



## OPEN-LABEL EXTENSION WEEK 96 INTERIM CLINICAL STUDY REPORT

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**Study Title:** A Phase 3, Randomized, Double-Blind, Multicenter Study of the Treatment of Antiretroviral-Naive, HIV-1-Infected Patients Comparing Tenofovir Disoproxil Fumarate Administered in Combination with Lamivudine and Efavirenz Versus Stavudine, Lamivudine, and Efavirenz

**Name of Test Drug:** Tenofovir Disoproxil Fumarate

**Indication:** HIV-1

**Sponsor:** Gilead Sciences, Inc.  
333 Lakeside Drive  
Foster City, CA 94404  
USA

**Study No.:** GS-99-903 (Open-Label Extension)

**Phase of Development:** Phase 3

**IND No.:** 52,849  
**EudraCT No.:** Not applicable

**Study Start Date:** 9 June 2000 (First Patient Enrolled)  
**Study End Date:** 7 December 2005 (Last Subject Observation for Open-Label Extension)

**Principal or Coordinating Investigator:** Name: José Valdez Madruga, MD  
Affiliation: AIDS Reference and Training Center  
São Paulo, Brazil

**Gilead Responsible Medical Monitor:** Name: Jeff Enejosa, MD

**Report Date:** 12 July 2006

**Previous Report Date(s):** 19 August 2002, 19 April 2004

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**CONFIDENTIAL AND PROPRIETARY INFORMATION**

This study was performed in compliance with the guidelines of Good Clinical Practice,  
including archiving of essential documents.

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## STUDY SYNOPSIS

**Gilead Sciences, Inc.**  
**333 Lakeside Drive**  
**Foster City, CA 94404**  
**USA**

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**Title of Study:** A Phase 3, Randomized, Double-Blind, Multicenter Study of the Treatment of Antiretroviral-Naïve, HIV-1-Infected Patients Comparing Tenofovir Disoproxil Fumarate Administered in Combination with Lamivudine and Efavirenz Versus Stavudine, Lamivudine, and Efavirenz

**Investigators:** Multicenter

**Study Centers:**

Open-Label Phase: 13 centers in Argentina, Brazil, and Dominican Republic

**Publications:**

Cassetti I, Madruga J, Suleiman J, Zhong L, Enejosa J, Cheng A. Tenofovir DF (TDF) in Combination with Lamivudine (3TC) and Efavirenz (EFV) in Antiretroviral-Naïve HIV-Infected Patients: A 4-Year Follow-Up. [poster]. 3rd IAS Conference on HIV Pathogenesis and Treatment; 2005 July 24–27; Rio de Janeiro, Brazil. Poster Number WePe6.3C05.

Cassetti, I., Madruga JVR., Suleiman, JMAH., Zhong, L., Cheng, AK. Tenofovir DF (TDF) in combination with lamivudine (3TC) and efavirenz (EFV) in antiretroviral-naïve HIV-infected patients: 4-year follow-up. [abstract]. 3rd IAS Conference on HIV Pathogenesis and Treatment; 2005 July 24–27; Rio de Janeiro, Brazil.

De Ruiter A, Pozniak A, Staszewski S, Gallant J, Yale K, Lu B, Enejosa J, Cheng A. Long-term safety and efficacy of tenofovir DF (TDF) versus stavudine (d4T) in combination with lamivudine (3TC) and efavirenz (EFV) in antiretroviral-naïve women: 144-week results. XV International AIDS Conference, Bangkok, Thailand, July 11–16, 2004; Abstract MoOrB1083.

Dore G, Cooper D, Pozniak A, Sayre J, Lu B, Enejosa J, Cheng A. Anti-Hepatitis B Virus (HBV) activity in HBV/HIV co-infected patients treated with tenofovir DF (TDF) and lamivudine (LAM) versus LAM alone: 144-week follow-up. XV International AIDS Conference, Bangkok, Thailand, July 11–16, 2004; Abstract MoPeB3308.

Dore GJ, Cooper DA, Pozniak AL, DeJesus E, Zhong L, Miller MD, et al. Efficacy of tenofovir Disoproxil fumarate in antiretroviral therapy-naïve and -experienced patients coinfecting with HIV-1 and hepatitis B virus. *J Infect Dis* 2004; Apr 1;189 (7):1185-92.

