ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 02/22/2013

Peripheral Body Fat Distribution After Switching Zidovudine and Lamivudine to Truvada (RECOMB)

This study has been completed.

Sponsor:	Gilead Sciences
Collaborators:	
Information provided by (Responsible Party):	Gilead Sciences
ClinicalTrials.gov Identifier:	NCT00324649

Purpose

This study evaluated changes in body fat distribution in human immunodeficiency virus type 1 (HIV-1) infected participants who either switched from a zidovudine- plus lamivudine- containing highly active antiretroviral therapy (HAART) regimen to a regimen containing Truvada® (a fixed-dose combination tablet of emtricitabine [FTC, 200 mg] and tenofovir disoproxil fumarate [TDF, 300 mg]) or who remained on a zidovudine- plus lamivudine-containing regimen. Subjects continued their protease inhibitor (PI) or nonnucleoside reverse transcriptase inhibitor (NNRTI).

Condition	Intervention	Phase
HIV-1	Drug: Truvada Drug: Zidovudine/lamivudine	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: Pilot Phase IV, Multicenter, Randomized, Open-label and Controlled Study to Assess the Evolution of Peripheral Body Fat Distribution After Switching From Zidovudine Containing Backbone to Truvada in HIV-1-infected Patients on HAART (RECOMB Study).

Further study details as provided by Gilead Sciences:

Primary Outcome Measure:

- Change From Baseline in Limb Fat at Week 48 [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Limb fat was measured by DEXA. Change = Week 48 value minus baseline value.

Secondary Outcome Measures:

- Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Oral Mucosa) [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Lymphocytes) [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Lactate Concentration [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Percentage of Days for Which Participants Were Compliant With Study Drug [Time Frame: Baseline to Week 72] [Designated as safety issue: No]
  Compliance = [1 - [(sum of days with a missed dose [per Question 6 study medication assessment questionnaire (SMAQ)])/(sum of days between SMAQ visits)]] *100 for visits with SMAQ data. An assessable visit is one where the number of missed days was reported [Question 6] and the number of days between SMAQ visits could be calculated.
- Percentage of Participants Who Maintain Confirmed HIV-1 RNA < 50 Copies/mL [Time Frame: 48 weeks] [Designated as safety issue: No]
- Percentage of Participants With HIV-1 RNA > 50 and < 400 Copies/mL [Time Frame: 48 weeks] [Designated as safety issue: No]
- Percentage of Participants With Virologic Failure [Time Frame: 48 weeks] [Designated as safety issue: No]
  Virologic failure was defined as two consecutive HIV RNA values > 400 copies/mL.
- Change From Baseline in Cluster Determinant 4 (CD4) Cell Count [Time Frame: Baseline to Week 48] [Designated as safety issue: No]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Fasting Serum Triglycerides [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Fasting Total Cholesterol [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Fasting Low Density Lipoprotein Cholesterol (LDL) [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Fasting High Density Lipoprotein Cholesterol (HDL) [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Change From Baseline in Hemoglobin [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Percent Change From Baseline in Hematocrit [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value expressed as median percent change.
- Change From Baseline in Waist Circumference/Hip Circumference Ratio [Time Frame: Baseline to Week 48] [Designated as safety issue: Yes]
  Change = Week 48 value minus baseline value.
- Percentage of Participants With Any Adverse Event [Time Frame: 72 weeks] [Designated as safety issue: Yes]
  Participants with treatment-emergent adverse events were analyzed. Adverse events were defined as any untoward medical occurrence in a clinical investigation subject administered a medicinal product and which did not necessarily have a causal relationship with study treatment, and were categorized using the Medical Dictionary for Regulatory Activities (MedDRA) Version 11. Treatment-emergent adverse events were events that met one of the following criteria: - Began or worsened in severity or relationship to study drug, on or after the date of the first dose of study drug and on or before the date of the last dose of study drug plus 30 days. - Had no recorded start date.
- Percentage of Participants Who Discontinue the Study Prematurely (Before Week 48) Due to Adverse Events. [Time Frame: 48 weeks] [Designated as safety issue: Yes]

