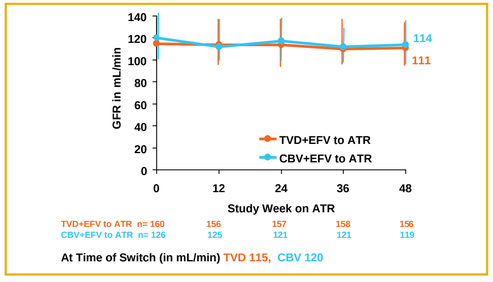
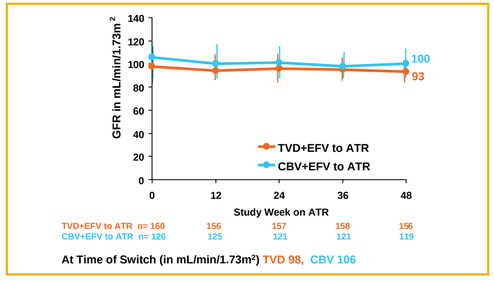


Figure 9. Median (IQR) Estimated GFR by MDRD (mL/min/1.73m^2) through Week 48 (Post-Switch)



Conclusions

- In patients receiving HAART for 144 weeks, virologic suppression was maintained 48 weeks after switching from TVD+EFV or CBV+EFV to a single tablet once-daily regimen of EFV/FTC/TDF (ATR)
- Decreases in fasting triglycerides and fasting cholesterol were seen 48 weeks after switching from CBV+EFV to ATR
- Limb fat prior to switch was significantly lower in CBV+EFV recipients, and no relevant changes were seen 48 weeks after switching from CBV+EFV to ATR
- Renal function remained stable through 48 weeks post-switch