## STUDY SYNOPSIS (CONTINUED)

### Publications: (continued)

Enejosa J, Zhong L, and Cheng AK for the 903E Study Team. Tenofovir DF (TDF) in Combination with Lamivudine (3TC) and Efavirenz (EFV) in Antiretroviral-Naïve HIV-Infected Patients: a 4-Year Follow-Up. 10th European AIDS Conference (EACS); 2005 November 17–20; Dublin, Ireland. Poster Number PE7.3/13.

Gallant J, Pozniak AL, Staszewski S, Lu B, Sayre J, Cheng A, et al. 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 [poster]. 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy; 2003 September 14–17; Chicago, Ill. Poster Number H-840

Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Suleiman JMAH, Miller M, Coakley DF, Lu B, Toole JJ and Cheng AK. Efficacy and Safety of Tenofovir DF vs Stavudine in Combination Therapy in Antiretroviral-Naive Patients A 3-Year Randomized Trial. JAMA 2004 July 14; 292 (2): 191-201.

Gallant JE, Staszewski S, Pozniak AL, DeJesus E, Lu B, Enejosa J, and Cheng A. Similar Renal Safety Profile Between Tenofovir DF (TDF) and Stavudine (d4T) Using Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault (CG) Estimation of Glomerular Filtration Rate (GFR) in Antiretroviral-Naïve Patients Through 144 Weeks. [poster]. 45th Interscience Conference on Antimicrobial Agents and Chemotherapy; 2005 December 16–19; Washington, DC.

Havlir DV, Strain M, Miller MD, Ignacio C, Lu B, Wong J, et al. HIV DNA as a predictor of residual viraemia in patients treated with tenofovir+lamivudine+efavirenz or stavudine+lamivudine+efavirenz [abstract]. Antivir Ther 2003;8 (Suppl 1):S66. Abstract 59.

Madruca J, Cassetti I, Suleiman J, Zhong L, Enejosa J, Cheng A. Improvement in Lipoatrophy and Lipid Abnormalities Following Switch from Stavudine (d4T) to Tenofovir DF (TDF) in Combination with Lamivudine (3TC) and Efavirenz (EFV) in HIV-Infected Patients: a 48-Week Follow-Up from Study 903E. [poster]. 3rd IAS Conference on HIV Pathogenesis and Treatment; 2005 July 24–27; Rio de Janeiro, Brazil. Poster Number TuPe2.B12.

McGowan I, Cheng A, Coleman S, Johnson A, Genant H. Assessment of bone mineral density (BMD) in HIV-infected antiretroviral treatment naive patients [poster]. 8th Conference on Retroviruses and Opportunistic Infections; 2001 February 4–8; Chicago, Ill. Poster Number 628.

Miller MD, Margot NA, McColl DJ, Tran S, Coakley DF, Cheng AK. Genotypic and phenotypic characterization of virologic failure through 48 weeks among treatment-naive patients taking tenofovir DF or stavudine in combination with lamivudine and efavirenz. In: Abstracts of the 6th International Congress on Drug Therapy in HIV Infection; 2002 Nov 17–21; Glasgow, UK. Abstract P205.

## STUDY SYNOPSIS (CONTINUED)

### Publications: (continued)

Miller MD, Margot NA, McColl DJ, Coakley DF, Cheng AK. Characterization of virologic failure through 96 weeks among treatment-naïve patients taking tenofovir DF (TDF) or stavudine (d4T) in combination with lamivudine (3TC) and efavirenz (EFV) [poster]. 2nd International AIDS Society Conference on HIV Pathogenesis and Treatment; 2003 July 13–16; Paris, France. Poster Number 553.

Pozniak AL, Staszewski S, Gallant J, Suleiman JMAH, DeJesus E, Lazzarin A, et al. Comparison of the efficacy and safety of tenofovir disoproxil fumarate (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in HIV-1 infected patients naive to antiretroviral therapy (ART) after 48 weeks of treatment (Study 903) [poster]. Sixth International Congress on Drug Therapy in HIV Infection; 2002 November 17–21; Glasgow, United Kingdom.

