



## FINAL CLINICAL STUDY REPORT

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**Study Title:** SWEET Study – Simplification With Easier Emticitabine and Tenofovir  
A Phase 3, Open Label, Randomized, Parallel Group Study to Compare the Effect on Prevention and Resolution of Treatment Related Adverse Events of a Simplified, Once Daily Regimen of a Fixed Dose Combination Tablet of Emtricitabine and Tenofovir DF Versus Twice Daily Co-formulated Zidovudine and Lamivudine (Combivir<sup>®</sup>) or Zidovudine and Lamivudine, in Virologically Suppressed, HIV Infected Patients Taking Efavirenz.

**Name of Test Drug:** Emtricitabine/Tenofovir disoproxil fumarate

**Dose and Formulation:** Emtricitabine/Tenofovir disoproxil fumarate tablet, 200 mg/300 mg

**Indication:** Human immunodeficiency virus type 1

**Sponsor:** Gilead Sciences Ltd.  
Flowers Building  
Granta Park, Great Abington  
Cambridge, CB21 6GT, United Kingdom

**Study No.:** GS-MC-164-0111

**Phase of Development:** Phase 3

**IND No.:** NA  
**EudraCT No.:** 2004-002254-59

**Study Start Date:** 10 June 2005 (First Subject Screened)  
**Study End Date:** 25 June 2007 (Last Subject Observation)

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**Report Date:** 21 May 2008

### CONFIDENTIAL AND PROPRIETARY INFORMATION

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

## STUDY SYNOPSIS

Gilead Sciences Ltd.  
Flowers Building  
Granta Park, Great Abington  
Cambridge CB21 6GT  
United Kingdom

**Title of Study:** SWEET Study – Simplification With Easier Emtricitabine and Tenofovir

A Phase 3, Open Label, Randomised, Parallel Group Study to Compare the Effect on Prevention and Resolution of Treatment Related Adverse Events of a Simplified, Once Daily Regimen of a Fixed Dose Combination Tablet of Emtricitabine and Tenofovir DF Versus Twice Daily Co-formulated Zidovudine and Lamivudine (Combivir<sup>®</sup>) or Zidovudine and Lamivudine, in Virologically Suppressed, HIV Infected Patients Taking Efavirenz

**Investigators:** Multicenter

**Study Centers:** Multicenter: 23 centers in the United Kingdom and one center in Ireland.

**Publications:**

Moyle G, Fisher M, SWEET Study Group. Switching from Combivir [CBV] (AZT/3TC) to Truvada [TVD] (TDF/FTC) preserves limb fat: results of a DEXA sub-study of a 48 week randomised study [poster N-214] [oral presentation]. 15th Conference on Retroviruses and Opportunistic Infections; 2008 February, 3–6; Boston, USA.

Fisher M, Moyle G, Ebrahimi R, and the SWEET Study Group. Switching from Combivir (CBV, AZT/3TC) to Truvada (TVD, TDF/FTC) maintains viral suppression, prevents and reverses limb fat loss, and improves biochemical parameters: results of a 48 week randomized study [oral #PS5/7]. 11th European AIDS Conference; 2007 October 24-27; Madrid, Spain.

Moyle G, Fisher M, and the SWEET Study Group. A randomized comparison of continued zidovudine plus lamivudine BID (AZT/3TC) versus switching to tenofovir DF plus emtricitabine (FTC/TDF) each plus efavirenz (EFV) in stable HIV infected persons: 48 week study – results of a planned 24 week analysis [poster number WEPEB028]. 4th International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention; 2007 July 22-25; Sydney, Australia.

Moyle G, Fisher M, and the SWEET Study Group. A randomized comparison of continued zidovudine plus lamivudine BID (AZT/3TC) versus switching to tenofovir DF plus emtricitabine (FTC/TDF) each plus efavirenz (EFV) in stable HIV infected persons: 48 week study – results of a planned 24 week analysis [poster number P24]. 9th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 2007 July 19-21; Sydney, Australia.

Moyle G, Fisher M, and the SWEET DEXA Sub-Study Group. Factors associated with low limb fat in a cohort of zidovudine-treated subjects [poster number P12]. 9th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 2007 July 19-21; Sydney, Australia.