Enrollment: 80
Study Start Date: May 2006
Primary Completion Date: March 2008
Study Completion Date: September 2008

Arms	Assigned Interventions
Experimental: Truvada Truvada + NNRTI or PI.	Drug: Truvada Truvada once daily with continuation of the current NNRTI or PI at randomization.
Active Comparator: Zidovudine/lamivudine Zidovudine/lamivudine + NNRTI or PI.	Drug: Zidovudine/lamivudine Continuation of the zidovudine + lamivudine containing regimen plus the current NNRTI or PI at randomization.

Detailed Description:

Standard care for the treatment of HIV infection involves the use of a combination of three antiretroviral drugs. The initial recommended regimen in antiretroviral-naive patients according to therapeutic guidelines of the US Department of Health and Human Resources (DHHS) includes two nucleoside reverse transcriptase inhibitors (NRTIs) and a third drug from another class (PI or NRTI).

The use of nucleoside analogues, especially stavudine and zidovudine, is associated with untoward side effects, including lipodystrophy hepatic steatosis/lactic acidosis syndrome, peripheral neuropathy, and anemia. However, Truvada has a low potential for both mitochondrial toxicity and fat distribution disturbances.

As described in the Consensus Document of the Spanish Group for the Study of AIDS (GESIDA), and the AIDS National Plan from the Spanish Ministry of Health "Recommendations on metabolic alterations and body fat distribution", studies should focus on the evaluation of body fat disturbances after antiretroviral drug substitutions, based on the basic assumption of virologic control of the patient and equivalence in potency of the new drug regarding virological control. In addition, studies based on selective substitution of antiretroviral drugs in HIV-1 infected patients under virological control, are recommended in the European Medicines Agency (EMA) in the "Guideline on the clinical development of medicinal products for the treatment of HIV infection".

In this study, stable, virologically controlled, HIV-1 infected participants receiving antiretroviral regimens containing zidovudine and lamivudine were randomized to switch to Truvada or to stay on their zidovudine- plus lamivudine-containing regimen. Participants in both groups continued the third drug of their antiretroviral regimen (either an NNRTI or PI). Changes in limb fat in the two groups were assessed using dual-energy x-ray absorptiometry (DEXA).

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- HIV-1 infection documented by confirmed positive HIV-1 antibody test and/or positive polymerase chain reaction for HIV-1 ribonucleic acid (RNA).
- Adult patients (over 18 years of age).
- Current HAART regimen containing zidovudine + lamivudine at usual doses for at least 6 months.
- Viral load < 50 copies/mL on the last two consecutive determinations, under zidovudine + lamivudine containing HAART regimen.
- For women of childbearing potential, negative urine pregnancy test at screening visit.
- Agreement to take part in the study and sign the informed consent.

- Patients on lipid lowering treatment were allowed to participate in the study only if the lipid-lowering treatment (either statins or fibrates) was stable for at least 8 weeks prior to screening and it was not expected to change during the first 3 months of the study.

Exclusion Criteria:

- Patients on current FTC or TDF therapy.
- Patients with previous history of virological failure on an FTC or TDF-containing regimen.
- Patients receiving a non-registered antiretroviral drug.
- Patients receiving a triple-nucleoside antiretroviral combination.
- Hypersensitivity to one of the components of the dosage forms of TDF or FTC, or previous history of intolerance to one of those drugs.
- Known history of drug abuse or chronic alcohol consumption
- Women who were pregnant or breast feeding, or female of childbearing potential who did not use an adequate method of contraception according to the investigator's judgment.
- Active opportunistic infection or documented infection within the previous 4 weeks.
- Documented active malignant disease (excluding Kaposi sarcoma limited to the skin).
- Renal disease with creatinine clearance < 50 mL/min.
- Concomitant use of nephrotoxic or immuno-suppressive drugs which could not be stopped without affecting the safety of the patient.
- Receiving on-going therapy with systemic corticosteroids, Interleukin-2 or chemotherapy.
- Patients who were not to be included in the study according to the investigator's criterion.