Pozniak AL, Gallant JE, Staszewski S, Suleiman JMAH, DeJesus E, Lu B, et al. Similar 96-week efficacy profile regardless of baseline characteristic variable for tenofovir disoproxil fumarate (TDF) versus stavudine (d4T) when used in combination with lamivudine and efavirenz in antiretroviral naive patients [abstract]. *Antivir Ther* 2003;8 (Suppl 1):S335. Abstract 559.

Pozniak A, Staszewski S, Gallant J, Lu B, Yale K, Enejosa J, Cheng A. Liver transaminase changes in Hepatitis C (HCV)/HIV co-infected antiretroviral-naïve patients treated with tenofovir DF (TDF) versus stavudine (d4T) in combination with lamivudine (3TC) and efavirenz (EFV). XV International AIDS Conference, Bangkok, Thailand, July 11–16, 2004; Abstract MoPeB3307.

Pozniak A, Gallant J, Staszewski S, Lu B, Yale K, Miller M, Enejosa J, Cheng A. Long-term efficacy and safety of tenofovir DF (TDF): a 144-week comparison versus stavudine (d4T) in antiretroviral naïve patients. 7th International Congress on Drug Therapy in HIV Infection, Glasgow, UK, November 14–18, 2004; Poster 130.

Pozniak A, Gallant JE, DeJesus E, Lu B, Enejosa J, Cheng A. The safety and efficacy of tenofovir DF (TDF) versus stavudine (d4T) in combination with lamivudine (3TC) and efavirenz (EFV) in hepatitis C (HCV)/HIV co-infected antiretroviral-naïve patients [poster number 22]. 2nd International Workshop on HIV and Hepatitis Co-infection; 2006 January 12–14; Amsterdam, The Netherlands.

Staszewski S, Gallant JE, Pozniak AL, Suleiman JMAH, DeJesus E, Sayre J, et al. Efficacy and safety of tenofovir DF vs. stavudine when used in combination with lamivudine and efavirenz in antiretroviral naive patients: 96-week preliminary interim results [poster]. 10th Conference on Retroviruses and Opportunistic Infections; 2003 February 10–14; Boston, Mass, USA. Poster Number 564b.

## STUDY SYNOPSIS (CONTINUED)

### Publications: (continued)

Staszewski S, Gallant J, Pozniak AL, Suleiman JMAH, DeJesus E, Koenig E, et al. Efficacy and safety of tenofovir disoproxil fumarate (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in HIV-1 infected patients naive to antiretroviral therapy (ART): 48-week interim results [poster/oral presentation]. XIV International AIDS Conference; 2002 July 7–12; Barcelona, Spain. Abstract Number 17.

Staszewski S, Gallant JE, Pozniak AL, Suleiman JMAH, DeJesus E, Lu B, et al. Favorable metabolic profile for tenofovir disoproxil fumarate (TDF) versus stavudine (d4T) when used in combination with lamivudine and efavirenz in antiretroviral naive patients: 96-week interim results [abstract]. 2nd International AIDS Society Conference on HIV Pathogenesis and Treatment; 2003 July 13–16; Paris, France.

Staszewski S, Gallant J, Pozniak A, Yale K, Lu B, Enejosa J, Cheng A. Three-year analysis of the renal safety of tenofovir DF (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in antiretroviral naïve patients. XV International AIDS Conference, Bangkok, Thailand, July 11–16, 2004; Abstract WePeB5917.

Staszewski S, Pozniak AL, Lu B, Cotton G, Enejosa J, Cheng AK. Similar Renal Safety Profile Between Tenofovir DF (TDF) and Stavudine (d4T) Using Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault (CG) Estimation of Glomerular Filtration Rate (GFR) in Antiretroviral-Naïve Patients Through 144 Weeks [poster]. 7th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 2005 November 13-16; Dublin, Ireland. Poster Number 93.

Staszewski S, Pozniak AL, Lu B, Enejosa J, and Cheng A for the 903 Study Team. Similar Renal Safety Profile Between Tenofovir DF (TDF) and Stavudine (d4T) Using Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault (CG) Estimation of Glomerular Filtration Rate (GFR) in Antiretroviral-Naïve Patients Through 144 Weeks. 10th European AIDS Conference (EACS); 2005 November 17–20; Dublin, Ireland. Poster Number PE9.7/10.