**Study Period:**

10JUN2005 (First subject screened)  
25JUN2007 (Last subject observation)

**Phase of Development:** Phase 3

**Objectives:**

The primary objective of this study was:

- To determine if switching from zidovudine plus lamivudine to a fixed-dose tablet of emtricitabine/tenofovir disoproxil fumarate (tenofovir DF) leads to changes in absolute hemoglobin at 24 weeks

The secondary objectives of this study were:

- To determine if switching from zidovudine plus lamivudine to a fixed-dose tablet of emtricitabine/tenofovir DF leads to changes in absolute hemoglobin at 48 weeks
- To determine whether switching from zidovudine plus lamivudine to emtricitabine/tenofovir DF backbone leads to an improvement in lipid profile or a delay in the time to lipid elevation
- To compare the immunological and virological outcomes
- To determine whether emtricitabine/tenofovir DF delays the time to treatment failure by improving virological efficacy, durability, and safety compared to zidovudine plus lamivudine therapy
- To assess the effect of using once daily emtricitabine/tenofovir DF on adherence using the Medication Adherence Self-Report Inventory (MASRI), on acceptability using the HAART (highly active antiretroviral therapy) Intrusiveness Scale (HIS) and Beliefs about Medicines Questionnaire (BMQ), and on quality of life using the Short Form 12 Version 2 (SF-12v2) Health and Well Being questionnaire
- To evaluate the health economics within the study using resource use data and the SF-12v2 Health and Well Being questionnaire

A substudy was included to determine whether therapy simplification with emtricitabine/tenofovir DF leads to improved fat recovery and fat sparing relative to zidovudine-based therapy, as measured by sequential dual energy x-ray absorptiometry (DEXA) scans.

**Methodology:** A Phase 3, open label, multi center, randomized, 48-week comparator study. Subjects receiving an antiretroviral regimen of zidovudine plus lamivudine with efavirenz were randomized in a 1:1 ratio to one of two treatment groups, either to switch the backbone therapy to once daily emtricitabine/tenofovir DF 200 mg/300 mg plus efavirenz 600 mg or to remain on their current twice-daily therapy of zidovudine (250 mg in the UK or 300 mg in Ireland) plus lamivudine (150 mg) plus once daily efavirenz 600 mg.

Subjects received study drug for 48 weeks and were assessed for efficacy and safety at Weeks 4, 12, 24, 36, and 48.

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

Planned: 220 randomized subjects  
Randomized: 250 subjects  
Analyzed: Efficacy 232  
Safety 234

**Diagnosis and Main Criteria for Inclusion:** Adult ( $\geq 18$  years) male and nonpregnant female subjects infected with human immunodeficiency virus (Type 1) (HIV-1) who had been maintained on stable antiretroviral therapy consisting of efavirenz given with zidovudine plus lamivudine for at least 6 months and who had viral loads  $\leq 50$  copies/mL on last two consecutive testings and  $< 400$  copies/mL for  $\geq 3$  months. Subjects requiring a lipid-lowering agent had to be established on a stable dose/frequency for at least 12 weeks prior to baseline and were expected to continue at a stable dose/frequency for the duration of the study.

**Duration of Treatment:** 48 weeks

**Test Product, Dose, Mode of Administration, and Batch No.:** Emtricitabine/tenofovir DF tablet (Truvada<sup>®</sup>) (200 mg/300 mg) taken orally without regard to meals with efavirenz (600 mg) taken orally. Subjects were instructed to take all study drugs once daily at the same time. Batch numbers: Truvada, V303B2, V303B2-A, V406B1, and V503B1; efavirenz was sourced from hospital supplies and batch numbers were not recorded.

**Reference Therapy, Dose, Mode of Administration, and Batch No.:** Zidovudine (250 mg in the UK or 300 mg in Ireland) plus lamivudine (150 mg), or Combivir (zidovudine/lamivudine, 300 mg/150 mg), taken orally twice daily with efavirenz (600 mg) taken orally once daily. Subjects were instructed to continue taking their daily dose of zidovudine plus lamivudine with efavirenz. Batch numbers: Combivir, zidovudine, lamivudine, and efavirenz were sourced from hospital supplies and batch numbers were not recorded.

**Criteria for Evaluation:**

**Efficacy:** Plasma hemoglobin; HIV-1 RNA (viral load) levels; CD4 and CD8 cell counts and percentages. Medication adherence was calculated by the MASRI, medication acceptability was assessed using the HIS and BMQ, and quality of life was assessed using the SF-12v2. Use of resources was also recorded.