Contacts and Locations

Locations

Spain

Gilead Sciences, S.L.

Madrid, Spain, E-28036

Investigators

Study Director:	Pedro Ferrer	Gilead Sciences, S.L.

More Information

Responsible Party:	Gilead Sciences
Study ID Numbers:	GS-ES-164-0154
Health Authority:	Spain: Spanish Agency of Medicines

Study Results

Participant Flow

Reporting Groups

	Description
Truvada	Truvada + nonnucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI).
Zidovudine/Lamivudine	Zidovudine/lamivudine + nonnucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI).

Overall Study

	Truvada	Zidovudine/Lamivudine
Started	39	41
Completed	37	36
Not Completed	2	5
Adverse Event	1	4
Withdrawal by Subject	0	1
Noncompliance	1	0

Baseline Characteristics

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Baseline Measures

	Truvada	Zidovudine/Lamivudine	Total
Number of Participants	39	41	80
Age, Continuous [units: years] Mean (Standard Deviation)	44 (10.6)	44 (7.4)	44 (9.0)
Gender, Male/Female [units: participants]			

	Truvada	Zidovudine/Lamivudine	Total
Female	11	4	15.0
Male	28	37	65.0
Race/Ethnicity, Customized [units: Participants]			
White	36	38	74.0
Black, of African heritage	1	2	3.0
Asian	1	0	1.0
Other	1	1	2.0
Region of Enrollment Spain [units: participants]	39	41	80.0
HIV-1 RNA Level [units: Participants]			
< 50 copies/mL	38	39	77.0
50 to < 400 copies/mL	1	2	3.0
Cluster determinant 4 (CD4) cell count [units: cells/mm^3] Median (Inter-Quartile Range)	655.0 (505.0 to 789.0)	504.0 (363.0 to 756.0)	600.5 (420.0 to 760.5)
Total limb fat [1] [units: grams (g)] Median (Full Range)	3565 (511 to 15932)	3589 (903 to 28155)	3589 (511 to 28155)
Years on zidovudine (AZT)/ lamivudine (3TC) [units: Years] Median (Inter-Quartile Range)	5.8 (4.2 to 7.2)	6.2 (4.7 to 7.2)	5.9 (4.6 to 7.2)

[1] Measured using dual-energy x-ray absorptiometry (DEXA). Total limb fat is the sum of the left arm, right arm, left leg, and right leg.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Limb Fat at Week 48
Measure Description	Limb fat was measured by DEXA. Change = Week 48 value minus baseline value.

Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Number of participants analyzed is those with baseline and post-baseline DEXA data. Last post-baseline observation carried forward (LOCF) method was used if the Week 48 limb fat value was missing.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	38	38
Change From Baseline in Limb Fat at Week 48 [units: grams (g)] Median (Inter-Quartile Range)	392 (-102 to 1056)	-257 (-751 to 148)

Statistical Analysis 1 for Change From Baseline in Limb Fat at Week 48

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0014
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Oral Mucosa)

Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	34	35
Change From Baseline in the Mitochondrial DNA/ Nuclear DNA Ratio (Oral Mucosa) [units: Ratio] Median (Inter-Quartile Range)	62.0 (20.0 to 212.0)	97.0 (20.0 to 197.0)

Statistical Analysis 1 for Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Oral Mucosa)

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9713
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Lymphocytes)
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	36	35
Change From Baseline in the Mitochondrial DNA/ Nuclear DNA Ratio (Lymphocytes) [units: Ratio] Median (Inter-Quartile Range)	36.0 (2.0 to 89.5)	43.0 (1.0 to 72.0)

Statistical Analysis 1 for Change From Baseline in the Mitochondrial DNA/Nuclear DNA Ratio (Lymphocytes)

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9725
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Lactate Concentration
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	27	30
Change From Baseline in Lactate Concentration [units: mmol/L] Median (Inter-Quartile Range)	-0.23 (-0.55 to 0.00)	0.09 (-0.12 to 0.43)

Statistical Analysis 1 for Change From Baseline in Lactate Concentration

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0078
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]

	Comments	No adjustments were made.