Suleiman, J., Lu, B., Enejosa, J., and Cheng, A. Improvement in Lipid Parameters Associated with Substitution of Stavudine (d4T) to Tenofovir DF (TDF) in HIV-Infected Patients Participating in GS 903. [poster]. 44th Interscience Conference on Antimicrobial Agents and Chemotherapy; 2004 October 30–November 2; Washington, DC. Poster H-158.

Tam J, Zhong L, Ho V, Enejosa J, Cheng A, for the Study 903E Team. Improvement in lipoatrophy and lipid abnormalities following switch from stavudine (d4T) to tenofovir DF (TDF) in combination with lamivudine (3TC) and efavirenz (EFV) in HIV-infected patients: A 48 week follow up from Study 903E. [poster]. Treatment and Management of HIV Infection in the United States Conference; 2005 September 15–18; Atlanta, GA.

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**STUDY SYNOPSIS (CONTINUED)**

**Publications: (continued)**

Zhong L., Cotton G., Enejosa J., Cheng A. Improvement in Lipoatrophy and Lipid Abnormalities Following Switch from Stavudine (d4T) to Tenofovir DF (TDF) in Combination with Lamivudine (3TC) and Efavirenz (EFV) in HIV-Infected Patients: a 48-Week Follow-Up from Study 903E. [poster]. 7th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 2005 November 13–16; Dublin Ireland. Poster Number 64.

Zhong L., Enejosa J., Cheng A. Improvement in Lipoatrophy and Lipid Abnormalities Following Switch from Stavudine (d4T) to Tenofovir DF (TDF) in Combination with Lamivudine (3TC) and Efavirenz (EFV) in HIV-Infected Patients: a 48-Week Follow-Up from Study 903E. [poster]. 10th European AIDS Conference (EACS); 2005 November 17–20; Dublin, Ireland. Poster Number PE9.3/5.

**Study Period:**

9 June 2000 (First patient enrolled)

7 December 2005 (Last subject observation for 96-week interim analysis of open-label extension phase)

**Phase of Development:** Phase 3

**Objectives:**

The primary objective of this study was as follows:

- To assess the equivalence of tenofovir DF plus lamivudine plus efavirenz versus stavudine plus lamivudine plus efavirenz in the treatment of HIV-1-infected antiretroviral-naïve patients as determined by the proportion of patients in each regimen with plasma HIV-1 RNA levels < 400 copies/mL at Week 48.

The secondary objectives of this study were as follows:

- To assess the equivalence of the two treatment regimens with respect to the ability to achieve HIV-1 RNA levels < 50 copies/mL at Week 48.
- To compare the safety, efficacy, and tolerability of the two treatment regimens through 144 weeks of drug exposure.
- To evaluate the long-term efficacy, safety, and tolerability of tenofovir DF in combination with lamivudine and efavirenz through approximately 336 weeks of drug exposure.

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**STUDY SYNOPSIS (CONTINUED)**

**Methodology:**

Open-Label Phase: At selected sites, the blinded phase of the study was followed by an open-label phase starting at each patient's Unblinding Visit, for those patients who remained on blinded study drugs at the time of unblinding. These patients rolled over into a protocol extension, and tenofovir DF, lamivudine, and efavirenz were provided. The same visit schedule used in the third year of the blinded phase was followed. The open-label phase was extended twice for a total of 192 weeks of open-label treatment.

**Number of Subjects (Planned and Analyzed):**

Open-Label Phase:  
Planned: 180 patients  
Analyzed: 171

**Diagnosis and Main Criteria for Inclusion:** Antiretroviral-naive, HIV-1-infected patients with plasma HIV-1 levels > 5,000 copies/mL at screening.

**Duration of Treatment:**

Open-Label Phase: 192 weeks

**Test Product, Dose, Mode of Administration, and Batch No.:**

Open-Label Phase: Tenofovir DF 300 mg tablets QD, lamivudine 300 mg (two 150 mg tablets) QD, efavirenz 600 mg tablets QD, all for oral administration; nevirapine (NVP) 200 mg PO BID, was provided for patients who had it substituted for efavirenz prior to unblinding, due to EFV-associated CNS toxicity or rash. In addition, patients received calcium supplementation, containing 630 mg of elemental calcium (as calcium citrate) and vitamin D 400 IU, PO QD (as Citracal).