**Safety:** Adverse events (AEs), physical examinations, fasting lipid profile, hematology, biochemistry, calculated creatinine clearance, urinalysis; and DEXA scans.

**Statistical Methods:**

**Efficacy:** The primary endpoint of the study was the change from baseline in absolute hemoglobin at Week 24. Hemoglobin change from baseline to Week 24 was calculated and summarized using descriptive statistics and statistical tests. Analysis of the primary endpoint was based on the treated analysis set and the last observed postbaseline value up to Week 24 (i.e., last observation carried forward, LOCF), and compared between treatment groups using the two sample Student t-test. The mean and the 95% confidence intervals (CIs) for changes from baseline and the difference between treatment groups in change from baseline in hemoglobin were reported. The p-value from a one-sample paired t-test for the change from baseline in hemoglobin within each treatment group was also reported. A secondary analysis of the primary endpoint was performed using a missing=excluded analysis using the same statistical method.

Hemoglobin changes from baseline at Week 48 were analyzed using similar methods to those used for the Week 24. A categorical change from baseline in hemoglobin by study visit assessed the number (%) of subjects with non-missing data with changes from baseline of  $> 10$  g/L,  $\geq -10$  to  $\leq 10$  g/L; and  $< -10$  g/L. The Cochran-Mantel Haenszel (CMH) Row Mean Score test was used to compare the categories of change from baseline in hemoglobin between treatment groups.

Binomial efficacy endpoints related to viral load were summarized. Exact 95% CIs were calculated for each endpoint (e.g., the proportion of subjects who maintained virologic response up to Week 48) in each treatment group, and Fisher's Exact test was used to test for differences between treatment groups. The 95% CI for the difference of proportions was calculated based on the normal approximation.

Descriptive statistics were used to summarize continuous measures. For CD4 and CD8 absolute counts, the Wilcoxon Signed Rank test was used to test for changes from baseline within each treatment group. The Wilcoxon Rank Sum test compared the differences in changes from baseline between treatment groups at each visit.

The overall HIS index score, index scores for the utility (N scores) and safety (C scores) components of the BMQ-HAART (for subjects with  $\geq 80\%$  of questions completed) and standardized scores for each of the domains and physical and mental components of the SF-12v2 and the corresponding changes from baseline were summarized as continuous data. The Wilcoxon Signed Rank test was used to assess the change from baseline within a treatment group and the Wilcoxon Rank Sum test was used to assess differences between treatment groups. Absolute values and the change from baseline for re-scaled response scores for each HIS or BMQ-HAART question at each visit were summarized using descriptive statistics. The total number of general practitioner (GP) visits, total number of outpatient visits, and total number of days hospitalized for each subject while on study was summarized by treatment group and compared using the Wilcoxon Rank Sum test. In addition, the number (%) of subjects within each treatment group who had at least one GP visit, at least one outpatient visit, and were hospitalized for at least one day were presented by treatment group, and were tested for differences using Fisher's Exact test.

**Safety:** All safety analyses were based on the treated analysis set and summarized by the actual treatments received using descriptive statistics. Clinical and laboratory AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 10. Statistical tests were performed on a subset of clinical laboratory data (such as fasting lipid profile). The Wilcoxon Rank Sum test was used to compare the difference between treatment groups. The Wilcoxon Signed Rank test was used to assess the change from baseline within each treatment group.

In the treated analysis set with DEXA scans, absolute values at baseline and Week 48 and change from baseline in total grams of limb fat mass, trunk fat, and whole body fat were analyzed. Limb fat mass was calculated as the sum of the limb fat mass for the right arm, left arm, right leg, and left leg. Two-sided 95% CIs for each treatment regimen were presented for the absolute and change from baseline values along with descriptive statistics. Two-sided 95% CIs for the differences in DEXA markers between treatment groups were calculated based on the normal approximation. The changes from baseline at Week 48 in DEXA results were compared between treatment groups using the two sample Student t-test.

#### **SUMMARY – RESULTS:**

Subjects treated in this study were predominantly male (84%, 197 subjects) and had a mean age of 42 years (range 20 to 72 years). Overall, 62% were white (145 subjects), 34% were black (80 subjects), 3% were Asian (seven subjects) and  $< 1\%$  were of other race (two subjects). The two treatment groups had similar demographic characteristics, weight, and hemoglobin levels at baseline.

Median overall adherence was 100% for both groups (MASRI).