5. Secondary Outcome Measure:

Measure Title	Percentage of Days for Which Participants Were Compliant With Study Drug
Measure Description	Compliance = [1 - [(sum of days with a missed dose [per Question 6 study medication assessment questionnaire (SMAQ)])/(sum of days between SMAQ visits)]] *100 for visits with SMAQ data. An assessable visit is one where the number of missed days was reported [Question 6] and the number of days between SMAQ visits could be calculated.
Time Frame	Baseline to Week 72
Safety Issue?	No

Analysis Population Description
Treated participants.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Days for Which Participants Were Compliant With Study Drug [units: Percentage of days with compliance] Median (Inter-Quartile Range)	100.0 (99.8 to 100.0)	100.0 (99.6 to 100.0)

Statistical Analysis 1 for Percentage of Days for Which Participants Were Compliant With Study Drug

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: percentages of days with compliance in the two treatment groups are equal. Alternative Hypothesis: percentages of days with compliance in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6984
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Maintain Confirmed HIV-1 RNA < 50 Copies/mL
Measure Description	
Time Frame	48 weeks
Safety Issue?	No

Analysis Population Description

Treated participants. Missing values were treated as failure (i.e., as HIV-1 RNA greater than or equal to 50 copies/mL).

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Participants Who Maintain Confirmed HIV-1 RNA < 50 Copies/mL [units: Percentage of participants]	92.3	78.0

Statistical Analysis 1 for Percentage of Participants Who Maintain Confirmed HIV-1 RNA < 50 Copies/mL

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: treatment is not associated with the observed virologic response. Alternative Hypothesis: treatment is associated with the observed virologic response.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1165
	Comments	No adjustments for multiple comparisons were made.
	Method	Fisher Exact
	Comments	No adjustments were made.

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	14.3
	Confidence Interval	(2-Sided) 95% -0.9 to 29.4
	Estimation Comments	The difference is for Truvada minus zidovudine/lamivudine. The 95% confidence interval on the mean difference between treatment groups is based on the normal approximation.

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With HIV-1 RNA > 50 and < 400 Copies/mL
Measure Description	
Time Frame	48 weeks
Safety Issue?	No

Analysis Population Description
Treated participants.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Participants With HIV-1 RNA > 50 and < 400 Copies/mL [units: Percentage of participants]	0	5

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Virologic Failure
Measure Description	Virologic failure was defined as two consecutive HIV RNA values > 400 copies/mL.
Time Frame	48 weeks
Safety Issue?	No

Analysis Population Description

Treated participants.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Participants With Virologic Failure [units: Percentage of participants]	0	0

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Cluster Determinant 4 (CD4) Cell Count
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	No

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	36	34
Change From Baseline in Cluster Determinant 4 (CD4) Cell Count [units: cells/mm^3] Median (Inter-Quartile Range)	60.5 (-6.5 to 159.0)	9.0 (-61.0 to 106.0)

Statistical Analysis 1 for Change From Baseline in Cluster Determinant 4 (CD4) Cell Count

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0789
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

10. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting Serum Triglycerides
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	34	31
Change From Baseline in Fasting Serum Triglycerides [units: mg/dL] Median (Inter-Quartile Range)	1.5 (-31.0 to 17.0)	4.0 (-44.0 to 40.0)

Statistical Analysis 1 for Change From Baseline in Fasting Serum Triglycerides

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9633
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting Total Cholesterol
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	34	31
Change From Baseline in Fasting Total Cholesterol [units: mg/dL] Median (Inter-Quartile Range)	4.5 (-12.0 to 12.0)	1.0 (-19.0 to 21.0)

Statistical Analysis 1 for Change From Baseline in Fasting Total Cholesterol

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9686
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

12. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting Low Density Lipoprotein Cholesterol (LDL)
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48

Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	29	27
Change From Baseline in Fasting Low Density Lipoprotein Cholesterol (LDL) [units: mg/dL] Median (Inter-Quartile Range)	7.0 (-9.4 to 15.6)	5.0 (-14.0 to 16.0)

Statistical Analysis 1 for Change From Baseline in Fasting Low Density Lipoprotein Cholesterol (LDL)

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6638
	Comments	No adjustments for multiple comparisons were performed.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

13. Secondary Outcome Measure:

Measure Title	Change From Baseline in Fasting High Density Lipoprotein Cholesterol (HDL)
Measure Description	Change = Week 48 value minus baseline value.

Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	31	28
Change From Baseline in Fasting High Density Lipoprotein Cholesterol (HDL) [units: mg/dL] Median (Inter-Quartile Range)	-2.0 (-7.0 to 2.0)	2.0 (-7.0 to 7.0)

Statistical Analysis 1 for Change From Baseline in Fasting High Density Lipoprotein Cholesterol (HDL)

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2907
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

14. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hemoglobin

Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	36	33
Change From Baseline in Hemoglobin [units: g/dL] Median (Inter-Quartile Range)	0.9 (0.0 to 1.2)	0.3 (-0.5 to 0.7)

Statistical Analysis 1 for Change From Baseline in Hemoglobin

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0072
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

15. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Hematocrit
Measure Description	Change = Week 48 value minus baseline value expressed as median percent change.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	36	33
Percent Change From Baseline in Hematocrit [units: Percent change in hematocrit] Median (Inter-Quartile Range)	2.7 (1.5 to 4.3)	1.0 (-0.9 to 2.0)

Statistical Analysis 1 for Percent Change From Baseline in Hematocrit

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0006
	Comments	No adjustments for multiple comparisons were made.
	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

16. Secondary Outcome Measure:

Measure Title	Change From Baseline in Waist Circumference/Hip Circumference Ratio
Measure Description	Change = Week 48 value minus baseline value.
Time Frame	Baseline to Week 48
Safety Issue?	Yes

Analysis Population Description

Treated participants. Missing values were excluded. Assessment of waist and hip circumference was added to the study schedule via protocol amendment part way through the study. This resulted in small numbers of subjects having data available for this analysis.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	28	25
Change From Baseline in Waist Circumference/Hip Circumference Ratio [units: Ratio] Median (Inter-Quartile Range)	-0.01 (-0.03 to 0.02)	0.01 (-0.01 to 0.04)

Statistical Analysis 1 for Change From Baseline in Waist Circumference/Hip Circumference Ratio

Statistical Analysis Overview	Comparison Groups	Truvada, Zidovudine/Lamivudine
	Comments	Null Hypothesis: changes from baseline in the two treatment groups are equal. Alternative Hypothesis: changes from baseline in the two treatment groups are different (two sided).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1785
	Comments	No adjustments for multiple comparisons were made.

	Method	Other [Wilcoxon Rank Sum test]
	Comments	No adjustments were made.

17. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Any Adverse Event
Measure Description	Participants with treatment-emergent adverse events were analyzed. Adverse events were defined as any untoward medical occurrence in a clinical investigation subject administered a medicinal product and which did not necessarily have a causal relationship with study treatment, and were categorized using the Medical Dictionary for Regulatory Activities (MedDRA) Version 11. Treatment-emergent adverse events were events that met one of the following criteria: • Began or worsened in severity or relationship to study drug, on or after the date of the first dose of study drug and on or before the date of the last dose of study drug plus 30 days. • Had no recorded start date.
Time Frame	72 weeks
Safety Issue?	Yes

Analysis Population Description
Treated participants.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Participants With Any Adverse Event [units: Percentage of participants]	77	85

18. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Discontinue the Study Prematurely (Before Week 48) Due to Adverse Events.

Measure Description	
Time Frame	48 weeks
Safety Issue?	Yes

Analysis Population Description
Treated participants.