Tenofovir DF batch numbers: J201B1, J205B2, J305B1, J307B2

Lamivudine batch numbers: B10108, B11544, B12955, B14031, B104263B, B110001A, B068575-1, B068575-6, B071994, B079075+, B136886&, B138166G, R174770A, R168054B, R159439V

Efavirenz batch numbers: 420LC, 936LD, 20NC, 407LC, 407LF, 407LG, 642LA, 949LD, R361MA, 339LA, 949LJ, H237, TP176A, 529PB, 87PC, J440

Nevirapine batch numbers: S0463, S0600, T0433, S0317A, T0239, T0520, T0966

Citracal batch numbers: 3G102, 3K132, 4G054, 4J108, 5F021

**Reference Therapy, Dose, Mode of Administration, and Batch No.:**

Open-Label Phase: Not applicable

## STUDY SYNOPSIS (CONTINUED)

### Criteria for Evaluation:

**Efficacy:** The primary endpoint was the proportion of patients with HIV-1 RNA levels < 400 copies/mL at Week 48. The secondary endpoints included the proportion of patients with HIV-1 RNA levels < 400 copies/mL and < 50 copies/mL; the change in HIV-1 RNA levels and CD4 cell count from baseline; and the proportion of patients with virologic failure.

Endpoints for the open-label Week 96 (Week 240 for the TDF/TDF group) analyses are the proportion of patients achieving and maintaining HIV-1 RNA levels < 400 copies/mL and < 50 copies/mL, change from baseline (double-blind and open-label baselines for TDF/TDF and d4T/TDF patients, respectively) in CD4 cell count, time to loss of virologic response (TLOVR), and time to pure virologic failure.

**Safety:** Adverse events, clinical laboratory tests, bone densitometry, whole-body DXA scan.

Open-Label Phase: Laboratory analyses every 12 weeks after unblinding until open-label Week 192. Bone densitometry was obtained at unblinding (if not performed within 1 month before unblinding) and every 24 weeks thereafter until open-label Week 192. Whole-body composition DXA, if performed during the Blinded Phase, was obtained at unblinding (if not performed within 1 month before unblinding) and every 48 weeks thereafter until open-label Week 192.

### Statistical Methods:

**Efficacy:** The results of the primary endpoint analysis (achievement of HIV-1 RNA < 400 copies/mL at Week 48) have been previously described in both the 48-week and 144-week Clinical Study Reports and are not repeated in this interim open-label phase study report. Analyses of secondary efficacy endpoints for the open-label phase were summarized for this report using descriptive statistics.

**Safety:** Safety analyses were performed using the safety population. Incidence of adverse events was summarized by treatment group, body system, preferred term, maximum severity, and relationship to study drug. Incidence of laboratory toxicity was summarized by treatment group and maximum severity.

### SUMMARY – OPEN-LABEL EXTENSION WEEK 96 RESULTS:

A total of 86 patients who had originally been randomized to tenofovir DF in the double-blind phase of Study 99-903 continued on open-label treatment in the extension phase (the TDF/TDF group). Of patients who had originally been randomized to stavudine in the double-blind phase, 85 started treatment with tenofovir DF in the open-label phase (the d4T/TDF group). As of Week 96 of the open-label phase, 9 TDF/TDF patients and 2 d4T/TDF patients had discontinued study.

Data are presented in this report only for patients who rolled over into the open-label extension phase. In addition, this report focuses on data related to tenofovir DF treatment; therefore, data are principally presented for the double-blind and open-label phases of the study for the TDF/TDF group and for the open-label phase only for the d4T/TDF group.

## STUDY SYNOPSIS (CONTINUED)

### **Efficacy Results:**

In HIV-infected, antiretroviral-naïve patients, the regimen of tenofovir DF + lamivudine + efavirenz demonstrated potent and durable efficacy through a mean of 248 weeks of treatment. The percentage of patients with plasma HIV-1 RNA concentrations < 400 copies/mL and < 50 copies/mL at Week 240 was 87% (75 of 86 patients) and 83% (71 of 86), respectively.