**Efficacy Results:** Switching treatment from zidovudine plus lamivudine to emtricitabine/tenofovir DF resulted in increases (improvements) in hemoglobin concentrations in this study. Differences between groups in the change from baseline in absolute hemoglobin were statistically significant at Weeks 24 and 48 when assessed using LOCF or missing = excluded methods (Week 24 difference for emtricitabine/tenofovir DF minus zidovudine plus lamivudine: LOCF 3.7 g/L, 95% CI 1.5 – 5.8 g/L,  $p < 0.001$ ; missing = excluded 3.6 g/L, 95% CI 1.3 – 5.9 g/L,  $p = 0.003$ ). Within groups, there was a statistically significant increase in absolute hemoglobin in the emtricitabine/tenofovir DF group (Week 24:  $4.6 \pm 8.79$  g/L,  $p < 0.001$  [LOCF]), compared to no statistically significant change from baseline in the zidovudine plus lamivudine group (Week 24:  $0.9 \pm 7.83$  g/L,  $p = 0.19$  [LOCF]). At Week 48, more subjects in the emtricitabine/tenofovir DF group (22 subjects, 22%) compared to the zidovudine plus lamivudine group (two subjects, 2%) had increases in absolute hemoglobin that could be considered clinically relevant, i.e.,  $> 10$  g/L; fewer subjects (two subjects, 2%) in the emtricitabine/tenofovir DF group compared to the zidovudine plus lamivudine group (eight subjects, 9%) had decreases in absolute hemoglobin of  $< -10$  g/L.

The majority of subjects in this study maintained virologic control. There were no statistically significant differences between groups in the numbers of subjects with viral load  $< 50$  copies/mL at Weeks 24 or 48. Similarly, there were no statistically significant differences between groups for the numbers of subjects who maintained virologic response during the study (90% of subjects in the emtricitabine/tenofovir DF group and 84% of subjects in the zidovudine plus lamivudine group,  $p = 0.25$ ); one subject ( $< 1\%$ ) in the emtricitabine/tenofovir DF group and five subjects (4%) in the zidovudine plus lamivudine group experienced virologic rebound.

CD4 cell counts were similar in the two treatment groups during the study. Differences between groups for CD4 cell counts were not statistically significant at Week 48; however, the difference between groups in the change from baseline to Week 48 in CD4 cell counts was statistically significant (median changes from baseline: emtricitabine/tenofovir DF group  $-3$  cells/mm<sup>3</sup>, zidovudine plus lamivudine group 33 cells/mm<sup>3</sup>,  $p = 0.003$ ). This statistically significant difference is not considered clinically relevant. When subjects who received any vaccination were excluded from the analysis, the difference between groups in the change from baseline to Week 48 in CD4 cell counts was not statistically significant. CD4 cell percentages and changes from baseline in CD4% were similar for each treatment group throughout the study.

CD8 cell counts were higher in the emtricitabine/tenofovir DF group than in the zidovudine plus lamivudine group at baseline, but were similar in the two treatment groups at the end of the study. The difference between groups in the change from baseline to Week 48 in CD8 cell counts was statistically significant (median change from baseline: emtricitabine/tenofovir DF group  $-102$  cells/mm<sup>3</sup>, zidovudine plus lamivudine group  $-21$  cells/mm<sup>3</sup>,  $p < 0.001$ ). This statistically significant difference is not considered clinically relevant. CD8 cell percentages were similar in each treatment group at the end of the study.

Differences between groups for changes in HIS index scores, BMQ perceived utility scores, and SF-12v2 physical and mental composite scores were not statistically significant during the study. In the emtricitabine/tenofovir DF group, there were small but statistically significant increases (improvements) in HIS index scores during the study. Differences between groups for changes in BMQ perceived safety score were statistically significant at all postbaseline assessments. In the emtricitabine/tenofovir DF group, there was a trend of small improvements (approaching significance) in the BMQ perceived safety index score during the study. In the zidovudine plus lamivudine group there was a statistically significant small worsening in the BMQ perceived safety index score during the study. The impact for subjects of these small changes is yet to be determined. Resource use during the study was similar in the two treatment groups, as assessed by the numbers of general practitioner or outpatient visits, or hospitalizations.

**Safety Results:** No new or unexpected safety findings were reported during the study; emtricitabine/tenofovir DF was well tolerated in this study population of HIV-1 infected subjects.