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Measured Values

	Truvada	Zidovudine/Lamivudine
Number of Participants Analyzed	39	41
Percentage of Participants Who Discontinue the Study Prematurely (Before Week 48) Due to Adverse Events. [units: Percentage of participants]	3	10

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Truvada	Truvada + NNRTI or PI.
Zidovudine/Lamivudine	Zidovudine/lamivudine + NNRTI or PI.

Serious Adverse Events

	Truvada	Zidovudine/Lamivudine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/	3/
Cardiac disorders		
Acute myocardial infarction [A] *	0/39 (0%)	1/41 (2.44%)
Prinzmetal angina [A] *	0/39 (0%)	1/41 (2.44%)
Gastrointestinal disorders		
Diarrhoea [A] *	1/39 (2.56%)	0/41 (0%)
Infections and infestations		
Respiratory tract infection [A] *	0/39 (0%)	1/41 (2.44%)
Injury, poisoning and procedural complications		
Lumbar vertebral fracture [A] *	1/39 (2.56%)	0/41 (0%)
Radius fracture [A] *	0/39 (0%)	1/41 (2.44%)
Nervous system disorders		
Cauda equina syndrome [A] *	1/39 (2.56%)	0/41 (0%)
Respiratory, thoracic and mediastinal disorders		
Bronchospasm [A] *	0/39 (0%)	1/41 (2.44%)
Emphysema [A] *	1/39 (2.56%)	0/41 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 11

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Truvada	Zidovudine/Lamivudine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	24/	28/
Blood and lymphatic system disorders		

	Truvada	Zidovudine/Lamivudine
	Affected/At Risk (%)	Affected/At Risk (%)
Anaemia [A] †	1/39 (2.56%)	3/41 (7.32%)
Neutropenia [A] †	0/39 (0%)	3/41 (7.32%)
Gastrointestinal disorders		
Abdominal pain upper [A] *	2/39 (5.13%)	0/41 (0%)
Diarrhoea [A] *	3/39 (7.69%)	2/41 (4.88%)
General disorders		
Pyrexia [A] *	2/39 (5.13%)	0/41 (0%)
Infections and infestations		
Bronchitis [A] *	2/39 (5.13%)	0/41 (0%)
Investigations		
Alanine aminotransferase increased [A] †	8/39 (20.51%)	10/41 (24.39%)
Aspartate aminotransferase increased [A] †	4/39 (10.26%)	6/41 (14.63%)
Blood amylase increased [A] †	4/39 (10.26%)	8/41 (19.51%)
Blood creatine phosphokinase increased [A] †	3/39 (7.69%)	3/41 (7.32%)
Blood lactic acid increased [A] †	2/39 (5.13%)	4/41 (9.76%)
Gamma-glutamyltransferase increased [A] †	11/39 (28.21%)	10/41 (24.39%)
Lipase increased [A] †	1/39 (2.56%)	3/41 (7.32%)
Metabolism and nutrition disorders		
Hypercholesterolaemia [A] †	2/39 (5.13%)	4/41 (9.76%)
Hyperlactacidaemia [A] †	2/39 (5.13%)	0/41 (0%)
Musculoskeletal and connective tissue disorders		
Back pain [A] *	1/39 (2.56%)	3/41 (7.32%)
Renal and urinary disorders		

	Truvada	Zidovudine/Lamivudine
	Affected/At Risk (%)	Affected/At Risk (%)
Renal colic [A] *	0/39 (0%)	3/41 (7.32%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 11

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

After conclusion of the study and without prior written approval from Gilead, investigators in this study may communicate, orally present, or publish in scientific journals or other scholarly media only after the following conditions have been met:

- The results of the study in their entirety have been publicly disclosed by or with the consent of Gilead in an abstract, manuscript, or presentation form; or
- The study has been completed at all study sites for at least 2 years.

Results Point of Contact:

Name/Official Title: Pedro Ferrer
Organization: Gilead Sciences
Phone: +34 91 771 2478
Email: pedro.ferrer@gilead.com