Virologic response was maintained in patients who switched from stavudine + lamivudine + efavirenz to tenofovir DF + lamivudine + efavirenz through a mean of 99 weeks of open-label treatment. The percentage of patients with plasma HIV-1 RNA concentrations < 400 copies/mL and < 50 copies/mL at open-label Week 96 was 95% (81 of 85 patients) and 91% (77 of 85), respectively.

Two patients in the TDF/TDF group discontinued due to virologic failure. No patients who switched from stavudine to tenofovir DF experienced virologic failure during open-label treatment. No patients developed the K65R mutation during the open-label extension phase.

CD4 cell counts continued to increase during the open-label phase of the study in the TDF/TDF group (the mean increases from double-blind Baseline at Weeks 144 and 240 were 273 and 421 cells/mm<sup>3</sup>, respectively). Following switch from stavudine to open-label tenofovir DF, patients in the d4T/TDF group demonstrated continued improvement in CD4 cell count during the open-label phase (the mean increase from open-label Baseline at open-label Week 96 was 118 cells/mm<sup>3</sup>).

**Safety Results:** The mean number of weeks on tenofovir DF was 248.4 ± 19.82 weeks for the patients in the TDF/TDF group and 98.7 ± 12.80 weeks for patients in the d4T/TDF group.

All patients in the TDF/TDF group and most patients in the d4T/TDF group experienced at least one adverse event; most AEs were mild to moderate in severity and did not lead to treatment discontinuation.

No deaths were reported during the open-label phase of the study.

SAEs were generally consistent with those that might be expected in a study population consisting of HIV-infected patients receiving multiple concomitant medications. Only one SAE that was assessed as possibly/probably related to tenofovir DF was reported in each treatment group (gynecomastia in the TDF/TDF group and rhabdomyolysis in the d4T/TDF group). No patients in either group had an SAE of renal failure or renal insufficiency. One patient in the TDF/TDF group was discontinued from treatment during the open-label phase due to increased, but asymptomatic, serum amylase and lipase.

There was no evidence of a tenofovir DF effect on renal function; no patients in either group discontinued treatment due to renal adverse events; and no Fanconi syndrome or tubulopathy was reported in either group.

### STUDY SYNOPSIS (CONTINUED)

Fractures occurred in 2 patients in the open-label phase (one in each group); both were trauma related and were assessed as not related to tenofovir DF.

The results of BMD monitoring demonstrated small changes from baseline at the lumbar spine and hip through a mean of 248 weeks of double-blind and open-label treatment with tenofovir DF. The majority of the change occurred in the first 24–48 weeks of the study with little or no progression in loss of BMD for the remainder of the treatment period through Week 240. Mean changes in spine and hip BMD were -1.5% and -2.7% at Week 240 for patients in the TDF/TDF group and -0.7% and -2.8% at open-label Week 96 for patients in the d4T/TDF group. Calcium and vitamin D supplementation appear to have limited to no impact on bone mineral density during the open-label phase.

During the open-label phase, lipid parameters remained stable for the TDF/TDF group. Statistically significant decreases in triglycerides and total, LDL, and HDL cholesterol were observed from open-label Baseline to open-label Week 96 for the d4T/TDF group.

During the open-label phase, limb fat increased slightly in the TDF/TDF group. A marked increase was observed in the d4T/TDF group after the switch from stavudine to tenofovir DF.

### CONCLUSIONS:

- Tenofovir DF in combination with lamivudine and efavirenz demonstrated potent and durable efficacy through a mean of 248 weeks of treatment. Virologic failure was rare, occurring in only 2 patients in the TDF/TDF arm, with no emergence of K65R through 240 weeks of treatment.
- Switching patients from a regimen of stavudine, lamivudine, and efavirenz to tenofovir DF, lamivudine, and efavirenz was associated with maintained virologic response and no emergence of resistance.
- Tenofovir DF in combination with lamivudine and efavirenz was well tolerated through a mean of 248 weeks of treatment. There was no evidence of any clinically significant toxicity related to the use of tenofovir DF. The renal safety profile remained stable. Small changes in BMD were seen in the first 48 weeks in the TDF/TDF arm which were non-progressive.
- There was a significant improvement in the lipid profile and a marked increase in limb fat of patients who switched from stavudine to tenofovir DF in the open-label phase.