No deaths occurred during the study. Treatment-emergent SAEs were reported for fewer subjects in the emtricitabine/tenofovir DF group (3%) compared to the zidovudine/lamivudine group (8%). None of the SAEs reported was considered related to study drug. Three subjects (3%) in the emtricitabine/tenofovir DF group and six subjects (5%) in the zidovudine plus lamivudine group experienced treatment-emergent AEs that resulted in permanent discontinuation of study drug. AEs that led to study drug discontinuation were considered related to treatment for two subjects in each treatment group (emtricitabine/tenofovir DF: dizziness, nausea, insomnia, and depression; zidovudine plus lamivudine: atrophy and adverse drug reaction). One pregnancy was reported for a female subject in the emtricitabine/tenofovir DF group; a liveborn infant with no congenital abnormalities was delivered.

Treatment-emergent AEs were reported for 102 of 117 subjects (87%) in the emtricitabine/tenofovir DF group and 94 of 117 subjects (80%) in the zidovudine plus lamivudine group. Gastrointestinal disorders (35% versus 28%), respiratory, thoracic, and mediastinal disorders (21% versus 14%), and skin and subcutaneous tissue disorders (32% versus 24%) were reported more frequently in the emtricitabine/tenofovir DF group compared to the zidovudine plus lamivudine group. Infections and infestations were reported more frequently in the zidovudine plus lamivudine group compared to the emtricitabine/tenofovir DF group (54% versus 48%). The most frequently reported treatment-emergent AEs in the emtricitabine/tenofovir DF group were diarrhea (18%), headache (14%), nasopharyngitis (13%), lower respiratory tract infection (11%), and cough (10%). In the zidovudine plus lamivudine group, the most frequently reported treatment-emergent AEs were nasopharyngitis (17%), headache (12%), diarrhea (11%), and lower respiratory tract infection (10%). Diarrhea (18% versus 11%), nausea (9% versus 4%), and cough (10% versus 3%) were reported more frequently in the emtricitabine/tenofovir DF group compared to the zidovudine plus lamivudine group. Constipation was reported more frequently in the zidovudine plus lamivudine group compared to the emtricitabine/tenofovir DF group (5% versus 0%).

Eight subjects (7%) in each treatment group reported Grade 3 or Grade 4 treatment-emergent AEs. No Grade 3 or 4 treatment-emergent AE was reported for more than one subject, and no Grade 3 or 4 treatment-emergent AE was considered related to study drug by the investigator.

Treatment-emergent AEs considered related to study drug were reported for more subjects in the emtricitabine/tenofovir DF group (25%) than in the zidovudine plus lamivudine group (13%); more subjects in the emtricitabine/tenofovir DF group compared to no subjects in the zidovudine plus lamivudine group experienced gastrointestinal disorders (14%) and psychiatric disorders (5%) that were considered related to study drug.

No renal AEs or fractures considered related to study drug were reported. Skin and subcutaneous tissue disorders that were considered related to study drug were reported for four subjects in the emtricitabine/tenofovir DF group (rash [n = 2], night sweats [n = 1], pruritus [n = 1], and yellow skin [n = 1]) and for four subjects in the zidovudine plus lamivudine group (lipoatrophy [n = 3] and lipohypertrophy [n = 1]).

Among hematology parameters, statistically significant but not clinically relevant decreases in MCV and platelet count and increases in white blood cell counts were observed during the study in the emtricitabine/tenofovir DF group, compared to no changes in the zidovudine/lamivudine group. By Week 48, subjects in the emtricitabine/tenofovir DF group had mean MCV, mean platelet counts, and mean white blood cell counts within the normal range.

No graded serum creatinine abnormalities were reported. No Grade 3 or 4 serum phosphorus abnormalities were reported; similar percentages of subjects in each treatment group had Grade 1 or Grade 2 serum phosphorus abnormalities reported. In the emtricitabine/tenofovir DF group, there were small decreases in creatinine clearance and estimated GFR (median decrease of  $-4.75$  mL/min at Week 48) and estimated GFR (median decrease of  $-0.90$  mL/min/ $1.73$  m<sup>2</sup> at Week 48). Mean values remained within the normal range, and the small changes are not considered of clinical significance.

Treatment with emtricitabine/tenofovir DF resulted in decreases (improvement) in fasting total cholesterol and fasting triglycerides compared to treatment with zidovudine plus lamivudine. Differences between groups in the changes from baseline in fasting total cholesterol and fasting triglycerides were statistically significant at all visits except Week 48. Within groups, there were statistically significant decreases from baseline in fasting total cholesterol and fasting triglycerides at all visits for the emtricitabine/tenofovir DF group, compared to no statistically significant changes from baseline in the zidovudine plus lamivudine group. Changes from baseline for fasting total cholesterol in the emtricitabine/tenofovir DF group were largest at Week 4 (median  $-0.59$  mmol/L), but reduced by visit to Week 48 (median  $-0.22$  mmol/L). Changes from baseline for fasting triglycerides in the emtricitabine/tenofovir DF group were evident at Week 4 and remained relatively stable throughout the study (range of median changes from baseline  $-0.16$  to  $-0.24$  mmol/L [Weeks 36 and 24, respectively]). Overall, differences between groups in changes from baseline in other lipid profile parameters (LDL and HDL cholesterol, ratio of total over HDL cholesterol) were not considered clinically relevant.

Treatment-emergent Grade 3 or 4 laboratory abnormalities were reported more frequently in the zidovudine plus lamivudine group (19 subjects) than in the emtricitabine/tenofovir DF group (six subjects). Treatment-emergent marked laboratory abnormalities were reported more frequently in the zidovudine plus lamivudine group (nine subjects) than in emtricitabine/tenofovir DF group (one subject). The treatment-emergent marked rise in alkaline phosphatase at Week 12 in a subject in the emtricitabine/tenofovir DF group was not reported as an AE.

Differences between groups in the change from baseline to Week 48 in total limb fat mass were statistically significant (mean difference for emtricitabine/tenofovir DF minus zidovudine plus lamivudine: 448 g, 95% CI 57 – 839 g,  $p = 0.025$ ). Subjects in the emtricitabine/tenofovir DF group has modest increases (improvements) in limb fat that approached statistical significance (mean change from baseline 261 g,  $p = 0.054$ ), compared to subjects in the zidovudine plus lamivudine group having modest, statistically nonsignificant decreases in limb fat (mean median change from baseline  $-187$  g,  $p = 0.21$ ). There were no statistically significant differences between or within groups in the changes from baseline to Week 48 in trunk fat or whole body fat.

No clinically relevant changes in body weight or body mass index were recorded in either treatment group.

## CONCLUSIONS:

- Switching treatment from zidovudine plus lamivudine to emtricitabine/tenofovir DF resulted in improvements in hemoglobin concentrations, as indicated by the statistically significant differences between groups in the change from baseline in absolute hemoglobin at Weeks 24 and 48 (Week 24 difference for emtricitabine/tenofovir DF minus zidovudine plus lamivudine: LOCF 3.7 g/L, 95% CI 1.5–5.8 g/L; missing = excluded 3.6 g/L, 95% CI 1.3–5.9 g/L). At Week 48, more subjects in the emtricitabine/tenofovir DF group (22 subjects, 22%) compared to the zidovudine plus lamivudine group (two subjects, 2%) had increases in absolute hemoglobin that could be considered clinically relevant, i.e., > 10 g/L; fewer subjects (two subjects, 2%) in the emtricitabine/tenofovir DF group compared to the zidovudine plus lamivudine group (eight subjects, 9%) had decreases in absolute hemoglobin of < –10 g/L.
- Subjects in both treatment groups maintained virologic suppression and immunologic control.
- Treatment with emtricitabine/tenofovir DF resulted in small improvements (significant or borderline significant) in HIS scores and in the BMQ perceived safety index score during the study; in the zidovudine plus lamivudine group there was a small worsening in the BMQ perceived safety index score during the study. The impact for subjects of these small changes is yet to be determined. There were no apparent effects of emtricitabine/tenofovir DF on treatment adherence (median overall adherence for three days recall across all visits was 100% in both treatment groups) or quality of life.
- Since few subjects failed therapy, time to treatment failure was not assessed.
- Treatment with emtricitabine/tenofovir DF resulted in improvements in lipid profile compared to treatment with zidovudine plus lamivudine, as indicated by decreases in fasting total cholesterol and fasting triglycerides in the emtricitabine/tenofovir DF group.
- Switching from zidovudine plus lamivudine to emtricitabine/tenofovir DF led to a preservation of limb fat, as indicated by the statistically significant difference between groups in the change from baseline to Week 48 in total limb fat mass (mean difference for emtricitabine/tenofovir DF minus zidovudine plus lamivudine: 448 g, 95% CI 57–839 g,  $p = 0.025$ ).